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CONTENTS

Seroepidemiology of Human Papilloma Virus and HPV Vaccination in Cervical Cancer–Era of New Hope: A brief review of article

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Abstract

Most of the cervical cancer are caused by with human papilloma virus (HPV), but risk associated with the various HPV types has not been adequately assessed. We searched literature from Pubmed, Embase and Medline with terms human papilloma virus, HPV, Cervical cancer, CIN and compiled data on seroepidemiological correlation of HPV in carcinoma cervix. There are 200 types of HPV viruses diagnosed by DNA sequencing. They are widely distributed through-out animal kingdom. It associates with various type of cervical lesion ranging from benign to malignant. The most common types observed among invasive cervical cancer cases were HPV 16 and HPV 18. This information is essential for planning prevention by HPV vaccines and for screening programs based on HPV testing.

Keywords: Human Papilloma virus, Cervicalcancer, Low risk, High risk, HPV vaccine

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Introduction

Papilloma virus tumorigenicity has been proven in animals. The epidemiologic suggestion of veneral transmission of an infectious agent involved in cervical cancer and molecular detection of papillomavirus DNAs in various human lesion, confirmed hypothesis of HPV involvement in genital cancer.[1] It associates with various type of disease ranging from benign to malignant. The incidence of HPV infection is increasing in trend. They are widely distributed throughout animal kingdom. There are 200 types of HPV viruses diagnosed by DNA sequencing.[2]

Aim

Seroepidemiology of HPV in cervical cancer and risk association with different types of HPV.

Material and Methods

We searched literature from Pubmed, Embase and Medline with terms human papilloma virus, HPV, Cervical cancer, CIN and thoroughly analyzed and summarized in this review article.

Review of Literature

Cervical cancer burden: Cervical cancer is the most commonly diagnosed cancer in women worldwide. There were 572,624 new cases of cervical cancer worldwide (4th most common cancer in women worldwide, accounting for 7.9% of all cancers in women apart from non-melanoma skin cancers. There were an estimated 265,672 deaths from cervical cancer worldwide (7.5% of the total number of cancer deaths in women, 4th most common cause of cancer-related deaths in women) in 2012.[3]

HPV Virology and Pathogenesis: The association between cervical cancer and HPV virus was first described by German virologist **Harold zurHausen**.[4] It is enveloped double strand DNA virus[5], HPV genome codes only for eight genes. Primary HPV oncoproteins are E6 and E7. These oncoproteins having various cellular target, HPVE6 mainly binds with p53 and inactivates it and increases the chance of cell survival by inhibiting apoptosis. Retinoblastoma (Rb) tumor suppressor gene is main target of E7 oncoprotein. Hence the inactivation of tumor suppressor gene in cells is central to cell transformation by HPV.

Sir Austin Bradford Hill proposed a general criteria[6] to establish causation between disease and environmental factor. Hill criteria are

1. Strength of association - how frequently a virus found in a tumor?
2. Consistency - has the association been observed repeatedly by different people in different place?
3. Specificity of association –is the virus or specific variant of virus uniquely associated with tumor?
4. Temporal relationship association –does virus infection precede tumor development?
5. Biologic gradient –is there a dose response relationship with virus load?
6. Biologic plausibility-is it biological feasible that virus could cause the tumor?
7. Experimental evidence –are there supporting laboratory results?

Seroepidemiolog has shown the association of cervical cancer and HPV fulfilled the Hill's criteria. The International Agency for Research on Cancer (IARC) concluded that four case–control studies in 1995 and sufficient evidence was collected to classify HPV types 16 and 18 as human carcinogens, but the evidence was limited or inadequate for other types.[7] Approximate 30 variants of HPV have been identified, that primarily infect cervix, vagina, vulva, and penis.

Priming step of pathogenesis is initiated by HPV infection of cervical epithelium during sexual intercourse. HPV exposure rate in sexually active women is very much high, but small proportion of them develop cervical cancer. Most of them successfully clear viral infection due to competent immune response.[8,9] The natural history of cervical cancer is a continuous process from CIN 1 to high-grade lesions (CIN 2/3) and finally invasive cancer. It usually associated with conversion of the viral genome to an integrated form from episome form, inactivation or deletion of the E2 region and expression of the E6/E7 product genes. Progression to malignant transformation generally takes place over a period of 10 to 20 years.[10]

Epidemiology of cervical cancer: Cervical cancer usually arises from cervical squamocolumnar junction between the columnar epithelium of the endocervix and the squamous epithelium of the ectocervix. In this transformation zone metaplastic changes is going on continuously. High ermetaplastic activity occurs during puberty and first pregnancy so the chances of HPV infection is higher during this period. High risk factors associated with HPV infection are multiple sexual partner, sexual activity at an early age, genital wart, history of STD, abnormal Pap smear, Age is also an important determinant factor. HPV infection is most common in sexually active young women age 18-30 years of age.[6]

High risk HPV alone is not responsible for development of cervical cancer. Various cofactors along with HPV infection are responsible for development of cervical cancer such as long term use oral contraceptive, smoking, coinfection with herpes simplex virus type 2 may play a role in the initiation of cervical cancer.[11] Cytomegalovirus (CMV), human herpesvirus 6 (HHV-6), and HHV-7 have also been detected in the cervix. Coinfection offers the opportunity for these viruses to interact with HPV.

Both squamous cell carcinoma and adenocarcinoma are caused by HPV infection.[12] About 99.7% of cervical squamous cell cancer are associated with HPV infection worldwide.[13] Genital HPV types have been subdivided into low-risk types and high risk group. Genital warts are mainly associated with low risk HPV and high-risk types which are frequently associated with invasive cervical cancer.[6,14] Nubia Muñoz *et al*[15] collected data from 11 case–control studies from nine countries involving 1918 women with histologically confirmed squamous-cell cervical cancer and 1928 control women to evaluate epidemiologic and phylogenetic classifications of HPV types. (Table 1, 2) A recent meta-analysis reported an overall prevalence of HPV DNA in 89.7% of invasive cervical cancer cases from Eastern Asia. HPV types detected[16]. Various studies[17] have been established the HPV types and cervical lesion, shown in Table 3.

Table 1: Phylogenetic & Epidemiologic classification of HPV Types

Phylogenetic Classification	Epidemiologic Classification	
	High Risk	Low Risk
High Risk	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 82, 26, 53, 66	70
Low Risk	73	6, 11, 40, 42, 43, 44, 54, 61, 72, 81, CP6108

Source of data: [Adapted from reference: N. Munoz et al.[15].

Table 2: Prevalence of the most common HPV types in cervical cancer by region

Sub Saharan Africa		Northern Africa		South Asia		Europe & North America		Central South America	
HPV	%	HPV	%	HPV	%	HPV	%	HPV	%
16	47.7	16	67.6	16	52.5	16	69.7	16	57.0
18	19.1	18	17.0	18	25.7	18	14.6	18	12.6
45	15.0	45	5.6	45	7.9	45	9.0	31	7.4
33	3.2	33	4.0	52	3.4	31	4.5	45	6.8
58	3.2	31	3.4	58	3.0	56	2.2	33	4.3

Source of data: [Adapted from reference: N. Munoz et al.[15].

Table 3: HPV types and cervical lesion association[17]

Cervical Lesion	HPV Type
Condylomaacuminata (Genital Warts)	6, 11, 30, 42, 43, 45, 51, 54, 55, 70
Cervical intraepithelial neoplasia	30, 34, 39, 40, 53, 57, 59, 61, 62, 64, 66, 67, 68, 69
Unspecified	6, 11, 16, 18, 31, 33, 35, 42, 43, 44, 45, 51, 42, 74
Low risk	16, 18, 6, 11, 31, 34, 33, 35, 39, 42, 44, 45, 51, 52, 56, 58, 66
High risk	
Cervical carcinoma	16, 18, 31, 45, 33, 35, 39, 51

Human papilloma virus vaccination

Cervarix, Gardasil, and Gardasil 9 are approved by FDA for prevention of HPV infection in females ages 9 -26 years. These vaccines are very effective in prevention of infection but not very much efficient in established infection.[18] These vaccines provide protection against the two main HPV types (16 and 18) that cause about 70% of cervical cancers worldwide. These vaccine are more effective in Asia, Europe, and North America.[19]

Conclusion

Data from above literature showed the growing evidence of HPV as necessary causative agent in cervical cancer. High risk types 16, 18, 45, 31, 33, 52, 58, and 35 accounted for 95 percent of the squamous-cell carcinomas positive for HPV DNA. So an effective vaccine against the five most common HPV would prevent about 90 percent of the cases of cervical cancer worldwide. Cervical cancer screening and vaccination programed is in rudimentary phase in developing countries. HPV vaccination and regular cervical screening is the most effective way to prevent cervical cancer. These three approved cervical cancer vaccines against prevention of cervical cancer are providing new hope to fight against cervical cancer worldwide.

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Music therapy for improving Bio-physiological and psychological outcomes in patients with cancer-A Review article

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Abstract

The diagnosis of cancer not only effects the person physically but also it disturbs the person psychological wellbeing. Anxiety and pain are the common problems usually experienced by the patients with cancer beginning from the diagnosis to the treatment part. There is a growing body of research documenting the effects of many alternative treatment modalities in cancer care, one among which is the music therapy. Research has proved that engaging in the music listening or music composing activities will reduce the overall health ailmnents which will arise due to the treatment part and increases the quality of life in terms of comfort, relaxation in patients with cancer.

Keywords: Cancer, Music therapy, Physical outcomes, Physiological outcomes, Psychological outcomes

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Introduction

Cancer is a staid, life-threatening disease.The diagnosis can make expressive and physical distress among the people. Patients with cancer experiences many side effects from diagnosis and treatment[1]. Apart from pharmacological management, Non-pharmacological agents are considerable in how the patients with cancer understand physical symptoms during treatment[2]. The importance of alternative system of medicine in present scenario has been increased to great extent, among which the music therapy is in the top[3], is one of the communicative therapies, which involves a trained music therapist, uses music to help the patients in improving their health status. Music therapy can be active or passive: during the early period, music therapist use to involve patients as an active participant in composing or playing the music, but at present, patients individually or in a group can listen to recorded music or they can listen to music played by the therapist. After world war II, music therapy established as profession and now its available globally in various health care institutions and hospitals including medicine, surgery, psychiatry, pediatrics, oncology, palliative settings etc[4,5]. When examining the usefulness of music as an intervention with the cancer patients, researchers highlighted that it is important to make clear similarity between music administered by health professionals and by the trained music therapist[6]. Music therapy has many forms including, singing, drumming, playing instruments, song writing. Substantive data signify that music interventions in terms of music therapy is more effective than using other terms like music medicine interventions for many outcomes[7]. Although several studies using music as interventions with cancer patients have a positive outcome though the treatment effect may be less and unimpressive to caregivers, patients with cancer, and their family members. Difference in study design, type of study, interventions used, duration intervention, and the role therapist in music therapy may produce changeable outcomes.

Methods

Identification of studies: A google search was carried out to find the studies related to music and cancer. Science direct, proquest, pubmed, cinhal and medline were also searched for the above mentioned type of studies. The terms used to search the studies are "music, music therapy, music intervention, music medicine, cancer, pain and radiation therapy, chemotherapy and oncology.

Inclusion criteria: Only randomized controlled trialswhich are published in English language are included in this review. No restrictions were made in selecting the review auch as age, gender, ethnicity, or type of setting. The review included all the trials in whcih music therapy was compared with (a) control group receiving only standard routine care, (b) standard care and other therapies, and (c) standard care with placebo. Placebo studies involved the use of headphones with no musical or any other type of auditory stimulus provided to participants.

Types of participants: This review included patients diagnosed with different type of malignant neoplastic disease. There were no limitations on age, gender,

background or type of setting. Participants those who were going gor biopsy, bone marrow biopsy and aspiration for diagnostic purposes were expelled from this review.

Types of interventions: The review incorporated all trials in which routine treatment combined with music therapy or music medicine interventions was compared with Standard care alone, Standard care combined with other therapies, Standard care with placebo.

Placebo treatment can involve the use of headphones for the patient wherein no music stimulus is provided or another type of auditory stimulus is provided such as sound of ocean waves etc.

Types of outcome measures

Primary outcomes: The primary outcomes looked in the selected trials includes psychological outcomes such as Depression, anxiety, anger, hopelessness, helplessness and relaxation and physical symptoms like Fatigue, nausea and pain.

Secondary outcomes: The secondary outcomes were mainly physiological parameters such asCortisol levels, immunoglobulin A (IgA) levels, Social and spiritual support likeFamily support, spirituality, social activity, isolation, communication includes verbalization, facial affect and gestures and Quality of life.

Study description and quality assessment: 38 eligible studies were selected in this review where patients with cancer recieved music therapy in various clinical setups such as during operations, chemo and radiotherapy sessions duration of music varied from trial to trial. Total 3,181 patients were randomized and most studies included most of the cancer types like breast cancer, lung cancer, maxillofacial cancers, cancer of nasopharynx and malignant tumors.

Total seven studies assessed the anxiety level of patients by using self rating anxiety scale (SAS), whereas two trials assessed the anxiety with the help of Hamilton anxiety scale (HAMA), Eight studies used Spielberger stat trait anxiety inventory (STAI). Seven trials assessed the depression by self rating depression scale (SDS). Two trials analyzed level of fatigue by using Profile of Mood States (POMS). Seven studies graded pain by using Numeric Rating Scale (NRS) and by Visual Analog Scale (VAS). Four trials assessed heart rate, three studies measured respiratory rate, five clinical trials assessed blood pressure, and two studies analyzed music effects on overall quality of life of patients with cancer.

Quantitative analysis of effects: Most of the studies reported that music therapy reduced level of anxiety and level of depression before, during, and after the medical/ surgical procedures or treatment, and to some extent, music therapy helped in improving the quality of life too.

Psychological outcomes: anxiety and depression: Nine trials (775 patients measured anxiety by SAS)[5,8-16] and seven trials (607 patients) provided useful data[8,9,11-13,15,16]. The mean difference was −12.84 (95% CI, −19.51 to −6.17; P<0.001; I20 98%). Three trials (597 patients) measured anxiety by HAMA[8,16,17]. The mean difference was −1.85 (95% CI, −3.43 to −0.27; P<0.05).

Eight trials (681 patients) measured anxiety by STAI[5,13,18-23]. All trials provided useful data. The mean difference of the data was −12.30 (95% CI, −18.93 to −5.68; P<0.001; I2098%). Depression Eight trials (739 patients) measured depression by SDS[8,9,12,13,15,20,23,24]. Seven trials involving 611 patients provided useful data[8,9,12,15,20,23,24]. The mean difference was −6.23 (95% CI, −8.85 to −3.60; P<0.00001).

Physical symptoms: pain and fatigue: Pain, Seven trials (535 patients) measured pain by NRS[17-19,23-26]. Five trials of 423 patients provided useful data[5,17,18,19,25]. Three studies (314 patients) measured pain by VAS[27-29]. However, only one (120 patients) provided useful data[28]. NRS and VAS rated pain intensity on a "zero to ten" scale (0, no pain; 10, worst pain). During the procedure, the utmost recorded value was recorded. The mean difference was −0.54 (95 % CI, −0.88 to −0.20; P<0.005). Just two trials (90 patients) measured fatigue by POMS[5], both the trials provided useful data. The mean difference of the data was 0.63 (95 % CI, −2.52 to 3.77; P00.70).

Physiological outcomes: Eight trials (581 patients) measured heart rate[5,10,11,16,19,26,27,30]. Four trials provided useful data[11,16,19,27]. The mean difference was −12.18 (95% CI, −22.47 to −1.89; P<0.05). four trials (283 patients) measured respiratory rate[10,16,19,27]. Three (203 patients) provided useful data[11,19,27]. The mean RR difference was −2.06 (95% CI, −2.84 to −1.28; P<0.00001). Seven trials (521 patients) measured systolic blood pressure[5,10,11,16,17,19,27]. Four trials provided useful data[11,16,19,27]. The mean blood pressure difference was −3.74 (95% CI, −20.56 to 13.08; P00.66). Blood pressure (diastolic) seven trials (521 patients) measured diastolic blood pressure[5,10,11,16-19,27]. Five trials of 365 patients provided useful data[5,11,16,19,27]. The mean blood pressure MM Hg difference was −2.48 (95% CI, −7.42 to 2.47; P00.33).

Quality of life: Two trials (268 patients) measured quality of life by QOLCA[5,31]. Both provided useful data. The mean score was 13.32 (95% CI, 11.01 to 15.62; P<0.00001).

Discussion

The music intervention reduces anxiety and depression before, during, and after cancer procedures but did not address the duration of positive effects. Few studies highlighted that music interventions will not produce significant changes in systolic or diastolic blood pressure but it helped in reducing heart and respiratory rates. The effect of music interventions on quality of life is positive. However, the effects of music interventions onother symptoms like fear, nausea, worry, psychological and physical outcomes like distress, socialization, orfunctional activity, and daily activities

remain unclear till the future investigation will be carried out.

A multidimensional outcome would provide a more comprehensive view of the benefits to music, possibly better than using just a single dimension but were not designed into these trials. Some degree of information was reported regarding the grounds and process of musical selections. Music therapy was not standardized procedure across all the trials, it was different in terms of mode of administration and duration. Most music medicine studies reported using headphones for music delivery. Duration and onset of the interventions varied. Further research is needed to decide the best possible duration for the music intervention. additional information regarding musical prefernce would be useful because selections varied by musical styles. Music preference is essential because individual difference make the person to like things they recognize and dislike theunwanted which may result in a negative effect on the outcome results[33]. Musical preferences differ across age, cultural backgrounds, etc. It is one of the important factors influencing benefits with music[34-36]. From a psycho-physiological point of view, music can promote relaxation, facilitate pleasurable experience, and it also reduces anxiety, heart rate and respiratory rate[37]. Physiological outcomes also may vary by the patients' musical preferences and past exposure to music[38].

The music as a therapy has important practical implications like it is safe to practice, it does not have any harmful side-effects, in expensive and easy to implement, and can be applied to different populations, from young children to the elderly. No adverse effects of music as atherapy wasreported in any of the studies. Therefore, music therapycan be considered as a potentially effective, inexpensive in addition to the standard care.

Conclusions

The effects of music therapy on psychological outcomes are positive, effects on physicalsymptoms, especially on blood pressure is less and donot give reason for its routine use. Music intervention reduces respiratory rate, but the quality of the evidence is low.

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Male Breast Cancer: An 8-year experience in a single tertiary oncology centre in India

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Abstract

Background and Objectives: Male breast cancer is a rare disease with a paucity of published literature on this topic. The purpose of this study was to report our experience with male breast cancer, focusing on the need of pooling of multi-institutional data for these patients.

Methods: A retrospective review of 23 male patients with carcinoma breast from 2008 to 2015 was performed. All documented data on patient and tumour characteristics, treatment and clinical outcome information were analyzed.

Results: The median age at diagnosis was 54 years. Majority of our patients had Stage III disease (52.2%) with infiltrating ductal carcinoma (82.6%) being the commonest histology. Estrogen receptor and progesterone receptor positivity was seen in 91.3% and 78.26% patients respectively while Her-2 (human epidermal growth factor receptor-2) positivity was seen only in one patient. All patients underwent surgery and adjuvant radiation therapy was used in 10 (43.5%) patients. All patients except one received systemic chemotherapy. The 5-year disease-free survival was found to be 78%. Median follow-up was 40 months (6 - 68 months).

Conclusion: Unfortunately, in the face of the limitation of current scientific knowledge in determining the optimal treatment strategy for male patients with breast cancer we recommend that there is an urgent need for publishing multi-institutional experience with these tumours. Hence, allowing the physicians in forming guidelines with the goal of improving clinical outcomes for these patients.

Keywords: Ductal carcinoma, Estrogen receptors, Male breast neoplasms, Progesterone, Retrospective studies.

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Introduction

Male breast cancer (MBC) is rare, accounting for about 1% of all malignancies in men and 1% of all breast cancers[1]. The incidence of MBC is increasing as in women, approximately about 26% rise over the past 25 years[2]. MBC patients usually have advanced disease at presentation, longer time to presentation, more Her-2neu positivity and triple negativity[3]. Invasive ductal carcinoma is the most common type of breast malignancy observed in males[4].

In clinical practice, the scarcity of cases has reduced the focus of research in this area as compared with female breast cancer[5]. The treatment strategies for MBC aren't based on prospectively or retrospectively conducted randomized controlled trials. Majority of the information regarding the biology, natural history, and treatment strategies of MBC has been extrapolated from the vast knowledge of female breast cancer[6]. Treating these male patients in a manner similar to female breast cancer may not be entirely applicable since the gender differences may affect the patient preferences with regard to treatment options, side effects as a result of treatment, and survival outcome[7].

In Indian patients, considering the lack of awareness, associated stigma and the rarity of MBC, it's challenging for the oncologists to get enough participants from a single institution to arrive at a definitive conclusion on the best evidence-based practice in the treatment of MBC. There is limited availability of data on MBC from India. The purpose of present article is to analyze the clinico-pathological data, treatment received and survival outcome of MBC patients presenting at a cancer research institute in India. In addition, we emphasize on the need of pooling of multi-institutional data for these patients.

Methods

A prospective, observational study on male patients with histopathologically proven carcinoma of the breast was carried out at our institute from 2008 to 2015. A total of 26 patients were retrieved from the records. The case records of patients were reviewed to extract the information on age, presenting symptom, site of primary tumour, treatment details, recurrence, and follow-up. The inclusion criteria for the study were as follows: a diagnosis of histologically confirmed male breast cancer, stage I – IV, availability of complete information on clinico-pathological data, treatment employed and survival outcome.

Pre-Treatment Evaluation: The pre-treatment evaluation included a complete history and physical examination, chest radiograph, bilateral breast mammogram, liver function tests including alkaline phosphatase, complete blood counts and abdominal ultrasound. Bone scan was considered only for symptomatic patients or those with elevated alkaline phosphatase. All patients underwent trucut biopsy, followed by determination of histopathology and estrogen receptor (ER), progesterone (PgR) and Her-2 status. The patients were staged according to American Joint Committee on Cancer – Tumour, nodes and metastasis staging system for female breast cancer, depending on the time period. After the complete staging work-up, all patients were evaluated by a multidisciplinary team including surgical oncologist, medical oncologist, radiation oncologist and pathologist.

Treatment plan: Patients presenting with early stage breast cancer, underwent either lumpectomy or modified radical mastectomy, followed by adjuvant chemotherapy (CT) and external beam radiotherapy (RT), if indicated. Patients with locally advanced breast cancer, received neoadjuvant CT (3 to 4 cycles) followed by assessment for tumour response. These patients underwent mastectomy followed by systemic CT and adjuvant RT. Depending on the receptor status, hormonal therapy in the form of tamoxifen was offered to the patients.

Chemotherapeutic regimens: CMF regimen was offered to 6 patients in view of Stage II disease as per the institutional protocol. Due to the higher stage (stage III and IV) at presentation, remaining patients received anthracycline- or taxane-based CT.

- CMF regimen

Cyclophosphamide 600 mg/m^2 i.v D1
Methotrexate 40 mg/m^2 i.v D1
5-Fluorouracil 600 mg/m^2 i.v D1
} Q3w x 6 cycles

- FAC regimen

5-Fluorouracil 500 mg/m^2 i.v D1
Adriamycin 50 mg/m^2 i.v D1
Cyclophosphamide 500 mg/m^2 i.v D1
} Q3w x 6 cycles

- FEC regimen

5-Fluorouracil 500 mg/m^2 i.v D1
Epirubicin 75 mg/m^2 i.v D1
Cyclophosphamide 500 mg/m^2 i.v D1
} Q3w x 6 cycles

- TAC regimen

Docetaxel 75 mg/m^2 i.v D1
Adriamycin 50 mg/m^2 i.v D1
Cyclophosphamide 500 mg/m^2 i.v D1
} Q3w x 6 cycles

Radiation therapy: Indications for post-mastectomy chest wall RT includes patients with four or more axillary lymph node metastasis, with a tumour size of 5 cm or more, and the presence of chest wall invasion[8,9]. These patients were planned on Acuity conventional simulator and treated with a linear accelerator of 6MV energy. Sites treated by RT included chest wall ± axilla, and supraclavicular regions, when indicated. Total RT dose consisted of 50 – 60 Gy at 2 Gy per fraction for 5 days in a week over 5–6 weeks with a two-field tangentially opposed photon beam arrangement for the chest wall. An additional direct anterior supraclavicular and axillary field were employed wherever indicated. Typically, the inferior border was located 1–2 cm below the inframammary fold, the superior border at the level of the suprasternal notch, the medial border at the mid-sternal line, and the lateral border at the mid-axillary line. In our setting, RT was recommended to patients with positive axillary nodes, large (≥ 5 cm) primary tumours and for those with chest wall invasion. Treatment was delivered daily, Monday through Friday.

Hormonal therapy: Hormonal manipulation in the form of tamoxifen 20 mg once a day for duration of 5 years was given to ER / PgR positive patients.

Follow-up: After completion of treatment, patients were called for follow-up 3 monthly for first 2 years, and then every 6 monthly for next 3 years and then annually. At each visit, evaluation included detailed history, physical examination and symptom directed investigations. Every 6 months, chest X-ray / abdominal ultrasound or computed tomography of chest and abdomen was done as a routine.

Statistical Analysis: The statistical analysis was performed using SPSS version 20.0. Disease-free survival (DFS) was defined as the time period from the date of initial diagnosis to the date of recurrence or last follow-up. DFS curve was calculated using Kaplan-Meier survival analysis. A p-value of 0.05 or less was considered as statistically significant. Univariate analysis was performed to assess if risk factors such as pathological T-stage and N-stage, lymphovascular invasion, grade of the tumour, close margin or extracapsular extension affect the occurrence of recurrence of disease.

Results

Twenty-six male patients were identified with a diagnosis of carcinoma of the breast. Among these, 23 patients were included in the study. Three patients were excluded as they did not complete the planned treatment because of personal reasons. The mean age (± standard deviation) of the overall study population was 56±9.65 years (range, 42 - 76 years). Metastatic sites were lung and bone. Twenty cases (86.9%) were classified as invasive ductal carcinoma of the breast (IDCA) while 2 (8.7%) patients had invasive lobular carcinoma of the breast. Only 1 (4.4%) patient had mucinous carcinoma of the breast (Table 1).

Table 1: The demographic and oncological characteristics

Patient characteristics	N = 23
Age (in years)	
Mean (range)	56±9.65 (42–76)
Habits	
Smoker	5 (21.7%)
Non-smoker	18 (78.3%)
Family history	
Negative	21 (91.3%)
Positive	2 (8.7%)
Symptoms	
Lump in the breast	23 (100%)
Axillary swelling	3 (13%)
Nipple retraction	3 (13%)
Side	
Right	9 (39.1%)
Left	14 (60.9%)
Site	
Central	17 (73.9%)
Upper Outer	5 (21.7%)
Upper Inner	1 (4.3%)
pT	
pT1	1 (4.3%)
pT2	7 (30.4%)
pT3	14 (60.9%)
pT4	1 (4.3%)
pN	
pN0	13 (56.5%)
pN1	7 (30.4%)
pN2	2 (8.7%)
pN3	1 (4.3%)
Stage	
Stage I	1 (4.3%)
Stage II	8 (34.8%)
Stage III	12 (52.2%)
Stage IV	2 (8.7%)
Receptor status	
ER positivity	21 (91.3%)
PgR positivity	18 (78.3%)
Her-2 positivity	1 (4.3%)

Table 2: Treatment characteristics

Treatment characteristics	N = 23
Surgery	
MRM	22 (95.7%)
Lumpectomy	1 (4.3%)
Chemotherapy	
Neo-adjuvant	7 (30.4%)
Adjuvant	20 (86.9%)
No chemotherapy	1 (4.3%)
Palliative	2 (8.7%)
Type of chemotherapy	
CMF	6 (26.1%)
FAC / FEC	14 (60.9%)
TAC	3 (13%)
Radiation therapy	
Adjuvant	10 (43.5%)
Not given	13 (56.5%)
Hormonal therapy	
Adjuvant	21 (91.3%)
Not given	2 (8.7%)

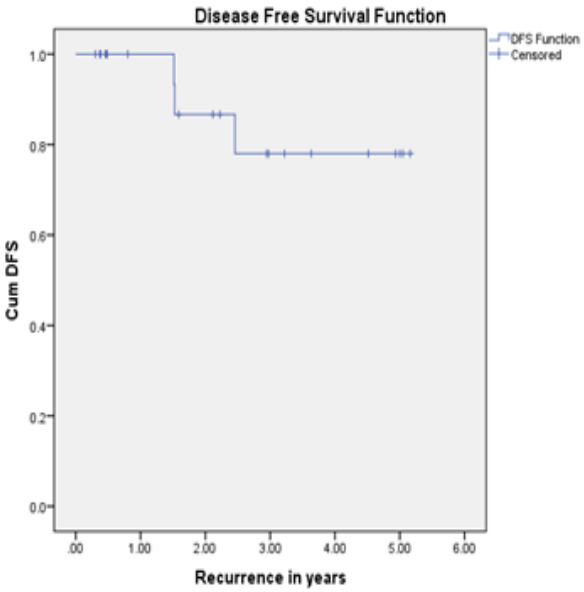

Fig. 1: Kaplan Meier survival analysis curve for DFS

Table 3: Kaplan Meier Survival analysis curve for DFS

Total N	N of Events	Censored		DFS at the end of 5 years
		N	Percent	
22	3	19	86.4%	78%

Univariate analysis of risk factors such as pathological T-stage (p = 0.24) and N-stage (p = 0.55), lymphovascular invasion (p = 0.91), grade of the tumour (p = 0.85), or extracapsular extension (p = 0.63) did not significantly affect the occurrence of recurrence of the disease (Table 4).

Table 4: Univariate cox regression analysis model

		No recurrence	Recurrence	p- value	Odds ratio	95.0% CI for Odds ratio	
Age		56.32±9.32	59.25±12.37	0.437	1.044	.937	1.162
HPE: T stage	1	1 (100.00%)	0 (0.00%)	.239	Variable		
	2	4 (57.14%)	3 (42.86%)				
	3	13 (92.86%)	1 (7.14%)				
	4	1 (100.00%)	0 (0.00%)				
HPE: N stage	0	12 (92.31%)	1 (7.69%)	.554	Variable		
	1	5 (71.43%)	2 (28.57%)				
	2	2 (100.00%)	0 (0.00%)				
	3	0 (0.00%)	1 (100.00%)				
Staging	1	1 (100.00%)	0 (0.00%)	.594	Variable		
	2	6 (75.00%)	2 (25.00%)				
	3	11 (91.67%)	1 (8.33%)				
	4	1 (50.00%)	1 (50.00%)				
LVI	No	13 (86.67%)	2 (13.33%)	0.913	1		
	Yes	6 (75.00%)	2 (25.00%)		0.875	.079	9.688
Grade	0	1 (100.00%)	0 (0.00%)	.853	Variable		
	1	2 (66.67%)	1 (33.33%)				
	2	11 (100.00%)	0 (0.00%)				
	3	5 (62.50%)	3 (37.50%)				
ECE	No	17 (80.95%)	4 (19.05%)	0.633	1		
	Yes	2 (100.00%)	0 (0.00%)		0.038	.000	26436.749

Discussion

MBC accounts for 0.5% of all diagnosed cases of breast cancer and less than 0.2% of all male cancers[10]. Due to the low Incidence of MBC, it has not been investigated thoroughly throughout the world[11,12]. Keeping this in mind, we reviewed our 8-year data of male patients with carcinoma of the breast focusing on clinical and pathological characteristics, treatment options, and disease outcome parameters.

Breast cancer is seen at a relatively early age in Indian males[5]. The mean age of 56 years in our study is in concordance with another study from India[13]. As per the literature, the most common location of the lump in female breast cancer is upper outer quadrant. Majority (73.9%) of our patients had lump involving the central portion. This difference in the location of the lump is likely to be due to paucity of breast tissue in males as compared to females[2].

We found ductal carcinoma (86.9%) as the commonest histology in MBC patients followed by 8.7% patients with lobular and only 4.4% had mucinous carcinoma. Similar findings of entire spectrum of histological variants of breast cancer seen in clinical practice have been reported[14]. Men with breast cancer tend to present at advanced stages of disease[15]. Consistent with this, approximately 60% of our patients had stage III or IV disease on diagnosis[16,17]. This tendency for advanced disease at presentation is attributed to ignorance about breast cancer in males, patients presenting with symptoms other than a lump, and often the patient presents for an unrelated condition[18].

There is a paucity of sufficient information in guiding the clinicians in choosing the optimal combination of surgery, RT, systemic therapy and/ or hormonal therapy. In most of the oncology centers, treatment of MBC is largely similar to established National Comprehensive Cancer Network guidelines for female breast cancer treatment. Hence, the standard therapy for MBC starts with mastectomy as majority of these patients present with locally advanced breast cancer[15,19]. Among our MBC patients, 95.7% underwent mastectomy while only one patient underwent lumpectomy.

After thoroughly searching the literature we found that the data regarding indications for adjuvant RT in male patients is limited. Men do tend to be treated with RT more often after mastectomy than women, perhaps because they are more likely to have nipple or skin involvement[20]. We have considered RT as a component of multimodality therapy for 43.5% patients undergoing mastectomy with these advanced features. We had 6 patients with axillary lymph node metastases, 3 patients with T3 tumour and only one patient with chest wall invasion.

Likewise, the information on the role of CT in MBC patients is limited by the number of cases. In a prospective study of 24 patients with node-positive stage II breast cancer, adjuvant CMF regimen was reported to be highly encouraging treatment option with 5-year survival rate of > 80% when compared to that of historical controls of similar stage in which 5-year DFS rates were < 30%[21]. Several retrospective series have provided supporting evidence that adjuvant CT lowers

the risk for recurrence in male patients[22,23]. In the largest case-control study comparing men and women treated for stage 0 - IIIB breast cancer, the results showed that male patients received systemic therapy comparable to that received by their female counterparts, and they had similar OS and DFS[24]. We have administered chemotherapy (neoadjuvant, adjuvant or palliative) to all patients except one with stage I disease.

Tamoxifen, a selective estrogen receptor modulator has been used to treat female breast cancer for more than 30 years[25], with the World Health Organization citing tamoxifen as an essential drug in breast cancer treatment[26]. Tamoxifen is generally accepted as the "Standard of care" for adjuvant hormonal therapy for MBC patients since 90% of these tumours express ER and 81–96% express PgR[13,27]. However, overall survival is not affected significantly if there is remarkably low hormone receptor expression for these patients[28]. In view of receptor positivity, twenty-one (91.3%) patients received hormonal therapy in the form of tamoxifen.

On comparing the survival rates for MBC with female breast cancer, the relative survival rates were found to be lower for men. This overall worse prognosis for patients with MBC could be attributed to older age as well as advanced stage disease at presentation[2], despite the fact that similar treatment options were considered for both MBC and female breast cancer patients. However, this difference in survival rate became less apparent when the cohorts were stratified according to various prognostic factors[2,29,30]. Estimated overall 5- and 10-year survival rates for MBC are 63% and 41%, respectively, ranging from 5-year survival rate of 78% for stage I disease to 19% for stage IV disease[2]. We found 5-year DFS of 78%. This could be because of small sample size. In addition, the limitations of our work include retrospective data, and single institutional experience.

Conclusions

MBC is an area of fertile research because of the limited knowledge available to guide its treatment. Majority of the information regarding this disease has been gathered from case reports and retrospective, single-institutional cohort studies. This evidence is low on the hierarchial levels of evidence, and a major pitfall in formulating guidelines for the optimal management of these patients. Therefore, MBC should be brought to the forefront of breast cancer research. We also emphasize on obtaining more information in order to provide complete landscape of this disease. However, rarity of the disease might be a serious problem. It is thus important to direct future efforts towards publishing multi-institutional experience with these tumours supporting the treatment decisions.

Conflict of interest

There are no conflicts of interest.

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Endoscopic and Histopathologic changes in Children with Chronic dyspepsia in a Rural Medical College Hospital in Melmaruvathur – Tamil Nadu

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Abstract

Introduction: Chronic pain abdomen and dyspepsia is the most common presenting symptoms in the paediatric outpatient department (OPD) after respiratory illnesses. It is increasing alarmingly both in the paediatric and adult population. We, therefore carried out a cross sectional study among children aged between 5 to 15 years, attending Paediatric OPD with chronic dyspepsia in a rural medical college hospital, Melmaruvathur, Tamil Nadu, South India.

Objective: To evaluate the gastroduodenal morbidity in children presenting to the paediatric department of a rural medical college hospital with chronic dyspeptic symptoms.

Methods: Forty six children between the age group of 5 to 15 years with chronic dyspeptic symptoms of at least one month duration were evaluated for their symptom profile, epidemiological profile, nutritional status, endoscopic appearance and histopathological changes. Data analysis was done using SPSS version 18.

Results: Of the 46 children studied, 43% were between the age group of 5-10 years and 70% were female children. Pain abdomen lasting for more than at least one month was the most common finding (93%) observed. Other common symptoms in the order of decreasing frequency were, early satiety (87%), Poor appetite (76%), Nausea (57%) and not thriving (57%). History of loss of appetite was significantly associated with chronic dyspepsia with an odds ratio of 68.9394 and 95% confidence interval 26.62 to 178.54, p value of <0.0001. Most of the children belonged to lower income group predominantly of a rural background. 33 (72%) children had under nutrition as per IAP (Indian Academy of Paediatrics) classification based on WHO growth charts. 10 (30%) Grade I, 15 (45%) Grade II and eight (24%) had Grade III malnutrition. 26 children (57%) had abnormal endoscopic findings. Antral mucosal biopsy done showed chronic lymphocytic gastritis in 44 (96%) cases. 38 of these 44 (86%) were H.pylori positive. H. pylori positivity in chronic dyspepsia was highly statistically significant with a p value of 0.0001.

Conclusion: The incidence of dyspepsia is common among children between the age group of 5-10 years with a female preponderance. The predominant symptoms noted among these rural children are abdominal pain and loss of appetite. We found that endoscopy has a very high pick up rate of macroscopic gastroduodenal pathology. Multiple gastric erosions is the most common finding observed endoscopically and H.pylori associated lymphocytic gastritis is the overwhelming finding in our children with chronic dyspepsia.

Keywords: Chronic dyspepsia, Endoscopy, Histopathologic examination(HPE) H. pylori, malnutrition

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Introduction

Chronic pain abdomen and dyspepsia is the commonest presenting symptom in the pediatric outpatient department OPD after respiratory illnesses and it is increasing alarmingly both in the pediatric and adult population. H.pylori is a ubiquitous infection of the stomach the world-over[(1)]. Over 50% of the world's population is infected with this organism[(2)]. Though the incidence is decreasing in developed countries, it is still very high in developing countries like India, where infection rates are around 80% in adult population[(2,3)]. Most of them are infected in childhood itself. There is a concern about carcinogenic effects of H.pylori which has been classified as a group 1 carcinogen by WHO[(3)]. The early pre neoplastic changes of gastric atrophy and intestinal metaplasia noted in many studies in the pediatric population itself is of concern as it may lead to gastric carcinoma in adults[(2,4,5)]. So this study is aimed to assess the endoscopic and histopathological changes in dyspeptic children of this rural area of Melmaruvathur.

Material and Methods

Children between the age group of 5 to 15 years presenting to pediatric OPD of a rural tertiary care hospital, Melmaruvathur with symptoms of chronic dyspepsia lasting at least for one month were included in the study. Detailed history of various symptoms, pertaining to the gastrointestinal system was taken including pain upper abdomen, nausea, vomiting, poor appetite, retrosternal pain and not thriving. The demographic data collected included age, sex, socio-economic strata and rural/urban background. History of antibiotic or proton pump inhibitors intake over the past month was obtained. Children with history of antibiotic intake over last month and proton pump inhibitors over last 2 weeks were excluded from the study.

General physical examination included evaluation of the anthropometry and clinical evidence of anemia. Per abdomen examination was done and presence of epigastric tenderness was recorded. Baseline investigations done included hemogram, urine analysis and ultrasound abdomen. Upper gastroduodenal endoscopy was done by a single physician and antral mucosal biopsy was sent for histopathological examination (HPE). Hematoxylin and eosin stain was done to assess histopathologic changes and the degree of inflammation in the antral mucosa. Giemsa staining was done to identify the presence of H.pylori and its density.

On HPE, the degree of chronic inflammation in the form of lymphocytic infiltration, degree of acute tissue injury in the form of neutrophilic infiltration and the presence and density of H.pylori infection was noted. Early pre neoplastic changes such as gastric atrophy and intestinal metaplasia were also looked for. Statistical analysis was done using chi square by SPSS software.

Results

Forty six children between 5 to 15 years were evaluated over a period of one year. The predominant age group affected were between 5-10 years (43%) and the average age was 10 (Fig. 1). Of these 14(30%) were male children and 32 (70%) were female children. Most belonged to lower income group of a rural background.

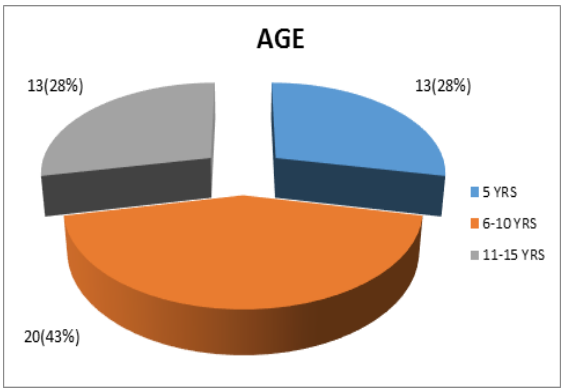

Fig. 1

Symptom Analysis

Pain abdomen more than one month was the common symptom seen in 43 (93%) children (Fig. 2) and three cases had other dyspeptic symptoms such as poor appetite, early satiety, nausea and vomiting. Other major symptoms found were early satiety 40 (87%), poor appetite 35(76%), nausea 27 (59%), failure to thrive 26 (57%), constipation 23 (50%), history of regurgitation of food in 22 (49%), retrosternal pain in 22 (49%), vomiting in 21 (46%), sensation of abdominal bloating in 14 (30%). Twelve (26%) children had history of recurrent fever and 10 (22%) had history of recurrent diarrhea and 25 (54%) had history of worms in stools.

History of loss of appetite was significantly associated with chronic dyspepsia with an odds ratio of 68.9394 and 95% confidence interval 26.62 to 178.54, p value of <0.0001. Only 13 (28%) children were normally nourished and remaining 33 (72%) were undernourished as per IAP classification (Fig. 3). Among the undernourished 10 (30%) were of Grade I, 15 (45%) of Grade II and 8 (25%) of Grade III malnutrition.

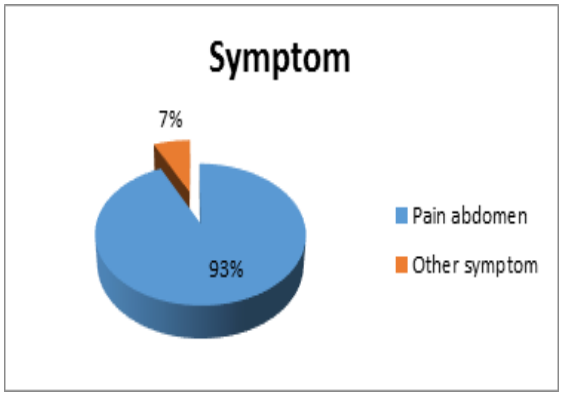

Fig. 2

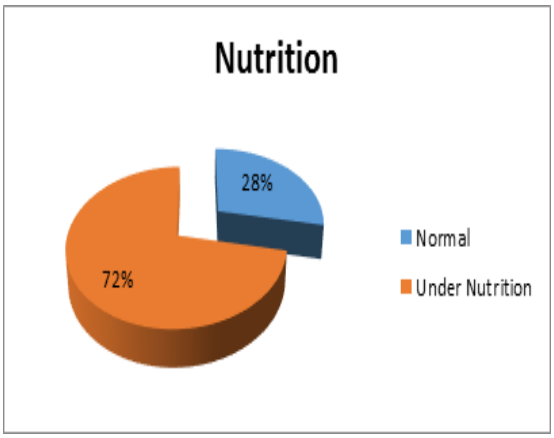

Fig. 3

Gross Endoscopic findings: Out of these 46 children, 26 children (57%) had abnormal endoscopic findings. Gastric erosions were seen in 21 (81%) children (Fig. 4, 5), duodenal erosions were seen in15 (58%) cases and duodenal ulcers were noted in 2 (8%) cases. Combined gastric and duodenal erosions were seen in 7 (27%) cases and one child had extensive erosions of esophagus, stomach and duodenum. Nodular gastritis was observed in one case (4%) and esophagitis in one case (4%). Three children (12%) showed incompetent esophagogastric junction (OGJ) and hiatus hernia was noted in four (15%) cases (Table 1).

Table 1: Nature and Distribution of endoscopic lesions

Site	Lesion	No. of Cases	Percentage of abnormal endoscopic findings
Esophagus (Total 8)	Incompetent OG Junction	3	12%
	Hiatus Hernia	4	15%
	Esophagitis	1	4%
Stomach (Total 21)	Antral gastritis alone	2	8%
	Nodular Gastritis	1	4%
	Erosive gastritis (more than one part of the stomach)	19	73%
	Pan Gastritis (involving all 3 parts)	13	50%
Duodenum (Total 17)	Duodenitis	15	58%
	Duodenal ulcer	2	8%
Combined	Gastric & Duodenal erosions	7	27%
	Gastric, Duodenal, Esophageal erosions	1	4%

Microscopic findings

Histopathologic examination (HPE) of antral mucosal biopsy was done in 46 children. Of these, 44 (96%) had abnormality on HPE and H.pylori associated chronic lymphocytic gastritis was noted in 38 cases (83%). Six cases (14%) showed chronic lymphocytic gastritis without evidence of H.pylori. H.pylori infiltration was mild to moderate in 31 (82%) (Fig. 6) and high in seven cases (18%). H. pylori positivity in chronic dyspepsia was highly statistically significant. Chi square value =168.941 with a $p < 0.0001$. Lymphocytic infiltration was mild to moderate in 28 (74%) and high in 10 cases (26%) (Fig. 7). Neutrophilic infiltration was noted in four cases (10%), mild to moderate in three cases(8%) and high in one case (3%). In our series no atrophy of mucosa was noted and intestinal metaplasia was noted in five cases (13%). (Table 2)

Table 2: Antral mucosal biopsy findings

Lesion	Mild to moderate		Severe		Total cases (46)
	Cases	Percentage	Cases	Percentage	
H.Pylori positive	31	82%	7	18%	38 (83%)
H.Pylori negative	-	-	-	-	6 (14%)
Normal	-	-	-	-	2 (3%)
Lymphocyte infiltration	28	74%	10	26%	38
Neutrophilic infiltration	3	8%	1	3%	4 (10%)
Intestinal metaplasia	5	13%	-	-	5

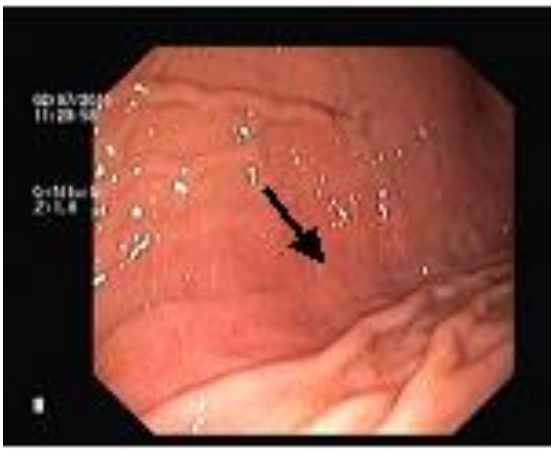

Fig. 4: Endoscopic Photograph shows body erosions (arrow)

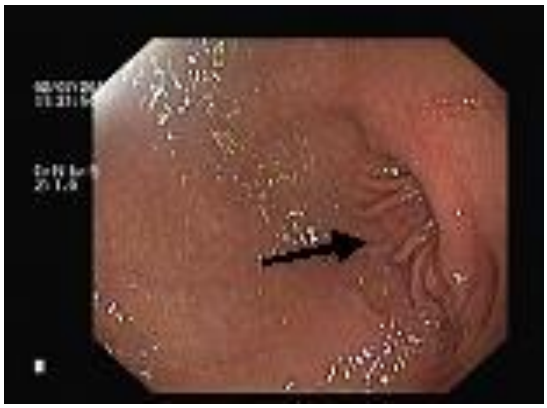

Fig. 5: Endoscopic Photograph shows antral erosions (arrow)

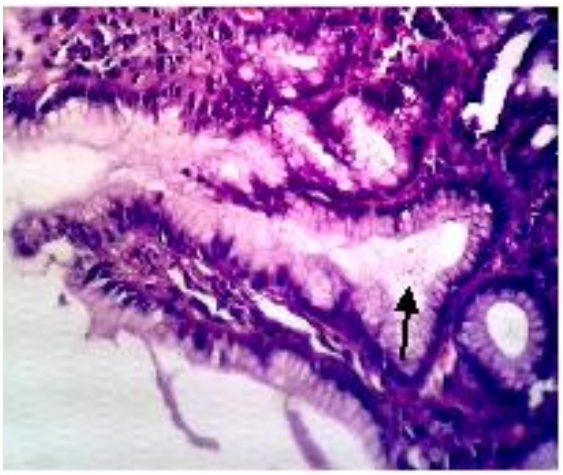

Fig. 6: Photomicrograph showing rod shaped Helicobacter pylori on mucosal surface (Arrow). (Hematoxylin and Eosin x 100)

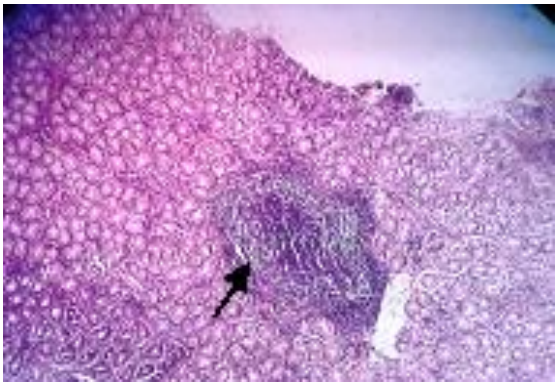

Fig. 7: Photomicrograph showing gastric mucosal glands with lymphoid follicles (Arrow) (Hematoxylin and Eosin x 40)

Discussion

The incidence of dyspepsia among children is common now days. In our study the predominant age group affected were between 5-10 years (43%) and female children (70%) were commonly affected. Symptoms of dyspepsia vary from pain abdomen, early satiety, poor appetite, nausea, vomiting, failure to thrive, gastrointestinal bleeding. In our study, pain abdomen was the most common finding in 43 (93%) children and other common symptoms found were early satiety (87%), poor appetite (76%), nausea (57%), and failure to thrive (57%). This was supported by studies done by Abdel Razak, Ozbey, et al, Oliveira et al who also observed pain abdomen as a common symptom in 67.5%, 57.4%, 34.6% cases respectively[2,6,7]. Gastrointestinal bleeding was observed in studies by Oliveira et al (13.4%), Ozbey, et al (11.9%), Motamed et al (9.8%), K Thakkar (5.8%), whereas we did not see any child with complaints of gastrointestinal bleed (2,7,8,9). Under nutrition and growth retardation was observed in dyspeptic children by Ozbey et al (21.8%) and K Thakkar (2.4%)[7,9]. In our series we found history of not thriving in 26 (57%) cases and a very high incidence of undernutrition in 33/46 (72%) children as per IAP classification. Ujjal Poddar has reinforced endoscopy as the most preferred method for evaluating children with chronic dyspeptic symptoms[1]. K Thakkar has reported chronic pain abdomen as the most common indication for endoscopy and has reported 38% pick up rate of gastroduodenal pathology by histopathology in their series on endoscopy[9]. In our study we had a very high pickup rate of both macroscopic and microscopic findings. Abnormal macroscopic endoscopic findings was observed in 26 (57%) children when evaluated for chronic dyspepsia and an astounding 44 (96%) cases had abnormal HPE. The predominant endoscopic findings in our study was gastric erosions (62%)in varying degrees including, only antral erosions (8%), erosions involving more than one part of gastric mucosa (73%) and pan gastritis involving the entire stomach (50%). This finding was supported by similar study done by Kumar et al who recorded 71% endoscopic antral gastritis and 85% histopathological antral gastritis[10]. In contrast to our findings, Deepak Bansal et.al observed no macroscopic lesions in the gastroduodenal mucosa & noted 16% incidence of esophagitis[11]. But our study showed esophagitis in one case (4%) only. Nodular gastritis which has been reported to be typical of H.pylori gastritis[6,8] was observed in only one case (4%) in our study whereas Ozbey, et al recorded antral nodularity in 54.5 % cases[7]. Duodenitis (58%) was the next common finding observed in our study (58%). Even though endoscopy was normal in 43% of the children in our study, histopathology was abnormal in all children except in two cases and all were reported as chronic lymphocytic gastritis. H.pylori positivity was observed in 38 cases (83%). This was supported by Ozbey et al. in their study which showed 63.2% H.pylori positivity and Rajindrajith et al who had reported 65.8% H.pylori positivity and chronic lymphocytic gastritis as commonest histological appearance in their series[7,12]. Our study showed high H.pylori infiltration in 7/38 cases (18%), high lymphocytic infiltration in 10 cases (26%) and high neutrophilic infiltration in one case (11%). In our series no atrophy of glandular mucosa was noted and intestinal metaplasia was noted in 5/38 cases (13%). But Guarner et.al in their series noted a high incidence of atrophy and/or intestinal metaplasia in 12/19 (63%) H.pylori positive patients. Atrophy in eight (42%) cases, intestinal metaplasia in two (11%) cases, both atrophy and intestinal metaplasia in two (11%) cases[5]. Oliveira, et al in their study found marked lymphocytic infiltration in < 5% of their series, marked neutrophilic activity in < 5% and marked H.pylori density in < 11%. They did not note pre neoplastic changes such as intestinal metaplasia, but noted mucosal glandular atrophy in 2/54 (4%) cases[2]. *Mukadder et al* have compared symptoms of H.pylori positive patients to H.pylori negative patients and found

dyspepsia and halitosis to be significantly higher in H.pylori positive patients[13]. In our study 84% children who underwent HPE for dyspepsia showed H.pylori positivity. It showed that there is a strong correlation of dyspepsia with associated H.pylori gastritis(p value of 0.0001). H.pylori has been implicated in various illnesses apart from gastric and duodenal ulcers and other forms of chronic gastro duodenal pathology. They include failure to thrive, refractory iron deficiency anemia and other less well established illnesses[3,6,8]. The increased association of under nutrition with dyspepsia noted in our study is a matter of concern to pediatricians as it may be a significant contributor to sluggish improvement in Millennium Development Goals (MDG)[14]. So the contribution of H.pylori gastritis to malnutrition in children between 5 to 15 years needs to be evaluated. Lydia et al have discussed that, in 1994 H.pylori has been recognized as group 1 carcinogen and the most common etiologic agent of infection related cancer by WHO International agency for research on cancer[4]. Our study finding of increased association of H.pylori gastritis in rural dyspeptic children is really an alarming sign that it may lead to later gastric malignancy later on. It is therefore suggested that further work up be done to assess the predisposing factors especially dietary habits for H.pylori gastritis in this rural children. Moreover comprehensive clinical assessment of children presenting with chronic dyspepsia and upper gastroduodenal endoscopy may pick up this gastroduodenal pathology early. This will be useful for the early identification and treatment of H.pylori gastritis in childhood itself and that may decrease the later incidence of gastric malignancy.

Conclusion

The incidence of dyspepsia is common among children between the age group of 5-10 years and female children were commonly affected. The predominant symptom noted among this rural children is chronic abdominal pain and loss of appetite. We found that endoscopy has a very high pick up rate of gastroduodenal pathology and gastric erosions involving more than one part of stomach is a frequent finding followed by duodenal erosion in dyspeptic children. H.pylori associated gastritis is the overwhelming finding observed in these rural children with chronic dyspepsia.

Acknowledgements

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Clinical profile of children presented with seizure in tertiary care hospital PMCH Patna, a retrospective study

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Abstract

Objective: To find the common causes of seizure and to classify seizure types in various age groups as well to predict outcome in relation to different variables.
Design: Retrospective hospital-based, analytic and descriptive study.
Setting: The Department of Paediatrics, PMCH, Patna.
Participants/patients: This study includes all children in the age group 6 months to 15 years presented in the department of paediatrics with seizure.
Outcome Measure(s): Demographic analysis and analysis of different seizure types, analysis of patient based on the cause of seizure as well as outcome of patient presented with seizure in relation to demographic, fever diagnosis and status epilepticus.
Results: The total number of patient presented with seizure are 956 of them 574 were males and 382 were females. 562 had fever on presentation and most of them were less than 5 years of age amount to 562. The most common clinical seizure type were generalized tonic- clonic (60.5%). Seizure disorder (14.4%), febrile seizures (16.1%), central nervous system infections and neurocysticercosis were common etiologies. Tubercular meningitis was more common etiology in 6–10 years age group. Neurocysticercosis were more common in 11-15 years age group. Encephalitis were more common in children below 5 years of age.
Conclusions: seizures are one of the common cause of hospitalization and high mortality. It can be inferred from this study that CNS infection are the most common cause of acute symptomatic seizure. Thus improvement in health care facilities like sanitation and immunization is warranted to prevent it.

Keywords: Generalized tonic-clonic seizures, Neurocysticercosis, Encephalitis, Tubercular meningitis

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Introduction

Seizures are the most common paediatric neurological disorder. Four to ten percent of children suffer at least one episode of seizure in the first 16 years of life. The incidence is highest in children less than 3 years of age, with a decreasing frequency in older children[1]. Seizures account for about 1% of all emergency department visits, and about 2% of visits of children's hospital emergency department visits[2]. The incidence of epilepsy (recurrent unprovoked seizures) in children and adolescents seems relatively consistent across all populations studied, ranging from 50 to 100/l00, 000 person-years[3]. In most of the studies, febrile seizures were reported to be the most common type seen in the paediatric population and account for the majority of seizures seen in children younger than 5 years of age[2-4].

Central nervous system (CNS) infections are the main cause of seizures and acquired epilepsy in the developing world[4,5]. Geographical variations determine the common causes in a particular region. Acute seizures are common in meningitis, viral encephalitis and neurocysticercosis and in most cases are associated with increased mortality and morbidity, including subsequent epilepsy[6-9]. The standardized mortality rate (SMR) in patients with a newly diagnosed unprovoked seizure ranges from 2.5 to 4.1 according to the study population and design. The SMR is highest in the youngest patients and in those with symptomatic seizure[10]. In most children with newly diagnosed epilepsy, the long-term prognosis of epilepsy is favorable, and in particular, patients with idiopathic etiology will eventually reach remission[11].

There are limited studies on causes and outcome of acute episode of seizure in developing countries. Most studies done so far have focused on epilepsy and clinical seizure types[12,13]. In this retrospective study, we therefore analyzed the prevalence of various etiologies, the clinical spectrum of seizure disorders and primary outcome of children admitted with a first attack of acute seizure disorder.

Methods

Patient population: A retrospective hospital-based analytic and descriptive study was conducted in the Department of Paediatrics, PMCH Patna. During a period of 1 year from Oct.31 2014 to Nov. 01 2015, where 8872 children admitted in the age group 6 months

to 15 years in the Paediatric Department. Among these, 956 children (10.8%) were admitted with complain of seizure who are included in the study. Children with seizure onset in hospital were excluded from this study.

Methods: All children admitted in the department of paediatrics with complaints of seizure in the age group of 6 months to 15 years were included (those who developed seizure during course of hospital stay were excluded). Furthermore children were divided into three age groups (6months-5years), (6years-10years), and (11years-15years). The medical record of patient were used to obtained the following data: Age, Sex, Type of seizure, If associated with fever, Final diagnosis, Final outcome recorded as discharge after recovery, LAMA(Left Against Medical Advice), Expired and referred to other institutions.

Patient presented with fever and without fever comprises two group: Those who presented with temperature more than and equal to 38°C and those who presented with temperature less than 38°C.Clinically seizures were classified as generalized tonic-clonic (GTC), partial, myoclonic, absence, and other seizures types based on the 1993 International League Against Epilepsy criteria[14]. Febrile seizure was defined as seizures that occur between the age of 6 and 60 mo with a temperature of 38 ° C or higher, that are not the result of central nervous system infection or any metabolic imbalance, and that occur in the absence of a history of prior afebrile seizures"[14]. Status epileptics was diagnosed as, "a continuous seizure activity or recurrent seizure activity without regaining of consciousness lasting for > 30 min."

Meningitis and encephalitis were diagnosed on the basis of clinical presentation and laboratory investigation which were verified with standard references[15].

Seizure disorder is characterised two or more "unprovoked" seizures. Unprovoked seizures have what are considered natural causes, such as genetic factors or metabolic imbalances in your body. Diagnosis was made by observation, neurological examination, electroencephalogram (EEG), and in some cases more advanced brain imaging techniques and metabolic tests.

A stroke is caused by the interruption of normal flow of blood to the brain, either by a blockage or a rupture in the blood vessels. When a part of the brain doesn't receive its regular flow of blood that carries vital nutrients and oxygen, brain cells die, causing a loss of brain function. The diagnosis was made using different neuroimaging and other tests viz Head Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Ultrasound, Electroencephalogram (EEG), Electrocardiogram (ECG or EKG) done if a heart problem was present or suspected, blood samples taken to check for blood clotting problem.

Cerebral palsy was defined group of permanent disorders of the movement and posture development , causing limitation of activity and that are attributed to insult that occurred in the developing fetal or infant brain leading to non-progressive disturbances. The diagnosis of cerebral palsy was made on clinical ground by clinical assessment, laboratory testing or neuroimaging was not taken into consideration. The diagnosis was based solely on parent reports or observations of motor milestones attainment, such as head control, pulling to stand, sitting, and walking, as well as evaluation of muscle tone, posture and deep tendon reflexes.

Sample size calculation: For a large population with 95% confidence interval and significance level of 5% and margin of error of 5%, required sample size was calculated to be 383 or more[16].

Results

Demographics and clinical seizure types in children with seizure: There was a total of 8872 patient admitted in the age group of 6 months to 15 years of age during the study period of 1 year. Out of these 956 (10.8%) had seizure. Among 956 patient with seizure 520 (54.4%) was in the age group of 6 months to 5 years and was associated with fever in 382(68%) of patient (Fig. 1). Fever was present on admission in 562(58.8%) of children. Afebrile seizure was common 150 (78.1%) in age group of 11 years to 15 years. There was 574(60%) males and 382 (40%)females with a male: female ratio of 1.5:1. There was a decreasing trend in the incidence of seizure with age, 6 months-5yrs 520 (54.4%)> 6 - 10years 244 (25.5%)> 11-15 years 192 (20.08%). Generalized tonic-clonic seizure were the most common seizure type in this study 562 (58.8%) and among them 375(66.7%) were febrile. These were followed by partial seizure 350 (36.6%), Absence seizure 27(2.8%) and Myoclonic seizure 11(1.2%). Other seizure types (Tonic, atonic) comprised 6(0.6%). In children with partial seizure 212(60.6%) were afebrile while in children who presented with Absence seizure 27(100%) were afebrile. Status epilepticus (Fig. 3) was present in 48(5.02%) of children and among them 21(43.8%) were febrile (Table 1)

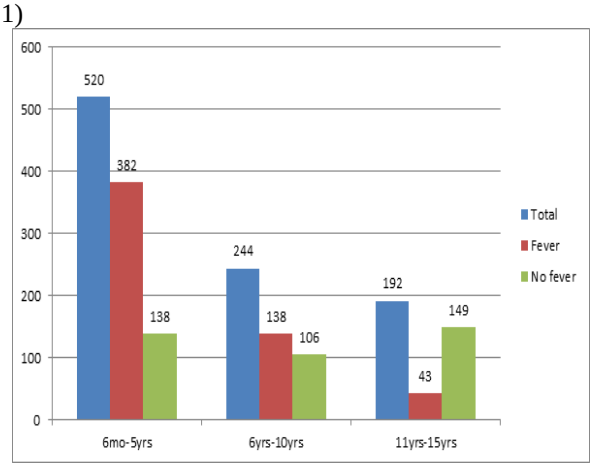

Fig. 1: Age & fever distribution of children with seizures

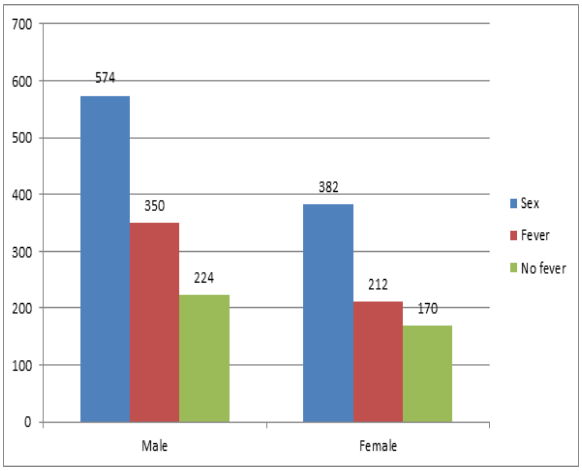

Fig. 2: Sex & fever distribution of children with seizures

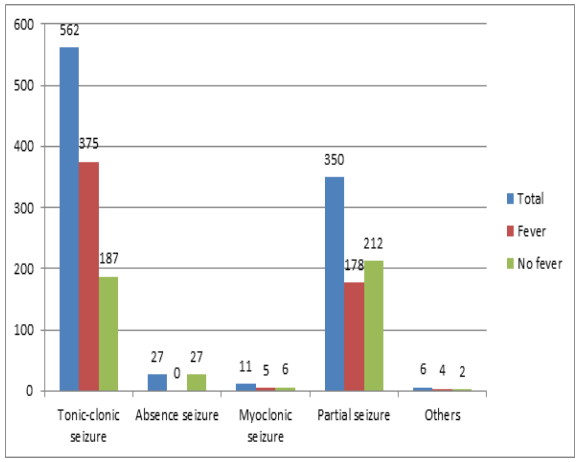

Fig. 3: Seizure type & fever distribution of children with seizures

Table 1: Demographic data and clinical seizure type of patients with seizure

		Fever (%)	No fever (%)	Total (%)
Sex	Male	350(62.3)	224(56.9)	574(60.04)
	Female	212(37.7)	170(43.1)	382(40)
	Total	562	394	956
Age	6 month -5yrs	382(68)	138(35)	520(54.4)
	6yrs -10yrs	138(24.6)	106(27)	244(25.5)
	11yrs -15 yrs	42(7.8)	150(38)	192(20.08)
	Total	562	394	956
Type of seizure	GTC	375(66.7)	187(47.5)	562(58.8)
	Partial	178(31.7)	172(43.7)	350(36.6)
	Absence	0	27(6.9)	27(2.8)
	Myoclonic	5(0.9)	6(1.5)	11(1.2)
	Status E	21(3.7)	27(6.9)	48(5.02)
	Others	4(0.7)	2(0.5)	6(0.6)
	Total	562	394	956

Analysis of patients based on etiology: Meningitis was the most common cause of seizure 170(17.8%) followed by febrile seizure 154(16.1%), Encephalitis 148(15.5%), Seizure disorder 138(14.4%), Tubercular meningitis 122(12.8%), Neurocysticercosis 101(10.6%).

Other diagnosis made were cerebral palsy 64(6.7%), stroke 17(1.8%) and miscellaneous etiologies includes electrolyte imbalance, neurocutaneous syndrome, brain abscess, hepatic and enteric encephalopathy, cerebral malaria, congenital CNS malformations accounting for 42(4.4%) of cases (Fig. 4).

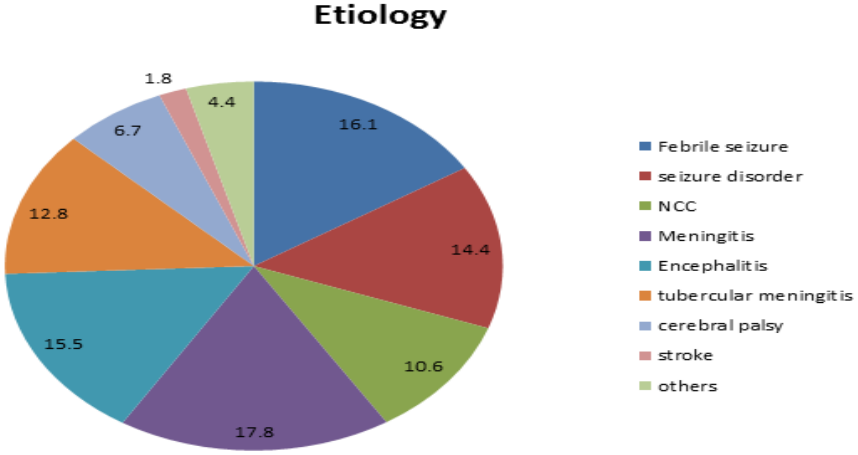

Fig. 4: Etiological diagnosis of children with seizures

Febrile seizure account for 29.6% of seizure in age group of 6 months - 5 years (Fig. 5) and was the most common etiology of seizure in this age group. NCC were more common in 11-15 years age group as against encephalitis which were common in 6 months to 5 years age group. Tubercular meningitis were more common in 6 -10 years age group (Table 2).

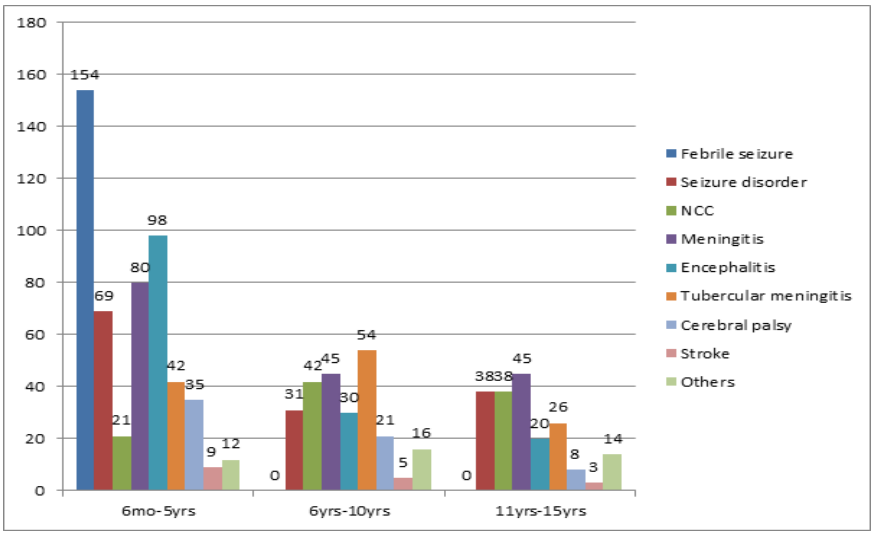

Fig. 5: Etiology & age group distribution of children with seizures

Table 2: Diagnosis of patients with seizure based on age groups

Diagnosis	6 month-5 years n (%)	6 years-10years n (%)	11years-15years n (%)	Total n (%)
Febrile seizure	154 (29.6)			154 (16.1)
Seizure disorder	69 (13.3)	31 (12.7)	38 (19.8)	138 (14.4)
NCC	21 (4.03)	42 (17.2)	38 (19.8)	101 (10.6)
Meningitis	80 (15.4)	45 (18.4)	45 (23.4)	170 (17.8)
Encephalitis	98 (18.8)	30 (12.3)	20 (10.4)	148 (15.5)
Cerebral palsy	35 (6.7)	21 (8.6)	8 (4.2)	64 (6.7)
Stroke	9 (1.7)	5 (2.05)	3 (1.6)	17 (1.8)
Tubercular Meningitis	42 (8.07)	54 (22.1)	26 (13.5)	122 (12.8)
Others	12 (2.3)	16 (6.6)	14 (7.3)	42 (4.4)
Total	520 (54.4)	244 (25.5)	192 (20.08)	956

Outcome in relation to gender, fever, status and diagnosis: The final outcome was made as discharge, death during stay in hospital, those who left against medical advice and those referred to other specialty centre for further management. 750 (78.5%) were discharged after successful treatment, 89 (9.3%) of children died during stay in hospital, 99(10.4%) had left against medical advice, and remaining 18(1.9%) cases were referred to other speciality centre for further management. The outcome between male (Expired 8.5%) and female (Expired 10.5%) were insignificant as with those presented with fever(Expired 10.5%) or without fever(Expired 7.6%). Among 48 children with status epileptics 20 (41.7%) expired. Most of the children who were diagnosed as neurocysticercosis (96%) and febrile seizure (96.8%) recovered and discharged successfully. Mortality was nil in patient with NCC. High mortality rate was found in Children who diagnosed as encephalitis, stroke and tubercular meningitis 25%, 17.6% and 13.1% respectively (Table 3).

Discussion

This was a hospital based retrospective analytic and descriptive study of children presented with seizure in a tertiary care centre PMCH Patna from October 31, 2014 to November 1, 2015. This study aimed to analyse demographics, clinical seizure types, etiologies and outcome of those children. This study excludes neonates and infants under 6 months of age because frequently they comprise one spectrum of diseases like septicemia, hypoxic-ischemic encephalopathy, and metabolic disorders[17].

Demographics and clinical seizure types: Many studies done before shows high incidence of seizure in

younger age group of children and a decreasing trend in older ones as well as more common incidence of seizure in males[2,5]. In our study also most children were younger than 5 years of age, even though not very significant but males had higher prevalence compared to female. Seizures presented with fever in 58.8% of cases. Generalized tonic-clonic seizure was found to be the commonest clinical seizure type and had higher incidence among children presenting with febrile seizure which is in accordance with the previous studies[4,5,7]. In the setting of higher incidence of meurocysticercosis in developing countries partial seizure is common[8]. Partial seizures represented 350 (36.6%) of children in the current study.

Etiological profile: First attack of seizure can have many possible etiologies, neurologic/developmental causes, infection, metabolic disturbances, traumatic head injury, toxins, febrile seizure etc[4-6]. One of the most common cause of seizure attack was reported to be due to febrile seizure[2-4]. In our study febrile seizures constitute (29.6%) and was found to be main the etiology of a first attack of seizure in children less than 5 years of age. Overall, meningitis was found to be the commonest etiology in children aged 6 months to 15 years (17.8%) followed by febrile seizure (16.1%), encephalitis(15.5%) and seizure disorder (14.4%).

Primary outcome of acute seizure: In our study the mortality rate during hospital stay among children admitted with acute episode of seizure was found to be similar with the mortality reports from other developing countries and amounting to 9.3%[4]. The difference in outcome among male (expired 8.5%) and female (expired 10.5%) was not so significant. Fever was found to be independently associated with increased mortality during the acute illness (mortality among febrile patient 10.5% and among afebrile patient with seizure 7.6% which is not similar to the reports from other studies, this may be due to Bihar being endemic for encephalitis which present with fever and has high mortality. Meningitis and encephalitis causes significant childhood mortality and morbidity[4,6]. There was poor outcome in children diagnosed with encephalitis and status epilepticus[18] there was good outcome in those children diagnosed with febrile seizure and neurocysticercosis.

As evident from this study first acute attack of seizure due to neurocysticercosis and CNS infections comprises a big bunch of cases. With improvement in sanitation and routine immunization for Hib and Japanese encephalitis vaccine most of these can be prevented. So attempt should be made towards these preventive measures to decrease the mortality from seizure, more over further intensive study need to be done to identify the burden of other etiological agents of CNS infections, so that appropriate targeted preventive measures can be taken and at the same time health care facilities need further preparedness for emergency management of seizure to decrease mortality and morbidity associated with seizure.

Limitations of the study

In this study outcome was defined as mortality during stay in hospital. Morbidities like neurological dysfunction and impact on scholastic performance were not studied in follow up. The details of other causes contributing for seizures could not be specified due lack of investigations (e.g. Inborn error of metabolism). Multicentric prospective study is needed to find out details regarding these problems.

Conclusion

Acute episodes of seizures are among the commonest cause of hospitalization with high mortality. It can be inferred from this study that most of acute symptomatic seizures are caused by CNS infections like meningitis, encephalitis, tubercular meningitis and neurocysticercosis as well as by febrile seizure which can be prevented with improvement in health care facilities like sanitation and immunization and preparedness to deal with acute episodes of seizure.

Already Known: There are limited studies on causes and outcome of acute episode of seizure in developing countries. Most studies had done so far have focused on epilepsy and clinical seizure types[12,13].

What this Study Adds: In this study, we have also analyzed the prevalence of various etiologies of seizure and primary outcome of children admitted with acute seizure disorder.

Authors' contributions: AKJ designed the study, TI drafted the manuscript, deduced the data and revised it. AK planned the study with TI, AK and TI conducted the data analysis, interpreted the data, and revised the manuscript. AKJ and AK critically revised the manuscript. All the authors approved the final document.

Conflict of interest: None

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Perceived understanding of informed consent among PG students and patients undergoing major abdominal surgeries in a selected hospital

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Abstract

Informed consent was developed as an ethical guideline 150 years ago. The concept began to take shape in 1914, when U.S. Supreme Court Justice Benjamin Cardozo stated, "Every human being of adult years and sound mind has a right to determine what shall be done with his own body, and a surgeon who performs an operation without his patient's consent commits an assault for which he is liable." Whatever we believe informed consent embodies, it has become first and foremost a legal system document designed to protect the patient from the physician. The quality of the administration of informed consent determines whether it is used as a prosecutorial or defense weapon in legal proceedings. Informed consent has evolved over the past 85 years to its current standardized form. Physicians contemplating surgical intervention are required to disclose a description of the problem and its natural history. They must explain the proposed treatment and alternatives to treatment. Risks general to the surgery and specific to the patient are to be delineated. Finally, outcome probabilities and postoperative expectations must be discussed.

Purpose: The main aim of the study was to know the perceived understanding of informed consent among PG students as well as among Patients undergoing major abdominal surgeries**.**

Method: A descriptive survey design was used for the study. A dyad sample of PG students and patients undergoing major abdominal surgeries participated in this study. Samples were selected through purposive sampling technique. Data was collected from PG students by administering a rating scale on perceived understanding of informed consent, and the data from patients undergoing major abdominal surgeries was collected by using structured interview techniques with the help of rating scale.

Results: The study result showed that 84% of the PG students and 40% of the patients undergoing major abdominal surgeries were having good perceived understanding about informed consent. 16% of the PG students and 52% of the patients were having average understanding of informed consent, whereas, 8% of the patients were having poor understanding of the informed consent. There was a association between the perceived understanding and the demographic variables of both PG students and the patients undergoing major abdominal surgeries.

Keywords: PG Students, Major abdominal surgeries, Perceived understanding, Informed consent

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Introduction

On the continuum of human life, many times the individual fall sick. It may be from a simple fever to life threatening illness which requires hospital stay, and there it begins different diagnosis, procedures, and surgeries etc. Most of the time the health care professionals treats the individual without providing enough information about the condition and what the treatment is being given. Patients need to be informed well about their condition once they come to the health care setting.

Performing surgical procedures is a routine event for the operating surgeon, while obtaining informed consent is an integral component leading up to the actual operation[1]. The principles of autonomy, beneficence and justice make up the basis of informed consent[2]. This usually involves a frank, interactive discussion between patient and surgeon regarding the proposed treatment, indications, risks and benefits, and alternative treatment options, if any. This is to equip the patient with the knowledge required to make an informed choice. Yet despite a physician's best efforts, informed consent may be ineffective[3]. This may be due to an overestimation of the level of patient comprehension during the informed consent process[4].

Informed consent is a process of communication in which the health care provider educates patients about the nature of their conditions and the possible solutions to their particular problems[3], and, in turn, the patient consents to the proposed treatment regimen. This process depends on a patient not only having, but also understanding, the appropriate information before treatment can be agreed upon and consented to[5,6]. Although the use of an informed consent document has become common practice in both the medical and dental professions, the process of educating patients so that they are truly informed has not[7]. As a result, many patients who sign a consent form are not actually informed.

Many health care professionals even today follow the paternalistic approach while treating the patient and they feel what they are doing[8] that is best for their patients. But they will not think from the patient's point of view what they really need to explain to them.

Keeping in view of the above findings in literature, the investigator wanted to know how much the PG students understand about the importance of informed consent and how much the patients get the information before they put their signature on the informed consent. The following objectives are formulated to carry out the study:

1. To assess the perceived understanding of informed consent among PG students.
2. To assess the perceived understanding of informed consent among patients undergoing major abdominal surgeries.
3. To find the association between perceived understanding of informed consent among PG students, patients undergoing major abdominal surgeries and selected variables.

Materials and Methods

The quantitative research approach was adopted and the descriptive survey design was followed. The study was carried out in Yenepoya Medical College Hospital, Yenepoya University, Mangaluru, Karnataka, India. The population for the study was PG students and the patients undergoing major abdominal surgeries. The sample (dyad) comprised of 25 PG students from different area of specialization and the patients who are admitted to undergo for major abdominal surgeries. The sampling technique used in this study to select the sample is non probability purposive sampling technique. The inclusion Criteria for selection of sample was PG students working in surgical wards, available at the time of data collection and Patients who are, **a**dmitted in the surgical wards**, a**vailable at the time of data collection

The instruments used for this study were "Rating scale on PG students perceived understanding of informed consent" and "Structured interview schedule for patients undergoing major abdominal surgeries using rating scale".

The above mentioned tools were prepared by the investigator and the reliability of the tools was obtained by Chron Bach's Alpha, and it was 0.8 for both Rating scale.

Method of data Collection

The investigator had obtained written permission from the director of the hospital prior to the data collection. The investigator approached each participant individually and explained about the project and signature was taken on the informed consent. PG students were given with the rating scale and asked them to respond by placing the tick (√) mark on the five point scale. Same way the investigator approached the patients undergoing abdominal surgeries admitted in the surgical wards and gynecology ward. Participants were informed about the study and signature was taken on the consent form. The investigator conducted a structured interview schedule with the help of a rating scale. Questions were asked to the patients from the rating scale and the response of the patients was put on the five point scale by using tick (√) mark.

Results

Table 1: Frequency and percentage distribution of subjects (PG students) according to their baseline characteristics(N=25)

	Variable	Frequency (f)	Percentage (%)
1.	**Age (in years)**		
	20-25	06	24
	26-30	18	72
	31-35	-	-
	36-40	01	04
2.	**Gender**		
	Male	15	60
	Female	10	40
3.	**Education**		
	MS	15	60
	MD	10	40
	Year of study		
	I Year	09	36
	II Year	07	28
	III Year	09	36
4.	**Area of Specialization**		
	Surgery	03	12
	Medicine	03	12
	Pediatrics	02	08
	Ophthalmology	05	20
	ENT	07	28
	Psychiatry	02	08
	Dermatology	03	12

Table 2: Frequency and Percentage Distribution of Patients According to their Baseline Characteristics (N=25)

	Variable	Frequency (f)	Percentage (%)
1.	**Age (in years)**		
	20-30	06	24
	31-40	09	36
	41-50	06	24
	51-60	04	16
2.	**Gender**		
	Male	11	44
	Female	14	56
3.	**Education**		
	No formal education	09	36
	Primary education	08	32

	Variable	Frequency (f)	Percentage (%)
	Secondary education	06	24
	Pre university and above	02	08
4.	**Occupation**		
	Agriculture	04	16
	Business	04	16
	Govt. Employee	03	12
	Private Employee	01	04
	Unemployed	13	52
5.	**Type of surgery**		
	Esophagectomy	02	08
	Gastrectomy	04	16
	Appendectomy	07	28
	Pancreatomy	02	08
	Hysterectomy	09	36
	Cholecystectomy	01	04

Table 3: Frequency and percentage distribution of perceived understanding of informed Consent among PG students and patients undergoing major abdominal surgeries (N=25+25)

Perceived understanding	PG students		Patients	
	Frequency	Percentage	Frequency	Percentage
Poor	-	-	2	8
Average	4	16	13	52
Good	21	84	10	40

Association between perceived understanding of informed consent among PG students, patients undergoing major abdominal surgeries and selected variables

The association between perceived understanding of informed consent among PG students, patients undergoing major abdominal surgeries and selected demographic variables was analyzed by using Chi-square test and the hypothesis was tested at 0.05 level of significance. The result showed that there is a strong association between the PG students understanding about informed consent, patients undergoing major abdominal surgeries and selected demographic variables.

Interpretation and conclusion

The study attempted to assess the perceived understanding of informed consent among PG students and the patients undergoing major abdominal surgeries. (84%) of the PG students and 40% of the patients undergoing major abdominal surgeries were having good perceived understanding about informed consent. 16% of the PG students and 52% of the patients were having average understanding of informed consent, 8% of the patients were having poor understanding of the informed consent. There was a significant association between perceived understanding and the selected demographic variables of PG students and the patients.

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Micropenis & Leucocyturia: a pointer to underlying urological anomaly?

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Abstract

UTI is common childhood infection yet frequently missed. The anomalies of genito-urinary tract are important predisposing factor for UTI. Certain anomalies of external genitalias points towards these internal urogenital anomalies. Present case an infant of 11 months with predominant presentation of bronchiolitis also had micropenis, which lead to focused renal screening and detection of multiple urological anomalies. Infant responded well to the treatment and is doing well on follow up.

Learning Points: Careful genital examination for external genital anomalies can help to unmask serious yet asymptomatic underlying urological malformation, if present should be followed by urine R/M +/-C/S.

Keywords: UTI, Micropenis, Urological anomaly.

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Introduction

UTI is commoner and usually recurrent in children with congenital anomalies of urinary tract, such children have greater risk of consequent renal scarring.[1,2] Primary renal damage in such children can be linked to obstructive uropathy or associated VUR or repeated UTI leading to renal scarring in a hypodysplastic kidney. Timely identification and detailed evaluation of such children will be of utmost importance. The difficulty lies in the fact that even serious anomalies can be completely asymptomatic. Certain clinical features suggesting of underlying functional or urological anomaly have been given by Indian society of pediatric nephrology but they have not included micropenis.

We are presenting an infant with bronchiolitis in whom presence of micropenis leads to renal screening and unmasking of the asymptomatic multiple urological anomalies.

Case Report

An 11 months old male infant brought with high grade fever along with poor feeding, cough, decreased urinary output for the past 4-5 days. He has received treatment for the same from another hospital. He was born as full term, AGA to primigravida mother and had non consanguineous parentage. Child was doing well except for two such similar episodes in the past for which he underwent treatment. He had normal bowel habits, normal urinary stream. No h/o abnormal frequency, dribbling or straining was present. Circumcision was delayed by parents due to micropenis.

On Examination: Child had toxic look, pallor, marked respiratory distress (tachypnea, chest wall retraction), coarse crepts bilaterally. On general physical examination following features were noted - brachecephaly, micropenis (stretched penile length = 1.5cm, normal SPL -2SD at 6- 12 months =2.3cms)[3] bifid scrotum, both testicles palpable (normal volume)rest systemic examination was normal. BP was normal for age along with normal anthropometry and development for age.

Initial Investigations done were **CBC** and **CXR PA** view. In view of micropenis **Urine R/M** and **C/S** was further advised. The CBC reports revealed polymorphonuclear leukocytosis and Urine R/M examination showed 20-25 pus cells per high power field but urine C/S was sterile. Chest X Ray revealed bilateral hyperinflation and increased broncho vascular marking (suggestive of bronchiolitis). In view of urine R/M findings renal function tests were done which were normal.

He improved after 7 days course of I.V antibiotics and was discharged on antibiotic prophylaxis. In follow up further renal imaging was advised.

USG KUB revealed B/L double ureters. No hydronephrosis and normal bladder wall was seen.

On **IVP**: Both kidneys normal

Right sided pelvicalyceal system duplicated (duplex kidney)

Right sided and left sided Duplicated Ureters (partial) which were joining at L2-L3 level on right as well as left side.

No hydronephrosis was seen.

MCUG: UB distended but normal morphology, position, capacity and outline, no f/o VUR were seen on either side, there was well defined, smooth, slit like filling defect in distal position of prostatic urethra with mild dilatation of proximal posterior urethra. Diagnosis

of PUV was made with no VUR and no hydronephrosis. During the entire follow up period of 9 months the patient took antibiotic prophylaxis initially for a period of 3 months, as he was undergoing renal imaging. He has been asymptomatic throughout.

He is under regular follow up for penile length and 6 monthly USG (KUB) will be done. Detailed endocrinological evaluation to determine the cause of micropenis to its level in the hypothalamic- pituitary-testicular- axis is being postponed due to the reluctance of parents.

Discussion

Urinary tract infections are common in children with highest prevalence in infancy[4], which is often missed or delayed due to minimal /non-specific symptoms leading to serious renal damage. Timely diagnosis[5] & regular follow up of such cases can be helpful in preventing renal complications in the long run.

Structural anomalies of genito urinary tract[6,7,8] are important predisposing factors for UTI & these are common in male infants[3] .

Although Indian Society of Pediatric Nephrology[3] has included few anomalies of external genitalia(tight phimosis, vulval synechiae, patulous anus) which point towards under lying urological anomalies, micropenis is not included. Focused renal evaluation of such infants for UTI can be helpful in detecting underlying urological abnormalities.

The above mentioned case presented with bronchiolitis but due to the presence of micropenis, urine r/m & urine c/s was advised. The investigations revealed leucocyturia but urine c/s was sterile (probably due to treatment with iv antibiotics from outside for 3 days prior to admission Detailed renal workup was planned & it revealed multiple urogenital anomalies namely, right sided duplex kidney, bilateral partial duplicated ureters with PUV with no VUR & no hydronephrosis & normal functioning kidneys.

So we suggest that anomalies of external genetalia i.e. micropenis can be included as a pointer to underlying urological anomalies.

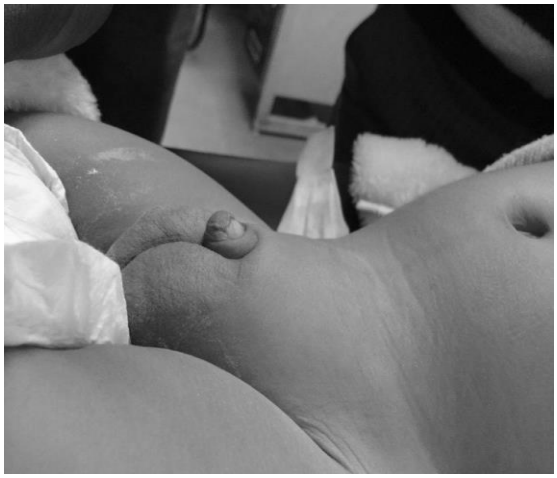

Fig. 1: Genitalia of the newborn

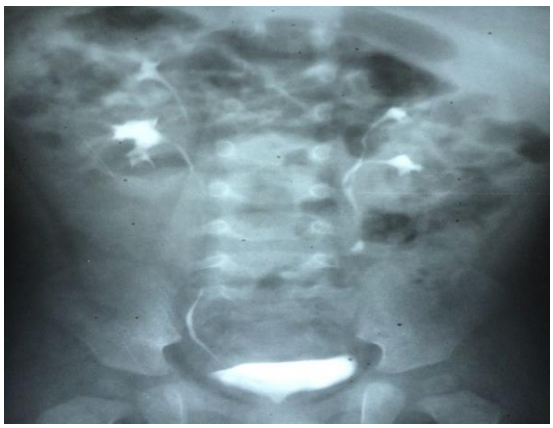

Fig. 2: IVP image of the infant

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Spindle Cell Carcinoma of the Tongue: A Case Report and Review of Literature

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Abstract

Spindle cell carcinoma (SpCC) or sarcomatoid carcinoma of the tongue is rare and aggressive variant of squamous cell carcinoma with incidence of <1%. It is characterised by proliferation of epithelial and mesenchymal components. It is important to diagnose this variant of SCC, because of its tendency to recur and early metastasis.

We are reporting this rare tumor with an unusual location in a forty year old gentleman to contribute in part to the better understanding and awareness of this rare malignancy.

Keywords: Spindle cell carcinoma, Biphasic, Sarcomatoid, Squamous

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Introduction

Spindle cell carcinoma (SpCC) is a rare variety of squamous cell carcinoma with aggressive behaviour in which usually upper aerodigestive tract is affected.[1,2] It accounts for almost 3% of all the SCCs in the head and neck region mainly involving larynx, hypopharynx and the mucous surface of oral cavity, but the SCC of the tongue is very rare.[3] It usually occurs in men (85%), during sixth and eighth decade of life.[3,4] It is usually associated with cigrette smoking, alcohol abuse, or any prior history of radiation.[2,4] We are hereby presenting a case report of spindle cell carcinoma of tongue in a male of 40 years old.

Case Report

A 40 year old gentleman presented with complain of ulcer on right lateral border of tongue for 2months progressive increasing in size associated with difficulty in chewing for 2 months and is not associated with bleeding from the lesion. Patient was a chronic tobacco chewer. There was no past history of tuberculosis, diabetes mellitus or any other chronic illness. MRI of face and neck was suggestive of well-defined lesion of 3.1*2.2*2.2cm on lateral aspect of anterior two-third of right side of tongue.[Fig. 1] Lesion is crossing midline to involve adjacent left side of tongue. There are multiple subcentimeter size discrete lymph node in submental and bilateral submandibular region. Patient underwent wide local excision with right sided supra onmohyoid neck dissection on 17 October, 2015.

HPE was suggestive of tumor size of 4*2.5*1.8 cm. All margins are more than 1 cm except deep resected margin that was .4cm. zero out of 11 lymph nodes were positive. On immunohistochemistry, tumor cells were positive for p63 and vimentin. Final diagnosis of Spindle cell carcinoma of tongue with pathological stage of pT2N0 was made.

Patient was then referred to our department for adjuvant treatment. Case was discussed in multidiscipilanary clinic and was planned for adjuvant radiation therapy upto a dose of 60 Gy in 30 fractions. He completed the entire treatment in November 2015 and is now on regular follow up. Follow up CECT (base of skull to insertion of diaphragm) was normal.

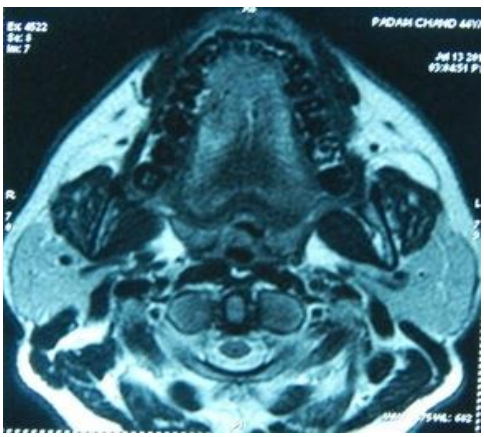

Fig. 1

Discussion

Spindle cell carcinoma is a biphasic tumor which is composed of both malignant epithelial and malignant mesenchymal components. The histogenesis of SpCC is very controversial, inspite of use of immunohistochemical electron microscope and genetic studies. As per the most recent theory, SpCC is a monoclonal epithelial neoplasm with the sarcomatous component derived from squamous epithelium with divergent mesenchymal differentiation.[5]

SpCC is mainly affects men between sixth and eighth decade of life.[2,4] In a study by Viswanathan S et al, 21.35% of the patients were in between 20 to 40 years of age.[4] The most common sites affecting SpCC are larynx, hypopharynx, nasal cavity and it rarely occur in tongue.[2,3,4] In the present case SpCC arises from the tongue of a young male of 40 years old. Potential risk factors include the history of tobacco use, poor oral hygiene, alcohol abuse, and previous ionizing irradiation of the area.[2,4] In the present case report, the patient was a chronic tobacco chewer.

SpCC is an aggressive disease and the chances of its recurrence or metastasis to lungs and other distant organ is very high.[4,6] Therefore it should be treated aggressively. Surgery is the standard definitive treatment for majority of oral cavity cancer. Along with surgical excision, radiotherapy plays a key role in the management of early stage and locally advanced cancer either alone or, in combination with surgery and/or chemotherapy, which provide an efficient adjuvant treatment.[4,6] Our patient had undergone wide local excision with ipsilateral supra omohyoid dissection followed by adjuvant radiotherapy with no evidence of recurrence and/or metastasis till date.

To conclude, although rare, the diagnosis of SpCC of tongue should always be keep in mind if on HPE malignant spindle cells are seen along with epithelial component and immunohistochemistry should be advised and the case should be treated aggressively.

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Periampullary Carcinoma with Skull Metastasis: A rare case report

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Abstract

Periampullary cancer consist of pancreatic cancer, carcinoma of ampulla of vater, distal common bile duct and duodenum. With the use of multimodality treatment, the prognosis of periampullary carcinoma has been improved. Skull (calvarium) metastasis is uncommon presentation. Only few cases of periampullary carcinoma with skull metastasis are available in English literature. Although rare, metastatic periampullary adenocarcinoma should be considered as a differential diagnosis in patients presenting with abnormal scalp swelling and tenderness. We reported a case of 48 year old female who presented with lytic expansile bony lesion with associated soft tissue mass in left parietal region with no neurological defecit 18 months after the whipples procedure.

Keywords: Periampullary Carcinom; Scalp Metastasis; Skull Metastasis

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Introduction

The global annual incidence rate for carcinoma of pancreas is about 8/100,000 persons[1] and is currently the fourth leading cause of cancer mortality in the United States It is anticipated that it become the second by 2020.[2] Skull (calvarium) metastasis is common from malignancies like breast, lung colon, prostate, kidney and ovary.[3] Gastrointestinal and pancreatic cancer rarely metastasized to brain and skull.[4]

However there are only few anecdotal reports in which ampulla of vater adenocarcinoma had metastasis to skull.[5,6] Here we are presenting a case of carcinoma head of pancreas with expansile osteolytic calvarial metastasis.

Case Presentation

A 48 years old post-menopausal female was diagnosed with periampullary carcinoma, underwent whipple surgery and feeding jejunostomy.[Fig. 1] Histopathology was suggestive of moderately differentiated adenocarcinoma, R0 resection with node positive. Case was discussed in multidispilanry clinic and planned for adjuvant chemotherapy. She had received adjuvant chemotherapy with Gemcitabine and Cisplatin till Sept 2014 and was kept on follow up. After 11 months of follow up, she developed swelling on left side of forehead, which was progressive increasing in size with mild pain. No complain of discharge from swelling, vomiting, headache, seizures, decrease of vision. On examination 5x5 hard fixed swelling present on left side of forehead with tense shiny skin, non-tender, temperature over the swelling not raised. Biopsy from the swelling was suggestive of metastatic carcinoma. CECT Scan of skull showed permeative lytic expansile bony lesion with associated soft tissue mass approximately 4.6X3.5 cm in left parietal region possibly metastasis. CECT thorax and abdomen was reveaed heterogenous enhancing irregular soft tissue mass esion in the retroperitoneum closely abutting right renal vessels approximately 2.5X2.2 cm suggestive of recurrent lesion with norma choedocho-jejunal, gastro-jejunal and pancreatico-jejuna anastomosis. Patient then received palliative radiotherapy to the skull lesion and is now on palliative chemotherapy. Good palliation was achieved.

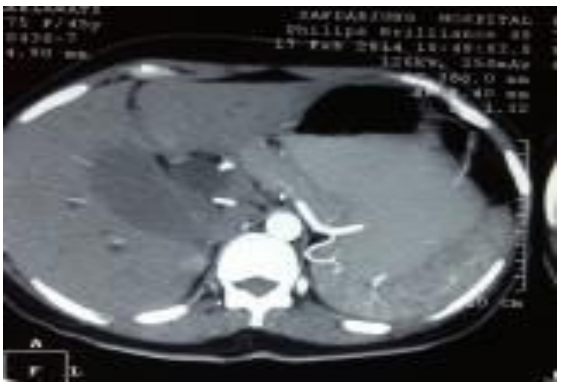

Fig. 1: CECT abdomen showed heterogenous enhancing irregular soft tissue mass lesion in the retroperitoneum

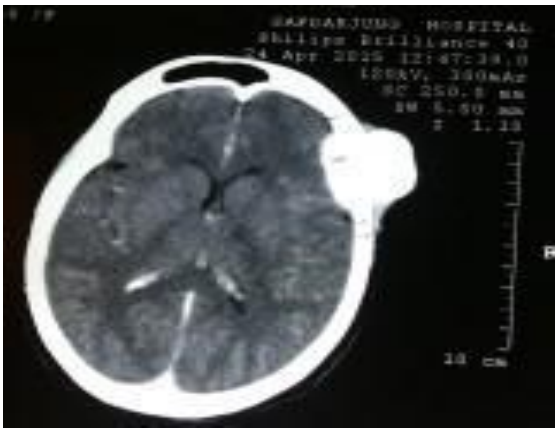

Fig. 2: CECT Scan of skull showed permeative lytic expansile bony lesion with associated soft tissue in left parietal region

Discussion

Periampullary cancer consist of pancreatic cancer, carcinoma of ampulla of vater, distal common bile duct and duodenum. Periampullary cancer are usually managed by radical operative procedures in early stages. However 80% of patients present with disease that cannot be cured with radical surgery.[7] In a study by Lee and Tatter, patients with carcinoma pancreas and periampullary cancer invariably present with metastasis to abdominal lymph node, liver and lung.[8] Cutaneous metastases is present in 0.7% to 9% of all patients with cancer, and is common in breast, lung, and colon cancer but are uncommon in pancreatic cancer.[9] In pancreatic carcinoma cutaneous metastasis are usually multiple and are confined to periumbilical region.[10] Isolated non umbilical metastasis are uncommon.[11] Pancreatic cancer with cutaneous metastasis to the scalp is rare.

So far to the best of our knowledge, there are only 7 cases of pancreatic cancer with scalp metastasis which are documented in literature.[5,6,12,13,14,15,16] Out of these there are only 5 cases including present study, in which skull is involved. In a study by Miyahara *et al*, 20 patients out of 22 reported with cutaneous metastasis prior to diagnosis of pancreatic cancer. In 11 of these, skin involvement was the first presentation.

Hopf S *et al* reported a case of cancer of ampulla of vater with right frontal skull metastasis 5 years after pylorus preserving pancreaticoduodenectomy.[1] In another study, by Jeon JY *et al* 65 year old Koren man presented with parietal scalp swelling after whipple procedure.[10] Aydin *et al* also reported a case of a 65-year-old woman, presented with painless frontoparietal scalp swelling which developed within three months and is the first presenting symptom of pancreatic adenocarcinoma.[26] (Table 1)

Table 1: Studies showing Metastatic periampullary carcinoma

Study	No. of patients	Sex	Site
Miyahara et al[12]	43	M	Uncus
Ambro et al.[13]	65	M	Ductal
Bhat W et al.[14]	59	F	Tail
Bdeiri K et al[15]	70	F	Tail
Aydin MV et al[16]	65	F	Tail
Hopf S et al[6]	54	F	Ampulla of vater
Jeon JY et al[5]	65	M	Ampulla of vater
Present study	48	F	Periampullary carcinoma

In the present study, patient of periampullary carcinoma developed skull metastasis 18 months after the curative whipples procedure, with no neurological deficits other than mild headache and scalp swelling despite adjacent dura is involved and underlying cortex is compressed.

Conclusion

With the use of multimodality treatment, the prognosis of periampullary carcinoma has improved, although rare, metastatic periampullaryl adenocarcinoma should be considered as a differential diagnosis in patients presenting with abnormal scalp swelling and tenderness.

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Neonatal candida guilliermondii sepsis-An unusual bug in neonatal intensive care unit

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Abstract

Fungemia particularly due to candida species is a well-recognized entity in Neonatal Intensive Care Units(NICU). A cause of concern is the increasing occurrence of sepsis due to non-albicans candida species. These are associated with increasing morbidity and drug resistance.

We report a rare case of neonatal sepsis due to Candida Guilliermondii, a yeast which was considered to rarely cause infection in humans. The neonate, born in an outreach facility, was admitted in NICU with features of systemic, CNS and dermatological manifestations. The initial investigation revealed thrombocytopenia with positive CRP and CSF suggestive of infection for which empirical antibiotic therapy**(Vancomycin+Meropenem)** in meningitic doses was started. Initial blood culture was sterile. Thrombocytopenia progressively worsened and patient manifested dermatological lesions in the form of hyperpigmented macular lesions over face which progressed caudally. In view of clinical sepsis, persistent thrombocytopenia and dermatological manifestations, a fungal etiology of sepsis was suspected. Blood and urine culture for fungus was sent and patient was started on IV Fluconazole along with topical antifungal ointment (Clotrimazole). Blood culture grew Candida Guilliermondii which was sensitive to Caspofungin, Micafungin, Flucytosine and resistant to Fluconazole and Amphotericin B. As the patient had already been on fluconazole therapy for 4 days on which she had shown clinical improvement in the form of improved activity, some regression of hyperpigmented patches and thrombocytopenia, IV fluconazole along with topical clotrimazole was continued for 3 weeks. After three weeks of antifungal therapy, there was normalising of haematological parameters in the form of resolving of thrombocytopenia, negative CRP and CSF studies within normal limits.

The neonate was treated successfully with intravenous Fluconazole, in spite of antibiotic sensitivity pattern suggesting its resistance in-vitro. This demonstrates a difference in in-vivo and in-vitro efficacy of drugs and the necessity of exercising clinical judgement before rapidly changing antibiotic therapy which could in the long run stem development of drug resistance.

Keywords: Candida Guilliermondi, Neonatal non-albican candida sepsis, Antifungals

Introduction

Fungemia particularly due to candida species is a well-recognized entity in Neonatal Intensive Care Unit(NICU). A cause of concern is the occurrence of non-albicans Candida species which were hitherto considered as contaminants and are now increasingly recognized to be associated with disease and increasing morbidity particularly in the immunocompromised patients. These are associated with drug resistance and increasing disease burden.

We report a rare case of Candida Guilliermondii sepsis in a neonate admitted in NICU with features of systemic as well as dermatological manifestation of infection. The infant was treated successfully with intravenous Fluconazole, in spite of antibiotic sensitivity pattern suggesting resistance to it. This demonstrates a difference in in-vivo and in-vitro efficacy of drugs. It also amply demonstrates the necessity of clinical judgement taking precedence and the need to exercise restraint of frequent change of antibiotics which could lead to development of increasing drug resistance.

Case Report

A term male baby was born to a 25yrs old G3P2L2 mother by elective LSCS with no history of maternal illness at a rural birthing centre. Baby was roomed in with mother. On day 7 of life the baby was admitted in NICU with features of sepsis in the form of fever, lethargy and poor feeding, multiple seizures with respiratory distress of two days duration.

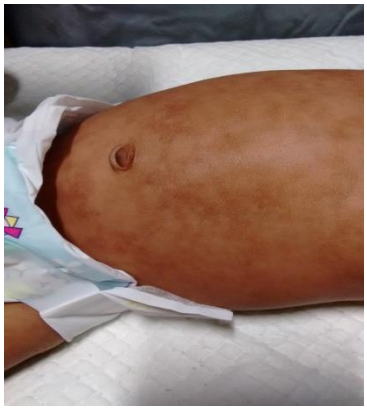
Clinical examination at admission revealed a lethargic term neonate with respiratory distress(Downe's score-5) and suffering repeated subtle seizures .Baby was euthermic, normotensive and SPO_2 was 80% in room air. There was no organomegaly detected, anterior fontanelle was flushed and there was no focal neurological deficit.

Baby was euglycemic. Haematological parameters revealed normal haemoglobin, total and differential white blood counts, thrombocytopenia (62,000/cumm) was present with no shift to left in peripheral smear. CRP was 34 mg/l. Serum Electrolytes, Calcium, magnesium and blood sugar levels were normal. CSF examination revealed Sugar-30mgm% (Blood sugar-108mg/dl), protein-115mgm% Cell count-58(neutrophils-50%, lymphocytes-50%) which was suggestive of meningitis. Blood & CSF culture were sterile.

- Cranial USG was normal.
- EEG showed bihemispherical epileptogenic foci.

A clinical diagnosis of sepsis with CNS involvement was made. Broad spectrum antibiotics (Vancomycin+Meropenem**)** were commenced in meningitic doses. Supportive care in the form of parenteral nutrition, trophic feeds and temperature management was instituted. Anticonvulsant therapy was started with Phenobarbitone which was stepped up to maximum dosages. In view of repeated seizures, Levitiracetam and Phenytoin needed to be provided to control seizures over a period of 36 hours.

Repeat haematological parameters monitoring showed a worsening of thrombocytopenia to 10,300/cumm with associated ecchymosis and GI bleeding. Therefore SDP transfusions were provided. By the 3rd day of hospitalization, baby developed hyperpigmented macular eruptions over face which progressed caudally.[Fig. 1] In view of continuing downhill course worsening thrombocytopenia and dermatological manifestation, a suspicion of fungal sepsis was considered and antifungal therapy (IV Fluconazole and Topical Clotrimazole) commenced after obtaining blood and urine for fungal culture. Patient showed gradual improvement over the next few days.[Fig. 2]



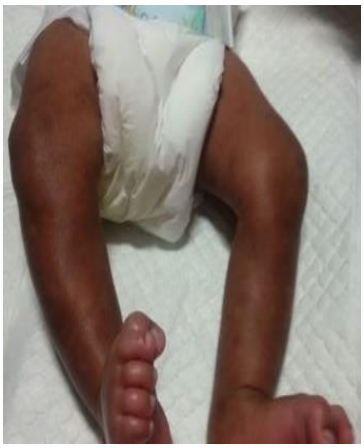
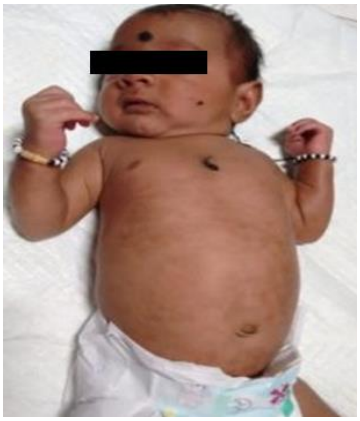


Fig. 1: Clinical photograph demonstrating dermatological manifestations of Candida Guilliermondii sepsis viz macular, hyperpigmented patches over face, trunk and extremeties



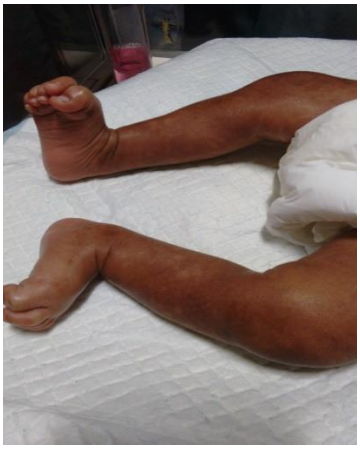


Fig. 2: Clinical Post Treatment Photograph of Patient Regression of Skin Lesions

Blood culture report which came in four days later revealed growth of Candida Guilliermondii sensitive to Caspofungin, Micafungin, Flucytosine and resistance to Fluconazole and Amphotericin B.

The patient meanwhile showed a clinical improvement in the form of improved activity, feed tolerance, reducing skin lesions and seizure control. Haematological parameters too showed an improvement in the form of increased platelet count and normalising WBC counts. Hence the same antibiotics and antifungal therapy was continued with biweekly monitoring of haematological parameters. Antimicrobial therapy was continued for 3 weeks duration. Repeat CSF examination showed normalization. The patient was discharged on one anticonvulsant (Phenobarbitone). Follow up at 6 weeks and 3 months showed a neuro-developmentally normal infant with normal haematological parameters and complete regression of skin lesion.

Discussion

Fungal infection due to candida albican in intensive care units has been a worrisome issue, particularly so in immunocompromised patients. Of concern is the recent emergence of non-albican candida species e.g. *Candida Tropicalis, C. Parapsilosis, C. Glabrata* and *C. Krusei*

causing disease, particularly in the intensive care settings. These strains were earlier considered contaminants but are now causing disease and are associated with increasing morbidity and mortality. Emergence of these uncommon species as pathogens in NICU has been a cause of worry.[1,2,3]

C. Guilliermondii is considered an uncommon clinical isolate globally.*C. Guilliermondii* ranks fourth behind *C. Albicans*, *Candida Tropicalis*, and *C. Parapsilosis* and ahead of both *C. Glabrata* and *C. Krusei.*[4]

Candida Guilliermondii is an uncommon species of *Candida* that is most often associated with onychomycosis[5]. It has been associated with poor clinical outcomes and hematologic malignancies[6]. It may be found on human skin and as part of the genitourinary and gastrointestinal tract flora. It has been documented to cause infection in patients undergoing surgical procedures, endocarditis in intravenous drug users and fungemia in immunocompromised patients. C. Guilliermondii has also been isolated in urinary tract infections[7]. Few reports of its isolation from bloodstream is particularly restricted to patients of hematological malignancy.

Only recently there are scant reports of its isolation from NICUs. These include a report of pseudoisolation in NICU. Exhaustive investigation on the blood culture practices revealed that when drawing blood for a culture from small infants, heparin flushes used was contaminated. Culture of a single lot of diluted heparin vials, grew between 10,000 and 15,000 colony-forming units of Candida Guilliermondii/ml[8].

Lately there are trends of its isolation from bloodstream and of CNS infection in adults and immunocompromised patients, particularly those with malignancies. However reports of sepsis in neonates with this fungi are few and far between. When it occurs, there are increasing reports of its resistance to Fluconazole[8]. *C. Guilliermondii* does appear to exhibit decreased susceptibility to fluconazole, and this pattern is seen in all geographic regions [9-12] It may also develop resistance to amphotericin B. The index case too demonstrated an in-vitro resistance to both fluconazole and amphotericin B.[13-14]

Antifungal Surveillance Program [ARTEMIS DISK] showed decreased susceptibility of Candida Guilliermondii to fluconazole, and voriconazole was more active in vitro against *C. Guilliermondii* than fluconazole.[15] It has also been seen that isolates of candida Guilliermondi from South Asian regions were most sensitive to fluconazole {77.4%} then other regions viz (Europe (73%), Latin America (77.0%), North America (67.7%). South Asian strains (7.9%) of Candida Guilliermondii showed least resistance to fluconazole therapy when compared to Europe(13%), Latin America(10.2%) and North America(8.8%). It has also been observed that in vitro resistance to fluconazole was the least in South Asia as compared to other antifungals.

Voriconazole has displayed more efficacy against *C. Guilliermondii* than fluconazole, irrespective of geographic region. However, its in vitro resistance rate has also been higher than fluconazole. Latest 2016 IDSA guidelines recommend Amphotericin B for treatment of disseminated candidiasis and Fluconazole as a reasonable alternative in patients who have not been on fluconazole prophylaxis.[16] Thus in view of these observation, fluconazole appears to be the most effective first line of therapy in South Asian regions.

Many NICUs adopt the policy of fluconazole prophylaxis because of high incidence of candida infection. But since in our unit fungal infections are uncommon, we do not use antifungal prophylaxis as a routine. This patient was provided IV Fluconazole on a clinical suspicion of a fungal septicemia. Our patient showed clinical improvement. Hence the same antifungal therapy was continued in spite of blood culture showing resistance to fluconazole. Also the high cost and side effects associated with use of Amphotericin and voriconazole were considered a limiting factor to its usage in our baby who had showed improvement on fluconazole. Further the use of fluconazole as a first line is in accordance with current recommended practice.[17]

Conclusion

We report a rare case of Candida Guilliermondii sepsis with CNS & dermatological involvement in a term neonate. We treated the baby successfully with IV Fluconazole in spite of blood culture showing resistance to it. This baby showed a progressive improvement. This reiterates a differing in-vivo and in-vitro efficacy of antimicrobials. It highlights the importance of clinical monitoring in deciding antimicrobial therapy and its efficacy in a given case. Furthermore, rapid changing of antimicrobials in a patient who is showing clinical improvement based on laboratory reports, would encourage development of drug resistance. Thus exercising clinical judgement and restraint from frequent change of antimicrobials would contribute greatly to improving healthcare in the long run.

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Pediatric optic ner-glioma: A case study

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Abstract

An **optic nerve glioma** is a type of brain tumor. There are multiple kinds with brain tumors and glioma's account for approximately one-third of brain tumors. They are **typically named after the kind** of cells they affect. It is a rare kind of cancer, they are considered low-grade and do not grow as quickly as other types of brain tumors. They are found in the optic chiasm, where the optic nerves cross or **surround** the optic nerves. They are also referred to as optic glioma or juvenile pilocytic astrocytoma. It is rarely found in individuals over the age of 20. It has also been associated with the genetic disorder neurofibromatosis Type 1, or NF1. Evidence suggests that adult malignant gliomas (glioblastoma) are rare & almost always occur in adult males with a very poor prognosis & almost certain death within one year. Optic-nerve gliomas comprise about 1% of all intracranial tumors and Optic nerve glioma is a slow-growing tumours, which typically affects children. 30% of patients have associated neurofibromatosis type 1 & those have better prognosis. However, optic nerve glioma of children is discussed in this article.

Keywords: Optic nerve glioma, Juvenile pilocytic astrocytoma, Brain tumors, Malignant glioma (glioblastoma) and intracranial tumors.

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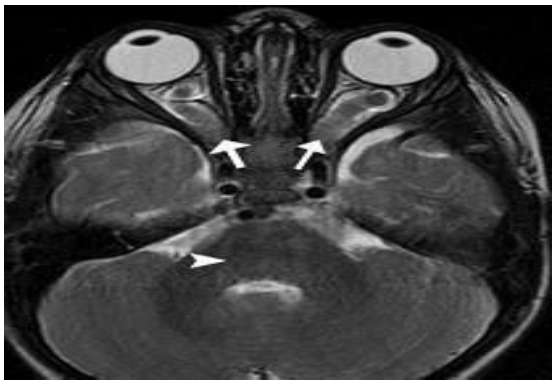
Introduction

A 7½ year old male child was admitted in the Peadiatric surgical ward on 12/02/2016 with the complaints of diminished vision from past 6 months and moderate to severe frontal head ache with one episode of vomiting. The child was apparently normal before 6 months, and his visual alteration was reported by his school teacher that he is unable to read words on blackboard. He went for routine eye checkup and suggested for improving diet and no other treatment measures were used. The symptoms progress and the child vision worsen with which he started banging on walls and doors. Due to progressive diminishing of vision made his parents to take him to ophthalmologic checkup twice and he was referred to tertiary care centre. Therefore the client came to AIIMS OPD with the above complaints for further treatment. There he underwent MRI and the child was diagnosed as brain tumor with other supportive investigations. The child underwent craniotomy and excision on 3rd march 2016 and the tumor was removed and culture was sent for histopathological examination. The incision was made from frontal area till the right ear, 13 sutures was made to close the incision. Based on the report of histopathological examination the diagnosis was conformed as **Optic Nerve Glioma**. Postoperatively the child's general condition was fair and was complaining of diarrhea and head ache.



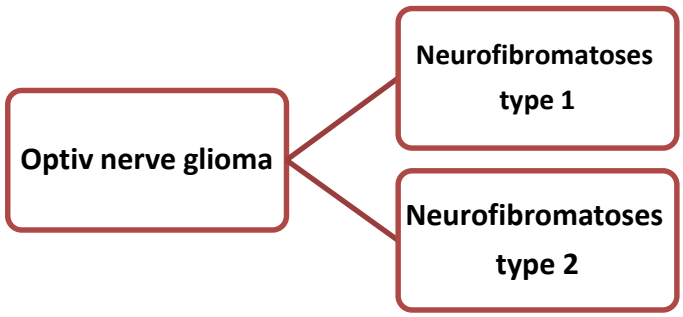
Back Ground: Optic Glioma

According to Literature	Patient Presentation
Definition: An optic nerve glioma (also called an optic pathway glioma) is a slow-growing brain tumor that arises in or around the optic nerve, which connects the eye to the brain. As the tumor progresses, it presses on the optic nerve, causing a child's vision to worsen. Blindness can occur, but only in about 5 percent of cases. The tumor sometimes produces additional symptoms as it grows. A low-grade form of this neoplasm, benign optic glioma, occurs most often in pediatric patients. While these are serious tumors, they have a high cure rate.	

Incidence:

- Peak incidence occurs in individuals aged 6-7years.
- Prevalence of 15% (range, 1.5–24%)
- benign optic glioma occur almost in children, better prognosis
- Aggressive glioma occurs almost in adult, poor prognosis.
- Genetic disorder neurofibromatosis Type 1, or NF1is commonest type in children.

Age 7 ½ years
Sex: male
Race: Asian



Types

The child's condition was classified as Neuro-fibromatoses type 1 after numerous diagnostics procedures.

Causes:
Exact cause is Unknown
Chromosomal abnormalities / hereditary genetic disorder,
Environmental or infectious causes can predispose.

Similar to the literature information, present case also did not depict any causative factor.

Pathology:

The NF-1 product, neurofibromin has GTPase-activating protein domain with the Ras protein, which is crucial in regulating signal transduction and cell proliferation and differentiation.

↓

Patient with NF-1 age at high risk for developing a number of different types of tumor because of this.

↓

Orpital portion of the optic nerve, a glioma often appears as a fusiform swelling

↓

Causes nerve compression and adjuscent structure compression

↓

Vision loss, head ache, and vomitting

Clinical manifestations

- **Headache**: due to increased intracranial pressure or hydrocephalus.
- **Nausea and Vomiting**: Classic projectile vomiting (frequently without nausea)
- **Vision loss**
  - Children are frequently unaware of significant vision loss; nevertheless, this symptom reportedly occurs in 20-60% of pediatric patients with craniopharyngioma at presentation.
  - Anterior extension to the optic chiasm can result in a classic bitemporal hemianopsia, unilateral temporal hemianopsia, papilledema, or unilateral/bilateral decrease in visual acuity. Classically, vision loss starts with a superior temporal field cut. However, the eccentric growth of these tumors can

Before surgery:
Head ache on frontal area
Vomiting
Partial Vision loss (bitemporal hemianopsia)
Unusual eye movement
After surgery:
Head ache
Diarrhea

result in varying patterns and severity of vision loss, including decreased acuity, diplopia, blurred vision, and subjective visual field deficits. Children are frequently inattentive to visual loss, and formal testing may be required.

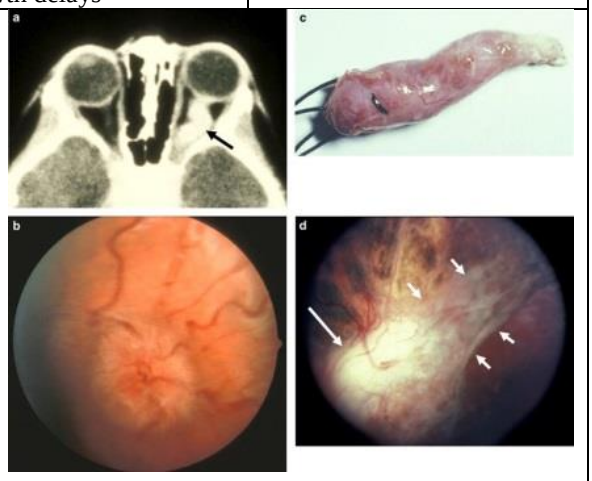
Balance problem

- **Seizures** due to Temporal lobe involvement
- **Hyperactive** children with unusual eye movements and even blindness due to extrinsic compression of the hypothalamus.
- **Endocrine deficiencies** leads to

short stature, Weight gain, Lethargy, Fatigue, Cold intolerance, Dry skin, Dry brittle hair, Slow teething, Anorexia, Large tongue, Deep voice, Myxedema, Delayed puberty, memory impairment, daytime sleepiness and growth delays

Diagnosis:

- History
- Physical examination with neurological exam.
- Preoperative intellectual or psychological assessment.
- Vision testing
- Serum electrolytes levels
- Hormonal studies
- Skull Radiography
- Head CT Scanning
- Brain MRI
- Cerebral Angiography
- Biopsy



The child presented with following findings:

History: The child natal history was apparently normal

- **General appearance:** Oriented, conscious, moderate body built.
- **GCS score:** Eye 4 verbal 5, and motor 6,
- **Vital signs:** stable
- **Anthropometr**y: height 154cm, weight 18kg, 1st degree malnutrition (according to Gomez classification).
- **Growth and development** seems to be normal. And child was mild hyperactive and have hurried in speech.
- **Head to foot:** surgery suture was healthy, partial visual acuity. Unusual eye movement, pupillary dilatation, partial optic atrophy. Extra ocular eye movement abnormalities. Slow teething and deep voice, weight loss.
- No other abnormal physical finding findings.

Investigations:

- **Haematological investigation**: Hb: 11.3gm/dl, RBC 4.56mc/cum,TLC 7500cells/cumm, DLC-N 90%,E-01%, L-05%, m-04%, platelet – 3.11 lacks/c/cumm, Hematocrit 34.8%.
- **Hormonal studies:** T3 level is elevated.
- **MRI**: suggestive of possibilities of Craniopharyngiomas.
- **Histo-pathological examination**: suggestive of optic nerve glioma

Treatment:

A treatment plan must be carefully individualized for each patient. This need consultation and team work.

Management:

Child was under continuous observation with possible supportive therapy to the family.

Medical management

He was on continuous medication till he undergo surgical management.
Tab valporate 200mg OD (morning)
Tab veona CR 300 mg OD (evening)
Tab pantop -20mg OD
Tab sporlac 120mg TDS

- **Surgical management**

Craniotomy and excision was done. Postoperatively the child was doing

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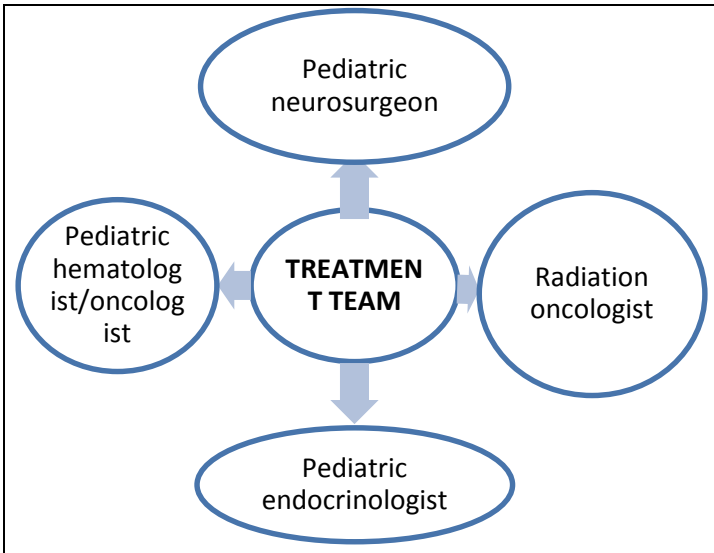

Observation only in presumed optic nerve glioma, particularly with good vision on the involved side; with careful follow up if the radiographic evidence.
Long-term hormone replacement is the primary medical treatment: intranasal vasopressin (desmopressin acetate [DDAVP]), corticosteroids, thyroid hormones, growth hormones, and sex hormones.
Combination chemotherapy using actinomycin D, vincristine, etoposide, bevacizumab and other agents has also been reported to be effective in patients with progressive chiasmal/hypothalamic gliomas to shrink the tumor and stabilize vision.
Radiation therapy as the sole treatment is considered if the tumor cannot be resected (usually chiasmal or optic tract lesions) and if symptoms (particularly neurological) progress or if the tumor is resistant to chemotherapy
Alternative medicine -(acupuncture/acupressure, therapeutic touch, herbal medicine, etc.) to control pain and treatment side effect.
Surgical Care-Surgery is usually not preferred for this type of tumor, but can sometimes relieve symptoms and/or improve vision. Surgical excision in case of rapid intra-orbital tumor growth to isolate the tumor from the optic chiasm and thus prevent chiasmal invasion. The surgeon should use an intracranial approach to obtain tumor-free surgical margins.
Radical surgery
Conservative surgery alone
Conservative surgery with postoperative radiotherapy

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<td>well and had satisfactory general condition.
No post-operative radiotherapy was given to the child.</td>
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<td>Complications:

Hormonal deficiency
Cognitive difficulties,
learning disabilities, and
impairments in growth

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<td>

TSH deficiency
Diencephalic syndrome (hyperactive with unusual eye movements)

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<td>Prognosis and recurrence

Variable
Optic nerve glioma recurrence may take place many years after initial treatment.
It usually recurs in the same place as the original tumor, but can also occur in other parts of the brain or spinal cord.
Local radiation therapy is the usual treatment if the patient has not previously been treated with this modality.

</td>
<td>After one month of hospitalization, the child was discharged with minimal deficit in activities of daily living.
The child was progressed positively according to the expectations. Supportive treatment and therapies have been provided. The child</td>
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• Chemotherapy and radiation therapy are options for patients who have only been treated surgically. • Child with NF-I tend to fare better with respect to growth and visual prognosis. • Most tumor grows slowly or having self-limited growth. • Some tumors are more aggressive, resulting in a rapid increase in ispilateral ptosis and visual loss.	recovered completely and was discharged after one month of surgery. He was advised for regular OPD checkups without fail.

Special consideration

- Identification of risk factors for exposure to radiation or chemicals that is carcinogenic.
- Identify the signs and symptoms are: headache, vomiting, and decreased vision or double vision.
- Identify any changes in client behaviour.
- Observation of hemiparese or hemiplegia.
- Changes in sensation: hyperesthesia, parasthesia.
- Observation of sensory changes: asteregnosis (not able to feel the sharp edges), agnosia (not able to recognize objects in general), apraxia (not being able to use the tool properly), agraphia (can't write).
- Observation of vital signs and level of consciousness.
- Observation circumstances fluid and electrolyte balance.
- Psychosocial: personality and behavioural changes, difficulty making decisions, anxiety and fear of hospitalization, diagnostic tests and surgical procedures, a change in the role.

Conclusion

Having cancer as a child can be socially and emotionally stressful. You or your child may benefit from counseling or a support group. Being around peers his or her own age can be a big support. The survival rate for optic pathway gliomas is near 90 percent. Older children and those with neurofibromatosis 1 have better outcomes. In fact, two-thirds of children with NF1 experience spontaneous remission of their optic pathway gliomas. Children may suffer a smaller field of vision, which means they do not have peripheral vision. The odds of complete blindness from these tumors, however, are less than 5 percent. As there is chance of recurrence after treatment, follow-up visits with doctor are necessary to check for any side effects and ensure the cancer has not returned.

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