



Unusual Tibial Site Metastases from a Muscle Invasive Urothelial Carcinoma: A Rare Case Report

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Abstract

Bladder cancer is a common malignancy of genitourinary tract with a considerable morbidity and mortality. Muscle invasive urothelial carcinoma is the most common type of cancer especially in ages over 65 years old. Though various metastases have been observed, bone localization is the second site metastases and is appeared in pelvis and spine. We present a case with tibial diaphyseal bone metastases from urothelial carcinoma as a rare manifestation and we review the literature among diagnoses and therapeutic management.

Keywords: *Bladder neoplasm, urothelial carcinoma, bone metastasis, tibia metastasis.*

Introduction

Bladder cancer is the most common type of malignancies in genitourinary tract and appears more often in older ages (over 65 years old), especially in male, predisposed to smoking and environmental factors and increases the propensity of urothelium for future malignant tumors ^[1]. In USA in 2013, an estimated number of 74,690 new cases were diagnosed and there were 15,580 deaths from bladder cancer ^[2]. Urothelial carcinoma is the most usual histologic subtype and accounts to 90% of cases in developed countries ^[3]. Non-muscle invasive Urothelial Carcinoma (U.C.) accounts to 70% of a new bladder cancer diagnosed while a percentage of 20-25% of the tumors appears to invasive in the muscularis propia ^[4]. Approximately 50% of patients with muscle-invasive disease will have a distant recurrence after radical cystectomy ^[5].

Shinagare et al (2010) report that the most common site metastases in U.C, are lymph nodes, bones and lungs ^[6]. The most frequent bone localization site includes the spinal column and the pelvis ^[7]. The aim of this report is to present an unusual bone metastases localization in diaphyseal of left tibia after an urothelial carcinoma and to review the literature among diagnoses and therapeutic management.

Case Report

A 58 year-old man, current smoker, was presented in emergency department with an intermittent pain on medial surface of left tibia. The pain in last three weeks appeared only during walking and

weight bearing while in the last week appeared during the night also and it was resistant in painkillers (paracetamol). The past clinical history of the patient was hypertension and a radical cystectomy 6 months before because of a bladder carcinoma. The biopsy revealed muscular invasive bladder cancer (MIBC), pT3bN0M0. The x-rays showed a lytic lesion of the medial surface of diaphyseal on left tibia. (fig 1(a)-1(b)). Radionuclide whole body bone scan demonstrated intense uptake at this point (tibia), with no other bony infiltration. Due to the lytic lesion of the tibia, which was not typical site metastases from urothelial carcinoma, we decided to do biopsy under computer tomography guidance which revealed metastatic invasion of urothelial cancer. According to Mirel's classification the score was 9 and for this reason we decided to do prophylactic static intramedullary nail of the tibia in order to avoid pathological fracture (fig 2(a)-2(b)). Two days postoperatively the patient started to walk with partial weight bearing and referred an ameliorisation of the past pain. Three weeks postoperatively the patient underwent chemotherapy (cisplatin/gemcitabine) which was administered in combination with lesion radiotherapy. After the administration of 6 cycles of chemotherapy, a disease progression was found and the patient initiated immunotherapy (Pembrolizumab) treatment. In re-examination at two months the patient was pain free and capable to do daily activities. Unfortunately at six months, in routinely medical examination, computer tomography revealed pelvic lymphadenopathy and pulmonary nodules.



Figure 1: Preoperative x- rays AP (a) and oblique (b) show a lytic lesion in diaphyses of left tibia (white arrow)



Figure 2: Postoperative x-rays AP (a) and profile (b) with intramedullary nail

Discussion

Urothelial carcinoma (UC) is the most common type of bladder carcinoma, has variable metastatic potential and almost any organ can be involved in metastasis [6]. The engaged metastases of UC represents a relatively rare but deadly event. However, the median overall survival of patients with metastatic UC, varies from less than 10 to more than 15 months according to the treatment protocol [8]. The most frequent locations of metastasis are lymph nodes, lungs, bones and adrenal glands. Dong F et al, studying 1862 patients with bladder cancer, report that the highest percentage of site metastases occurs in bone(42.9%), lung(38.9%), distant lymph nodes(34.2%) and brain(4.1%) [9]. In another study of 392 cases the most common site of metastases is referred in lymph nodes(69%) followed by bone(47%), lung(37%), liver(26%) and peritoneum (16%) [6].

Bone metastasis is the relatively usual location due to urothelial carcinoma. According to Ramos et al, only 5-15% of

patients with UC have solitary bone metastases and until today neither the prognosis nor the mechanism of development of bone-predominant metastatic from urothelial cancer have been clearly elucidated [10]. Taher et al (2006) suggest that bone site metastases depend on the degree of muscles invasions of the bladder neoplasm [7]. Another study suggests that possible mechanism of bone metastases is the genetic changes of the tumor which is associated with either specific treatment sensitivity or less aggressive disease phenotype [10]. Nathoo et al (2011) postulate that the propensity of bladder cancer to spinal bone metastases is due to anatomical relationship between the urological venous system and the vertebral veins(Batson's plexus) [12]. Concerning the age element, a study shows that patients over 65 years old had a higher frequency of single metastases, referring to bone and this may be indicative of a good prognosis [11]. The most frequent bone metastases location is spine and pelvis. In international bibliography sporadic case reports exist, with other bone metastases locations. Ramos et al (2014) report one case with peripheral bone metastases (in humerus

and in 5th rib sites), while Brennan et al(2013) report a case with a bone metastases at proximal medial tibial plateau [7,10]. Our case seems to be the second case reported in literature with solitary peripheral bone metastases after a UC in diaphyses of tibia.

Patients with bone metastases report extensive pain localized on site metastases, with gradually functional impairment, and increased risk for pathological fracture. While the first imaging examination is radiography, computer tomography (CT) and magnetic reasonable imaging (MRI) are represented as high specificity examination for the diagnosis of the malalignment. Bone scan is an examination with a high level of sensitivity, but presents lower specificity than CT or MRI. Oliver et al(2011) postulate that bone biopsy under CT guidance is the most specified examination, if there is a discrepancy in diagnosis and is an important factor for the therapeutic strategy management of the lesion [13]. In our case only with biopsy under CT/guidance, we confirmed that the tibial lesion was metastases from urothelial carcinoma.

Metastases indicates the advancing disease process while therapeutic management includes pain control, decrease the lesion progress, functional recovery of daily living and reduction of the risk of pathological fractures. Mirel's et al (1989) introduced a score based on lesion site, size, pain, severity and nature of the metastases with scope to decide a prophylactic osteosynthesis of long bones and to avoid the complications of metastatic lesion (fracture). In our case the Mirel's score was 9 and a prophylactic static intramedullary nail was applied to patient.

Conclusion

Bone metastases due to urothelial cancer are very frequent, especially in subtype with muscle invasive cancer. Clinicians in the emergency department must be suspicious that atypical manifestations of bone metastases from urothelial carcinoma could exist in patients who are presented with bone pain and impairment of daily functional activities. In this situations biopsy under CT guidance will determinate the diagnosis promptly. Therefore the goal of treatment of this disease such as interrupting disease process, pain relief, quick recovery and patients returning in daily activities, will be achieved on time.

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