Case Report

Primary Squamous Cell Carcinoma of a Tarsal Bone

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Abstract We describe a rare case of primary squamous cell carcinoma of the cuneiform bone of the foot in a 57-year-old man. In the appendicular skeleton, epithelial carcinomas of bone are usually metastatic deposits, primary squamous cell carcinomas of bone being found more frequently in the skull. A review of the English literature revealed only two other reported cases of primary squamous cell carcinoma outside the skull—one in the ilium and one in the tibia. In our patient, extensive metastatic

workup and monitoring during more than 2 years showed no primary focus, supporting the rare presentation of a primary squamous cell carcinoma of bone in the appendicular skeleton.

Introduction

Primary squamous cell carcinoma of bone is rare in the skeletal system other than in the skull, with only two such cases reported in the English literature [1, 3]. This is attributed to the absence of native squamous epithelium in bones. The majority of these carcinomas when found in the extremities are metastatic from another primary. In 1997, Gangopadhyay and Saha [3] reported a case of a primary squamous cell carcinoma of the left iliac bone, and in 2003, Abbas et al. [1] reported the case of a patient with a primary squamous cell carcinoma of the distal tibia. A followup of 10 months was reported in the first case, whereas there was no mention of followup in the second case. We report a case of a primary squamous cell carcinoma of a tarsal bone in which all examinations and a followup of 26 months have ruled out metastasis.

Case Report

A 57-year-old male judge first experienced nonspecific left foot pains after prolonged standing and ambulation. There was no history of antecedent trauma. Radiographs taken on consultation with an orthopaedic surgeon 4 months later showed a lytic lesion in the proximal third of the first cuneiform. The lesion had geographic borders with an intact bony cortex (Fig. 1A). The patient underwent curettage and iliac crest bone grafting. Osteoblastoma was

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Each author certifies that his or her institution has approved the reporting of this case report, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

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Fig. 1A–B (A) A radiograph shows the foot on initial presentation. (B) A preoperative radiograph shows the foot now with involvement of the entire first cuneiform.

diagnosed on histopathology and the patient was referred to our institution for further management.

On initial examination, there was diffuse swelling over the medial aspect of the left foot underlying the healed surgical incision. Repeat radiographs revealed an even larger lytic lesion now involving the entire first cuneiform, with permeative borders and without a matrix (Fig. 1B). MRI showed a heterogeneously contrast-enhancing mass with cystic changes involving the entire first cuneiform, hyperintense on T2-weighted images, with cortical breaks and a rim of enhancing soft tissue around the surrounding joints (Fig. 2). Differential diagnoses on review of histology slides from the initial operation included an aggressive osteoblastoma or an osteoblastic osteosarcoma, although the latter differential was considered unlikely because of the patient's age and the location of the lesion. A decision was made to excise the entire mass with margins adequate for a malignant tumor. No other lesions were detected on the chest CT scan and total-body bone scan.

The patient underwent wide excision of the first cuneiform mass and reconstruction of the resulting defect with interosseous wiring of an iliac crest autograft (Fig. 3). Surgical margins included the distal third of the navicular proximally, the lateral third of the second cuneiform and second metatarsal laterally, and the proximal third of the first metatarsal distally. The gross specimen measured $4.5 \times 2 \times 2$ cm, and the lesion within was a brown ovoid hard mass, cream-white and soft on cross section, originating from the first cuneiform. No connection to the epidermis was identified. Histologic examination showed sheets of malignant squamous cells. There were also foci of well-differentiated malignant squamous cells producing

Fig. 2 A T2-weighted MR image shows a heterogeneously contrast-enhancing soft tissue mass with cystic changes involving the entire cuneiform, with cortical break and rim of enhancing soft tissue.

keratin pearls with remnants of normal bone and reactive bone along the periphery (Figs. 4, 5). On immunohistochemical analysis, the tumor cells were positive for cytokeratin and nonreactive to vimentin (Fig. 6). The final histopathologic diagnosis was poorly differentiated squamous cell carcinoma of the first cuneiform bone. Considering the infrequency of this histology, slides were sent for a second opinion to the Mayo Clinic, Rochester, MN, where a similar interpretation was given.

At the same time, imaging was obtained to rule out the cuneiform lesion as a metastatic deposit. MRI of the abdomen and pelvis (to rule out bladder carcinoma); CT of the chest (lung carcinoma), head, and neck (esophageal and nasopharyngeal carcinoma); total-body bone scan; and

Fig. 3 A postoperative radiograph shows reconstruction with iliac crest autograft and interosseous wiring.

Fig. 4 A photomicrograph shows sheets of malignant squamous cells with keratin pearls (KP) and remnants of bone (B) along the periphery (Stain, hematoxylin and eosin; original magnification, $\times 100$).

referrals to an otorhinolaryngologist and a gastroenterologist showed no other lesions or signs of a possible primary. The diagnostic tests were repeated every 3 to 6 months.

Twenty-six months later, the patient remains disease free. A CT scan of the chest obtained at the 2-year followup was normal. The bony reconstruction has healed,

Fig. 5 A photomicrograph shows a keratin pearl typical of squamous cell carcinoma (Stain, hematoxylin and eosin; original magnification, $\times 400$).

Fig. 6A–B (A) Immunohistostaining with cyokeratin shows an intense reaction of tumor cells (Stain, cyokeratin; original magnification, $\times 400$). (B) The tumor cells had a negative reaction for vimentin (Stain, vimentin; original magnification, $\times 400$).

and the patient is able to ambulate with a cane. He has returned to work as a judge and continues to see us regularly for followup.

Discussion

Primary squamous cell carcinoma of bone usually is reported in the skull; it is rare elsewhere in the skeleton. A MEDLINE search from 1970 to 2008 with keywords “squamous cell carcinoma/cancer” and “bone/skeleton” listed only two cases outside the skull. The first report was of a case in the left iliac bone of a 20-year-old woman [3]. Extensive workup revealed no other foci of malignancy. Histologic analysis showed infiltration of bone tissue by malignant squamous cells with pearl formation. Treatment consisted of radiotherapy alone, as the tumor was deemed inoperable. The patient reportedly was in complete remission 10 months after treatment. The second case was in the distal tibia [1]. A 47-year-old woman had a well-differentiated squamous cell carcinoma apparently arising from malignant transformation of a preexisting epidermoid cyst in the distal tibia. The patient underwent a below-knee amputation, but no mention was made of metastatic workup and further followup. The authors remarked about the difficulty of relying on radiology and histology for the diagnosis and that a primary tumor elsewhere must be excluded.

In contrast, primary squamous cell carcinoma of bone of the head and neck region is much more common and has been reported in the maxilla [2, 15], mandible [4, 5, 10, 11], and temporal bone [7]. Squamous cell carcinoma in these bones has been theorized to arise *de novo* from epithelial remnants or from malignant transformation of epithelial lining of cysts commonly found in the substance of these bones [4, 5, 10, 11, 15]. Although rare, these cysts also may be found in bones of the appendicular skeleton, giving rise to the possibility of intraosseous epithelial carcinomas [1].

The occurrence of an epithelial carcinoma of bone in our patient probably can be explained by a similar pathology. Adamantinomas of the appendicular skeleton are uncommon primary bone tumors with epithelial lineage [8, 9]. Epithelial tumors are postulated to originate either *de novo* from aberrant epithelial cells in the bone substance or from traumatic inclusion of skin fragments with eventual malignant transformation [8, 9, 12]. The former is highly unlikely and mostly has been discarded as a possible explanation. The theory of traumatic inclusion of epithelial cells in the subperiosteal layer was described by Ryrie in 1932 [13] and is supported by the association of adamantinomas with a history of antecedent trauma and the fact that a majority of these tumors originate from the

anterior tibia [8, 9]. Ryrie further theorized shearing forces applied to bones with a superficial edge exposed to trauma (ie, the anteromedial surface of the tibia) could seed epithelial cells from the dermal layers and skin appendages into the lacerated periosteum, and in a process he describes as “thwarted repair,” these epithelial cells could undergo constantly frustrated reparative hyperplasia, eventually undergoing neoplasia [13].

Although our patient could not recall any specific episode of antecedent trauma, the subcutaneous location of the first cuneiform in an area exposed to shearing forces fits this profile.

The interpretation of osteoblastoma or osteosarcoma from the first surgery could be explained by a sampling of reactive bone from a superficial area of the lesion. However, monophasic epithelial synovial sarcoma was considered unlikely owing to the primarily intraosseous nature of the lesion, with minimal soft tissue involvement around the bone and in the surrounding joints. Furthermore there was an absence of glandular differentiation as might be expected of biphasic synovial sarcoma.

Although skeletal metastases occur in 20% to 30% of patients with malignancies, metastases to the foot and hand are uncommon (0.007%–0.3%), with foot metastases reported at only 1/2 to 1/3 the rate in the hand [6]. Furthermore, metastatic lesions in the hands and feet usually are associated with diffuse tumor spread and a grave prognosis, with a reported mean survival of 0.9 to 14 months after diagnosis [6, 14]. In our patient, the solitary lesion, extensive workup for a possible primary source, and the 26-month disease-free followup support our final diagnosis of a primary squamous cell carcinoma of bone.

Our case report shows the need to be vigilant in pursuing the histology of the lesion and the risks of automatically assuming a diagnosis of metastasis. It is important to exhaust all available diagnostic means and have an adequate followup to rule out metastasis.

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