BRIEF REVIEW

Update on the classification of hemangioma

Antony George, Varghese Mani[1], Ahammed Noufal
Department of Oral and Maxillofacial Pathology, MES Dental College, Perinthalmanna, [1]Department of Oral and Maxillofacial Surgery, Mar Baselios Dental College, Kothamangalam, Kerala, India

Address for correspondence:
Dr. Antony George,
Department of Oral and Maxillofacial Pathology,
MES Dental College, Perinthalmanna,
Malappuran - 679 338, Kerala, India.
E-mail: kavitamardi@yahoo.co.in

Received: 28-02-2012
Accepted: 06-06-2014

ABSTRACT

Despite the fact that a biological classification of congenital vascular tumors and malformations was first published in 1982 by Mulliken and Glowacki, significant confusion still prevails due to the indiscriminate and interchangeable use of the terms hemangioma and vascular malformation. Hemangiomas are true neoplasms of endothelial cells and should be differentiated from vascular malformations which are localized defects of vascular morphogenesis. On an analysis of various scientific articles and latest edition of medical text books an inappropriate use of various terms for vascular lesions was found, contributing further towards the confusion. The widely accepted International Society for the Study of Vascular Anomalies (ISSVA) classification differentiates lesions with proliferative endothelium from lesions with structural anomalies and has been very helpful in standardizing the terminologies. In addition to overcoming obstacles in communication when describing a vascular lesion, it is important that we adhere to the correct terminology, as the therapeutic guidelines, management and follow-up of these lesions differ.

Key words: Classification, congenital hemangioma, hemangioma, infantile hemangioma, international society for the study of vascular anomalies, vascular malformation

INTRODUCTION

The classification and the terminologies used for various vascular lesions have been very confusing despite the fact that a biological classification was first published in 1982 by Mulliken and Glowacki.[1] This classification was later adopted by the International Society for the Study of Vascular Anomalies (ISSVA) in their first workshop held in Rome during June 1996.[2] This continuing workshop now takes place every 2 years in various countries around the world. The ISSVA is an organization comprising of specialists in various disciplines interested in vascular anomalies and was founded in 1992 in Budapest with the aim of achieving consensus among health care professionals on the terminology, to further the knowledge of pathogenesis, diagnosis and treatment of these vascular lesions.[3] An analysis of various scientific articles and latest edition of text books showed that significant confusion still prevails due to the indiscriminate, inappropriate and interchangeable use of various terms.[3]

Access this article online
Quick Response Code:
Website: www.jomfp.in
DOI: 10.4103/0973-029X.141321

Classification

Historically benign vascular tumors were classified: (1) According to the type of fluid they contained as hemangioma (blood-containing lesion) and lymphangioma (lymph-containing lesion) and (2) according to the size of the vascular channels as capillary (small diameter vascular channels) and cavernous (large diameter vascular channels).[4] Mulliken and Glowacki described a biological classification based on endothelial cell characteristics, physical findings and natural history, that differentiates vascular lesions with endothelial cell proliferation (example hemangioma) from lesions with structural anomalies (vascular malformations).[1-5] The ISSVA modified it in their continuing workshops, differentiating vascular tumors from vascular malformations based on their clinical appearance, radiological features, pathological features and biological behaviour [Table 1].[2,3,5]

DISCUSSION

Hemangiomas grow by endothelial cell hyperplasia and should be differentiated from vascular malformations, which are not true neoplasms but are localized defects of vascular morphogenesis caused by dysfunction in embryogenesis and vasculogenesis [Table 2].[2-10] The Greek suffix ‘‘oma’’ means cellular proliferation of a

Table 1: Modified International Society for the Study of Vascular Anomalies (ISSVA) classification

Vascular tumors	Vascular malformation
Infantile hemangiomas	Slow (low) flow
Focal	Capillary malformations (CM)
Segmental	Port-wine stain
Indeterminate	Telangiectasia
Congenital	Angiokeratoma
hemangiomas	Venous Malformations (VM)
Rapidly involuting	Common sporadic VM
congenital	Bean syndrome
Hemangioma (RICH)	Familial cutaneous and mucosal
Non involuting	VM (VMCM)
congenital	Glomuvenous Malformation (GVM)
Hemangioma (NICH)	or Glomangioma
Tufted angioma	Maffucci syndrome
Pyogenic granuloma	Lymphatic malformation (LM)
Dermatologic acquired	Lymphedema
vascular tumors	Lymphangioma circumscriptum
Kaposiform	Lymphangioma cavernosum
hemangioendothelioma	Lymphangioma cysticum
Spindle cell	Fast (high) flow
hemangioendothelioma	Arterial malformation (AM)
Hemangioendothelioma	Arteriovenous fistula (AVF)
NOS	Arteriovenous malformation (AVM)
	Complex combined vascular malformations

NOS: Not otherwise specified

tumor and thus the term hemangioma is erroneous when used for malformations.[2] Hemangiomas are the most common benign soft tissue tumor of infancy and childhood, occurring in 12% of all infants and are found in greater frequency in girls, whites, premature infants, twins and are usually born to mothers of higher maternal age.[2-8] They occur most frequently in head and neck region (60%), followed by the trunk (25%) and the extremities (15%), which are grouped into Infantile Hemangiomas (IHs) and Congenital Hemangiomas (CHs).[2,3,8]

IHs (outdated term juvenile hemangioma) arises during the first 8 weeks of life as an area of discoloration or telangiectasia. The lesion exhibits a rapid proliferative phase during early childhood for 6-12 months and grows into a raised rubbery bright-red tumor (resembling a strawberry, hence outdated term strawberry hemangioma).[4,5,7,8] This is followed by gradual involution and a spontaneous regression by the age of 5-9 years. 50% of all hemangiomas will completely involute by the age of 5 years and 90% by the age of 9 years.[4,5,7,8] 40% of involuted lesions may either show scaring, wrinkling, telangiectasia, or loose fibro-fatty tissue.[5,6,8] IHs can be grouped into focal, segmental and indeterminate, or depending on the depth of the lesion from the skin surface as superficial, deep and mixed. Focal IHs are the most common variant, appearing as localized raised tumor-like lesion that tends to occur at the area of embryological fusion. Segmental IHs are flat plaque-like larger lesions that show a geographic segmental distribution and Indeterminate IHs shows characteristics of both focal and segmental IHs.[5] Color varies with the depth of the lesion; they can be bright red (superficial), purple, blue, or normal skin colour (deep).[3-5]

CHs are clinically present as fully developed lesions at birth and either rapidly involutes during the first year of life or may never show involution. These lesions do not exhibit a proliferative phase and do not grow after birth.[5,6] Rapidly Involuting Congenital Hemangiomas (RICH) are present at birth, either as red-purple color plaques with coarse telangiectasia, or as flat violaceous lesions, or as a raised greyish tumor surrounded by a pale halo with multiple tiny telangiectasia. RICH undergo a rapid regression phase and completely disappear by 12-18 months of age.[5,6] Non Involuting Congenital Hemangiomas (NICH) are also present at birth, appearing as pink or purple colored plaque-like lesions with prominent overlying coarse telangiectasia and peripheral blanching. NICH do not show a regression phase and grows proportionately with the growth of the child.[5,6] Main differences between congenital and infantile hemangiomas are summarised in Table 3.[2,4-7,10]

Apart from hemangiomas of soft tissue, scientific literatures have reported central hemangiomas (hemangioma of bone) and intramuscular hemangiomas. Many researchers in addition to the World Health Organization (WHO) believe that most if not all such proposed lesions are vascular malformations rather than true neoplasms.[9] ISSVA classification has not been applied for the categorization of these osseous vascular lesions.[9]

CONCLUSION

Therapeutic guidelines, management and follow-up of hemangiomas and vascular malformations differ and are beyond the scope of this article. A good classification is important for categorising information, recording data, proper communication, guiding treatment plans, obtaining prognostic information and should be easy to understand and applied by the clinicians. It is our duty to be consistent in our terminology and classification of vascular lesions in all our scientific writings and presentations in order to communicate effectively, understand its pathophysiology, promote research and develop newer therapeutics. Terms to be avoided when describing these lesions include angioma, birthmarks, capillary hemangioma, cavernous hemangioma, juvenile hemangioma, strawberry hemangioma and inappropriate interchangeable use of the terms hemangioma and vascular malformation.

Table 2: Differences between infantile hemangioma and vascular malformations

Characteristics	Infantile Hemangioma	Vascular Malformations
Age of occurrence	Develops between 2-8 weeks of life	Present at birth (may not be clinically detectable)
Gender prevalence	Female prevalence (5:1)	No gender prevalence
Course of lesion	Grows rapidly for approximately 6-12 months then undergoes slow involution Involute by 5-9 years	Grows proportionately with the child's growth Does not involute
Factors causing flare	None	Trauma, hormonal changes
Auscultation, palpation	No associated thrill, bruit, or pulsation	Thrill, bruit, or pulsation may be appreciated
Diagnosis	Clinical history, appearance and magnetic resonance angiography	Vascular imaging: Magnetic resonance angiography, doppler ultrasonography, angiography
Magnetic resonance angiography	Well-delineated tumor with flow voids	Hyper-signal on T2-sequences with VM and LM Flow voids without parenchymal staining with AVM
Cellular changes	Increased endothelial cell proliferation Increased number of mastocytes Thick basement membrane	Normal endothelial cell-cycle Normal number of mastocytes Normal basement membrane
Immunohistochemistry	GLUT-1 positive Proliferating hemangioma: PCNA +++, VEGF +++, bFGF +++, collagenase IV +++, urokinase ++, TIMP-1 –ve, LYVE-1/CD31 +++ Involuting hemangioma: PCNA –ve, VEGF +, bFGF ++, collagenase IV –ve, urokinase ++, TIMP-1 +++, LYVE-1/CD31 –ve	GLUT-1 negative Barely detectable: PCNA, VEGF, bFGF, urokinase Variable staining: TIMP-1 Negative staining: Collagenase IV
Treatment	Left untreated (observation) until puberty anticipating spontaneous involution. 90% of hemangiomas will completely involute by 9 years For functional and cosmetic reasons pulse-dye lasers, intra-lesional injection of sclerosing agents (sodium morrhuate, psylliate, glucocorticoids, interferon-α), surgical excision, or radiation therapy	Depend on site, size, stage and symptoms Slow flow lesions: From conservative to pulse-dye lasers, sclerotherapy with or without excision or surgery alone Fast flow lesions: From conservative to embolisation plus surgery or surgery alone

AVM: Arteriovenous malformation, bFGF: Basic fibroblast growth factor, GLUT: Glucose transporter, LM: Lymphatic malformation, LYVE: Lymphatic endothelial hyaluronan receptor, MRI: Magnetic resonance imaging, PCNA: Proliferating cell nuclear antigen, TIMP: Tissue inhibitor of matrix proteinases, VEGF: Vascular endothelial growth factor, VM: Venous malformation

Table 3: Differences between congenital and infantile hemangioma

Congenital hemangioma	Infantile hemangioma
Less common (30%)	More common (70%)
Present at birth	Develops between 2-8 weeks of age
Equal male and female prevalence	Female prevalence (5:1)
Growth is complete at birth or grows proportionately with the child's growth	Grows rapidly for approximately 6-12 months
Rapid involution (within 12-18 months) or no involution	Slow involution (over 5-9 years)
GLUT-1 negative	GLUT-1 positive

GLUT: Glucose transporter

ACKNOWLEDGEMENT

Manoj Vengal, Professor of Oral Medicine and C. S. Jayapalan, Professor of Oral Pathology, for their critical evaluation and valuable guidance in manuscript preparation and general support.

REFERENCES

1. Mulliken JB, Glowacki J. Hemangiomas and vascular malformations in infants and children: A classification based on endothelial characteristics. Plast Reconstr Surg 1982;69:412-22.
2. Enjolras O, Wassef M, Chapot R. Color Atlas of Vascular Tumors and Vascular Malformations. 1st ed., New York: Cambridge University Press; 2007.
3. Redondo P. Vascular Malformations [I] Concept, Classification, Pathogenesis and Clinical Features. Actas Dermosifiliogr 2007;98:141-58.
4. Donnelly LF, Adams DM, Bisset GS. Vascular malformations and hemangiomas: A practical approach in a multidisciplinary clinic. Am J Roentgenol 2000;174:597-608.
5. Restrepo R, Palani R, Cervantes L, Duarte A, Amjad I, Altman N. Hemangiomas revisited: The useful, the unusual and the new. Pediatr Radiol 2011;41:895-915.
6. Eivazi B, Ardelean M, Baumler M, Berlien H, Cremer H, Elluru R, *et al*. Update on hemangiomas and vascular malformations of the head and neck. Eur Arch Otorhinolaryngol 2009;266:187-97.
7. Dadras SS, North PE, Bertoncini J, Mihm MC, Detmar M. Infantile hemangiomas are arrested in an early developmental vascular differentiation state. Mod Pathol 2004;17:1068-79.
8. Murthy J. Vascular anomalies. Indian J Plast Surg 2005;38:56-62.
9. Bruder E, Perez-Atayde AR, Jundt G, Alomari AI, Rischewski J, Fishman SJ, *et al*. Vascular lesions of bone in children,

adolescents, and young adults. A clinicopathologic reappraisal and application of the ISSVA classification. Virchows Arch 2009;454:161-79.
10. George A, Jayapalan CS, Noufal A. Diagnosing hemangioma and vascular malformations of head and neck. Health Sciences 2014;3:JS002C.

How to cite this article: George A, Mani V, Noufal A. Update on the classification of hemangioma. J Oral Maxillofac Pathol 2014;18:117-20.
Source of Support: Nil. **Conflict of Interest:** None declared.