CASE REPORT

Metastatic transitional cell carcinoma of the tibia radiologically mimicking osteosarcoma

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SUMMARY

We report a case of a 73-year-old lady with transitional cell carcinoma and no evidence of metastatic disease presenting with gradual weight loss, pretibial swelling and painful weightbearing. Investigations revealed a lesion of the right tibial diaphysis. The radiological and clinical appearance was that of primary osteosarcoma. Biopsy results revealed metastatic transitional cell carcinoma of the tibia. Intramedullary nailing was performed which relieved pain on weightbearing. The patient declined radiotherapy and was started on a palliative care regimen. This case illustrates the importance of histological diagnosis in the treatment of diaphyseal lesions.

BACKGROUND

Common sites of transitional cell carcinoma (TCC) metastases include regional visceral lymph nodes, liver, lung, bone and adrenal gland.¹ Bony metastases most frequently localise to the pelvis and spine.² However, cases of isolated bony metastases of urothelial origin have been previously reported to the shoulder girdle,³ metatarsus⁴ and tibia.^{5 6} We report a case of a single distant bony metastasis of the tibia associated with TCC.

CASE PRESENTATION

A 73-year-old postmenopausal lady presented in March 2013 with a 6-month history of 10 kg weight loss, progressive pain on weightbearing and symptomatic pretibial swelling of her right tibial midshaft.

A history included hypertension, ex-smoker of 40 pack-years and atrial fibrillation with failed direct current cardioversion and warfarinisation. In 2009, the patient was diagnosed with high-grade non-muscle-invasive TCC (pT1G3). The patient refused radical cystectomy and instead consented to undergo a course of intravesical bacillus Calmette-Guerin. Regular transurethral resections of bladder tumour with deep muscle biopsies were performed to resect multiple non-muscle-invasive lesions. The latest transurethral resection was performed in June 2012 and confirmed similar lesions.

Clinical examination revealed a palpably tender mid-diaphyseal pretibial swelling. The patient was admitted under the medical team and investigated.

INVESTIGATIONS

Haematological investigation revealed a raised C reactive protein of 31 and a normal alkaline phosphatase level.

Standard anteroposterior and lateral radiographs of the right tibia showed an ill-defined mixed lytic and blastic lesion of the diaphyseal medulla with cortical and soft-tissue involvement (figure 1). CT of the thorax, abdomen, pelvis showed locally advanced bladder carcinoma with multifocal lesions protruding into the bladder lumen, but no pulmonary or abdominal metastases. A full-body isotope bone scan revealed extensive uptake in the right tibia (figure 2). MRI of the tibia showed a diaphyseal lesion 6 cm in craniocaudal length centred 12 cm proximal to the tibiotalar joint (figure 3). Radiologically, the appearances were in keeping with primary osteosarcoma.

A trephine bone biopsy was performed which revealed metastatic papillary-type carcinoma of urothelial origin (figure 4). The biopsy stained positive for TCC-specific markers CK7 and CK20 (figure 5), in addition to p63 and markers of epithelial differentiation CK AE1/AE3. The lesion scored 10 according to the Mirels scoring system.⁷

DIFFERENTIAL DIAGNOSIS

- ▶ Primary diagnosis: Metastatic disease.
- ▶ Secondary diagnosis: Osteosarcoma, osteomyelitis, lymphoma.

Figure 1 Standard lateral and anteroposterior radiographs of the right tibia showing an ill-defined mixed lytic and blastic lesion in the diaphyseal medulla with cortical and soft tissue involvement (arrows).

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Figure 2 Standard blood pool (top) and delayed (bottom) bone scan images of the right tibia at 3 h were acquired after the injection of 700 MBq (18 mCi) of Tc-99 m Oxidronate (HDP). There was prominent nearhomogenous, intense, generalised uptake in the early blood pool as well as delayed images of the mid right tibia.

TREATMENT

Intramedullary nailing was performed with good symptomatic relief. Histological analysis of reamings confirmed the diagnosis of metastatic disease.

OUTCOME AND FOLLOW-UP

The patient was followed up for 4 months and returned to full weightbearing mobilisation. The patient declined chemoradiotherapy for her tibial lesion and was started on a palliative care regimen.

Figure 3 Coronal (A) and axial (B) T2-weighted MR images of the right tibia demonstrating an intramedullary mass of heterogeneous signal intensity with cortical bony destruction and extension into the anterior tibial compartment. Findings were in keeping with osteosarcoma and bony metastases of the right tibial diaphysis.

Figure 4 The metastasis stained with H&E 100× magnification showing a high-grade transitional cell carcinoma invading the haversian systems of the tibial diaphysis.

Figure 5 The metastasis stained with cytokeratin 20 of 400× magnification showing a moderate and distinct cytoplasmic staining reaction in the majority of the neoplastic cells.

DISCUSSION

High-grade intramedullary osteosarcomas typically affect the metaphysis of long bones in the second decade of life, with the knee being affected in approximately 50% of cases.⁸ In patients over the age of 40, osteosarcomas tend to occur in atypical areas such as axial bones.

The differentiation between metastatic disease and osteosarcoma is particularly important in terms of surgical management. In lower extremity osteosarcoma, amputation may be performed to achieve local control of disease progression. Alternatively, limb-salvage procedures may be performed when adequate resection margins have been achieved with the use of various reconstruction techniques, such as arthrodesis, allografting or arthroplasty.⁹

Operative treatment of osseous metastases is indicated primarily to alleviate pain, to treat impending or actual pathological fracture and to maintain the patient's ability to walk by providing functional stability. Because pathological fractures are devastating and prophylactic surgical treatment has been shown to improve outcomes,¹⁰ Mirels⁷ devised a scoring system to quantify the risk of pathological fracture in the extremity based on degree of pain, lesional size, lytic versus blastic nature and anatomic location. Mirels recommended operative treatment in patients with a score of 10 or more.

At radiographic examination, bony metastases of urothelial origin have previously been described as extensive lytic destruction with cortical involvement and heterotopic bone formation in the adjacent soft tissues.⁵ An osteoblastic or mixed osteolytic-osteoblastic pattern of skeletal involvement has also been described.¹¹ In this case study, the lesion has the radiological features of a high-grade intramedullary osteosarcoma. These lesions have a rapid doubling time (20–30 days) and are often large (>6 cm) at the time of diagnosis. Other features include cloud-like opacities within the lesion, with mixed sclerotic and lucent areas characteristic of osteoid matrix production. Osteosarcomas of this nature have a growth pattern that tends to breach the cortex without expanding the osseous contours, and have an aggressive periosteal reaction (Codman triangle, laminated, hair-on-end or sunburst pattern) with associated soft tissue masses.¹²

In this case, the clinical staging of non-muscle-invasive TCC in June 2012 differs from the locally advanced and metastatic disease observed 9 months post-transurethral biopsy. It is unclear whether this is due to a clinical staging error or disease progression.

Significant clinical staging errors involving T1 tumours have been reported to occur in 24–62% of cases.^{13–18} To improve clinical staging and ensure complete resection of visible disease, repeat transurethral biopsy 4–6 weeks following the initial biopsy¹⁹ and early radical cystectomy¹³ have been proposed.

Learning points

- ▶ The diagnosis of metastases is difficult as radiological findings mimic other pathologies.
- ▶ Accurate histological diagnosis is necessary to plan treatment of diaphyseal lesions.
- ▶ Intramedullary nailing may relieve pain and maintain the patient's ability to walk in the treatment of tibial metastases by providing functional stability.

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Contributors LPC produced the manuscript and prepared the histological figure. BJO edited the initial manuscript and prepared the radiological figures. JFQ edited the second draft of the manuscript and was the consultant responsible for the care of the patient. All three authors were involved in the surgical procedure and aftercare of the patient.

Competing interests None.

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REFERENCES

- 1 Braendengen M, Winderen M, Fossa SD. Clinical significance of routine pre-cystectomy bone scans in patients with muscle-invasive bladder cancer. *Br J Urol* 1996;77:36–40.
- 2 Sengelov L, Kamby C, von der Maase H. Pattern of metastases in relation to characteristics of primary tumor and treatment in patients with disseminated urothelial carcinoma. *J Urol* 1996;155:111–14.
- 3 Weizer AZ, Shariat SF, Haddad JL, et al. Metastatic transitional cell carcinoma of the urinary bladder to the shoulder girdle. *Rev Urol* 2002;4:97–9.
- 4 Petkovic M, Muhvic D, Zamolo G, et al. Metatarsal metastasis from transitional cell cancer of the urinary bladder. *Coll Antropol* 2004;28:337–41.
- 5 Chinn D, Genant HK, Quivey JM, et al. Heterotopic bone formation in metastatic tumor from transitional-cell carcinoma of the urinary bladder. A case report. *J Bone Joint Surg Am* 1976;58:881–3.
- 6 Evison G, Pizey N, Roylance J. Bone formation associated with osseous metastases from bladder carcinoma. *Clin Radiol* 1981;32:303–9.
- 7 Mirels H. Metastatic disease in long bones. A proposed scoring system for diagnosing impending pathologic fractures. *Clin Orthop Relat Res* 1989;256–64.
- 8 Unni KK. Osteosarcoma. In: Unni K, Dahlin D, eds. *Dahlin's bone tumors: general aspects and data on 11,087 cases*. Philadelphia: Lippincott-Raven, 1996:143–83.
- 9 Simon MA, Aschliman MA, Thomas N, et al. Limb-salvage treatment versus amputation for osteosarcoma of the distal end of the femur. *J Bone Joint Surg Am* 1986;68:1331–7.
- 10 Hardman PD, Robb JE, Kerr GR, et al. The value of internal fixation and radiotherapy in the management of upper and lower limb bone metastases. *Clin Oncol (R Coll Radiol)* 1992;4:244–8.
- 11 Goldman S. Metastatic transitional cell carcinoma from the bladder: radiographic manifestations. *AJR Am J Roentgenol* 1979;132:419–25.
- 12 Mirra J. Osseous tumors of intramedullary origin. In: Mirra J, Picci P, Gold R, eds. *Bone tumors: clinical, radiologic, and pathologic correlations*. Philadelphia: Lea & Febiger, 1989:248–438.
- 13 Stein JP, Lieskovsky G, Cote R, et al. Radical cystectomy in the treatment of invasive bladder cancer: long-term results in 1,054 patients. *J Clin Oncol* 2001;19:666–75.
- 14 Soloway MS, Lopez AE, Patel J, et al. Results of radical cystectomy for transitional cell carcinoma of the bladder and the effect of chemotherapy. *Cancer* 1994;73:1926–31.
- 15 Pagano F, Bassi P, Galetti TP, et al. Results of contemporary radical cystectomy for invasive bladder cancer: a clinicopathological study with an emphasis on the inadequacy of the tumor, nodes and metastases classification. *J Urol* 1991;145:45–50.

- 16 Freeman JA, Esrig D, Stein JP, *et al.* Radical cystectomy for high risk patients with superficial bladder cancer in the era of orthotopic urinary reconstruction. *Cancer* 1995;76:833–9.
- 17 Amling CL, Thrasher JB, Frazier HA, *et al.* Radical cystectomy for stages Ta, Tis and T1 transitional cell carcinoma of the bladder. *J Urol* 1994;151:31–5; discussion 5–6.
- 18 Yiou R, Patard JJ, Benhard H, *et al.* Outcome of radical cystectomy for bladder cancer according to the disease type at presentation. *BJU Int* 2002;89:374–8.
- 19 Herr HW. Surgical factors in the treatment of superficial and invasive bladder cancer. *Urol Clin North Am* 2005;32:157–64.

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