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PRESENTATION OF NONSEMINOMATOUS GERM CELL TUMOR OF THE TESTIS WITH SYMPTOMATIC SOLITARY BONE METASTASIS. A CASE REPORT WITH REVIEW OF THE LITERATURE

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Metastatic bone lesions are exceptional at diagnosis in germ cell tumors (GCTs). Bone involvement is usually a late event combined with synchronous metastasis in the retroperitoneal lymph nodes, lung and liver. Bone examination is not considered a standard procedure in the staging of GCTs, and this may contribute to underestimation of the real proportion of bone metastases. Here we report a case of nonseminomatous GCT of the testis with a synchronous, symptomatic, solitary pubic bone metastasis that was completely controlled by systemic chemotherapy and locoregional radiation therapy. Solitary bone metastases from GCTs seem to be chemosensitive and radiosensitive, but we do not know their prognostic value. We reviewed the literature where 3 similar cases have been reported. We propose individualized management for symptomatic GCT patients including bone scintigraphy and/or PET examination at diagnosis and a combined cytotoxic approach with chemotherapy and radiation therapy

Key words: bone metastasis, chemotherapy, nonseminomatous germ cell tumor, PET.

Introduction

Bone metastasis as the first event in nonseminomatous germ cell tumors (GCTs) is very rare. We present the unusual case of a man submitted to orchiectomy because of progressive right scrotal swelling and concomitant thigh and hip pain that hampered his walking. A mixed nonseminomatous germ cell tumor confined to the right testis was diagnosed. The symptoms persisted after radical surgery. The result of standard staging procedures was irrelevant but a solitary osteolytic pelvic lesion was found by scintigraphy and specific CT scan. Fine-needle aspiration cytology revealed metastatic tumor cells in the pelvic lesion. Standard chemotherapy and locoregional radiation therapy produced complete remission of the disease but a few months later PET examination showed a relapse at the sacrum. A second schedule of platinum-based chemotherapy and radiation therapy completely controlled the disease. After 20 months the patient is alive without symptoms or disease.

Case report

A 49-year-old man had a recent history of progressive right scrotal swelling and concomitant thigh and hip pain that hampered his walking. Two weeks after a right orchiectomy, in March 2003, he was admitted to our institution. Pathological examination revealed a solid mass of 6.5 cm arising from the right testis. The tumor was limited to the testis without epididymus and cord involvement but with vascular thrombosis; microscopically, it showed areas of embryonal carcinoma, yolk sac tumor and teratoma, like malignant mixed germ cell tumors. After orchiectomy the thigh and hip pain persisted, spreading to the right leg. Imaging studies and blood tests were carried out. Computed tomography (CT) of the thorax, abdomen and retroperitoneal region excluded distant metastasis and pathological lymph nodes. Technetium bone scan revealed hot spots in the parietal bone and right ischiopubic ramus of the pelvis. Magnetic resonance imaging (MRI) excluded brain metastasis and identified a benign malacic lesion in the parietal bone; CT scan of the pelvis showed a solitary osteolytic lesion at the right ischiopubic ramus spreading to the surrounding soft tissues and muscles (Figure 1A). Fine-needle aspiration cytology of the pubic lesion was obtained and carcinoma cells consistent with metastasis from testicular tumor were harvested (Figure 2). Elevated tumor marker levels were measured before the orchiectomy: β-human chorionic gonadotropin (β-HGC) 252 mU/mL; α-fetoprotein 287 ng/mL; lactate dehydrogenase (LDH) 521 U/L. After surgery the β-HGC and LDH values returned to normal while α-fetoprotein remained elevated (606 ng/mL until the beginning of chemotherapy). Standard PEB (cisplatin, bleomycin, and etoposide) chemotherapy was given for 3 cycles, followed by a fourth PE cycle supplemented with 20 Gy of radiation therapy to the pubic lesion. The α-fetoprotein value returned to normal after the first cycle of chemotherapy. This treat-

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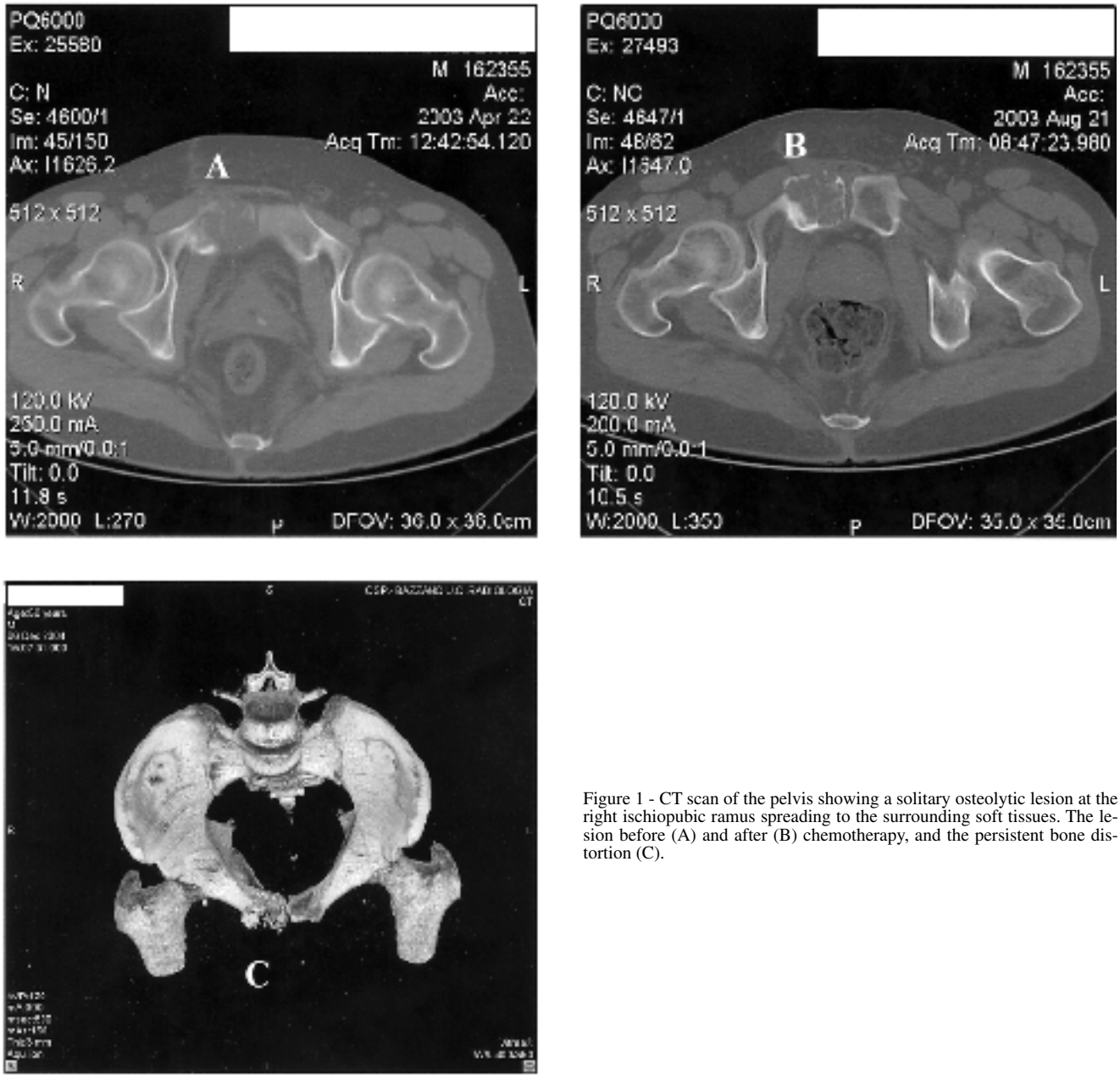

Figure 1 - CT scan of the pelvis showing a solitary osteolytic lesion at the right ischiopubic ramus spreading to the surrounding soft tissues. The lesion before (A) and after (B) chemotherapy, and the persistent bone distortion (C).

ment produced resolution of the pelvic pain, restoring normal walking. The pelvic CT scan showed a reduction of the pubic lesion, which was more evident in the soft tissue areas while there was persistent bone distortion (Figure 1B and 1C). Three months after the last cycle of chemotherapy the patient complained of lower back pain. A relapse was suspected but the tumor markers were in the normal range, X-ray of the pelvis was negative, and CT scan showed that the residual pelvic bone lesion was unchanged. Finally, positron emission tomography (PET) examination revealed an area of intense hyperactivity in the left part of the sacrum and a faint uptake in the right ischiopubic ramus (Figure 3A). A second line of chemotherapy was planned starting from January 2004 with a combination of ifosfamide, carboplatin, and etoposide for 4 cycles. A palliative dose (30 Gy) of radiation therapy was delivered to the sacral lesion. The patient obtained complete regression of the symptoms. The following PET examination confirmed the complete remission of the disease (Figure 3B). At present the patient is alive without disease.

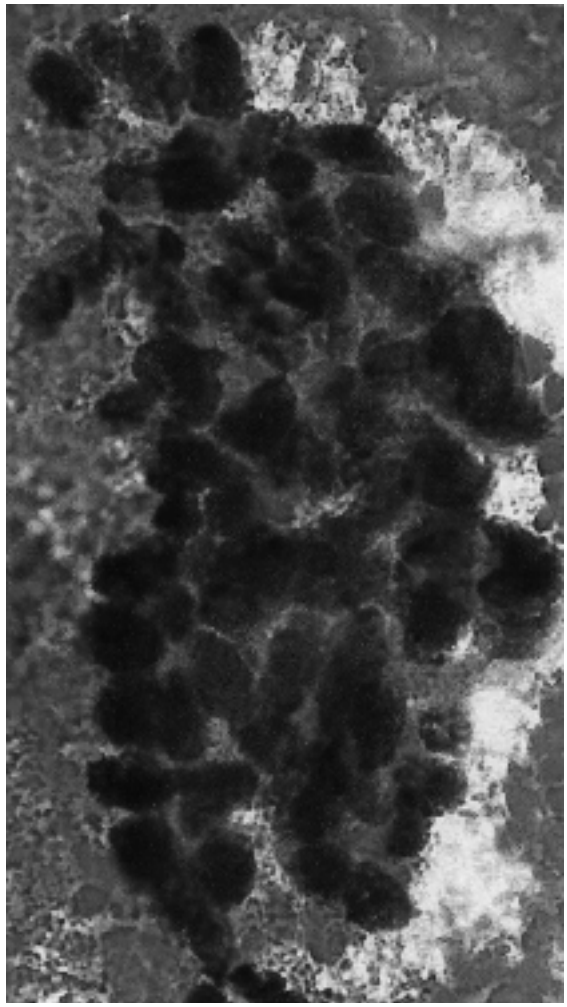

Figure 2 - Fine-needle aspiration cytology from the pubic lesion: carcinoma cells consistent with metastasis from testicular tumor.

Discussion

Hematogenous bone metastases have rarely been reported in nonseminomatous GCTs when compared with seminomas. Typical sites of involvement in nonseminomatous GCTs are the lung (89%), liver (75%), and brain (31%)[1-3]. Hitchins *et al.*[2] reported that in testicular and extragonadal GCTs bone involvement is the first presentation of disease or relapse in 3% and 9% of patients, respectively. However, all patients considered in these reports had synchronous metastasis in the retroperitoneal lymph nodes or lung. Bone scintigraphy is not routinely performed in the diagnosis of testicular cancer. This means that the incidence of bone metastases may be underestimated. In the report by Merrick *et al.*[4], 5 out of 8 GCT patients with bone metastases had seminomas and 6 of these patients died of their disease. The author recommended that all patients with recurrent tumor regardless of the initial stage undergo bone scintigraphy because it can identify patients with a poor prognosis, but he excluded a role for bone scintigraphy at the initial staging of testicular cancer. In our case, PET examination was determinant in finding the site of relapse. Recently, PET has been extensively studied in testicular cancer, particularly in the assessment of recurrent and residual disease. PET can differentiate an active tumor mass from fibrosis, necrosis or mature teratoma with high sensitivity and specificity and can identify the disease earlier in patients with raised marker levels[5]. In our case CT scan and MR imaging demonstrated the regression of the disease in the pelvic soft tissues but were unable to differentiate pelvic bone destruction and remodeling after therapy. The PET examination, on the other hand, was determinant in finding the site of the relapse as well as in demonstrating tumor regression in both the soft tissue and bone sites. Interestingly, the PET infor-

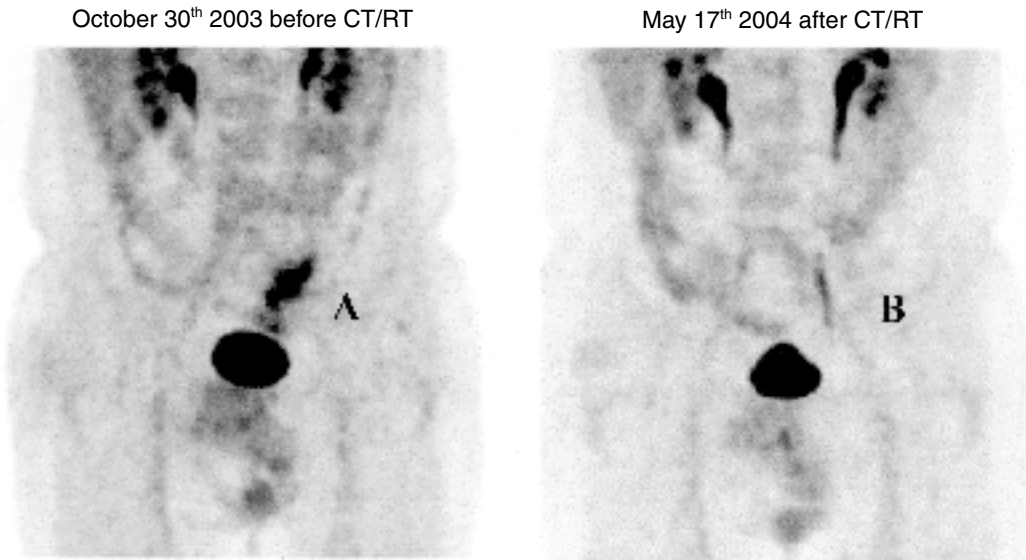

Figure 3 - PET examination showing intense hyperactivity at the left side of the sacrum (A), which disappeared after chemotherapy (B).

mation paralleled the clinical improvement and symptom resolution.

Our case represents a rare and unusual presentation of nonseminomatous GCTs. Only 2 cases of primary bone metastasis in nonseminomatous GCTs have been reported in the literature[6,7]. Interestingly, the pubic bone was the only metastasic site in these cases too. In these cases 2 different schedules of chemotherapy were used to obtain complete remission of the disease. We chose to administer both chemotherapy and radiation therapy to obtain rapid and persistent control of the symptoms a well as function rehabilitation of the right lower limb. Bone metastasis from GCT seems to be chemosensitive and radiosensitive but we do not know their prognostic value. We therefore emphasize the importance of accurate staging for GCTs and recommend that bone scintigraphy be used for symptomatic patients while PET examination could be usefully included among the standard staging procedures.

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