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CASE REPORT

Osteoblastoma of the clavicle at the site of a previous fracture—first case report and review of the literature

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Abstract

Osteoblastoma is a rare, benign primary tumor of bone, accounting for < 1% of all bone tumors. We report the case of a 27-year-old female who developed pain and swelling five and a half years after a clavicular fracture and was subsequently found to have an osteoblastoma arising at the fracture site. This is the first reported case of an osteoblastoma developing after a fracture, although osteoid osteomas, which are histologically indistinguishable from osteoblastomas, have been reported at prior fracture sites. This report demonstrates that secondary neoplasms such as osteoblastomas should be considered in the differential diagnosis for pain at a healed fracture site recurring years after the initial trauma.

Keywords Osteoblastoma · Bone tumor · Trauma

Introduction

A causative association between trauma and the development of bone tumors has been the subject of speculation, although never proven [1, 2]. There have been a number of case reports in which bone tumors occurred following trauma. Osteochondromas have been reported in a variety of anatomical locations following surgery and after Salter–Harris fractures [3–6]. The subungual exostosis, a closely related lesion, is commonly ascribed to trauma [7]. Osteoid osteomas have also been reported after fractures many times [8–16].

Osteoblastoma is a rare, benign primary tumor of bone. Although in the most recent WHO classification of tumors of soft tissue and bone, osteoblastoma and osteoid osteoma are listed as separate entities, these benign bone tumors can be histologically indistinguishable [17]. The distinction between osteoblastoma and osteoid osteoma is essentially based on radiological and clinical differences. However, the differential diagnosis is sometimes difficult [18].

To our knowledge, there are no previous reports in the literature of an osteoblastoma occurring at the site of trauma. We report the case of a 27-year-old female who developed an osteoblastoma at the site of a clavicle fracture five and a half years later.

Case report

A 27-year-old female sustained a displaced, traumatic fracture of the middle third of the clavicle as the result of a snowmobiling accident. Radiographs taken at the time of injury (Fig. 1) showed no evidence of a pre-existing lesion at the site. The fracture was treated by open reduction and internal fixation using a plate and screws. The patient was able to return to her normal activities, including resistance training, one and a half years after the injury.

Pain recurred at the fracture site two and a half years after the initial trauma. Radiographs obtained at this time demonstrated complete healing of the fracture. There was no evidence of an underlying bone lesion (Fig. 2). The pain persisted for 6 months. It was thought to be secondary to the hardware, and consequently the plate was removed. Radiographs

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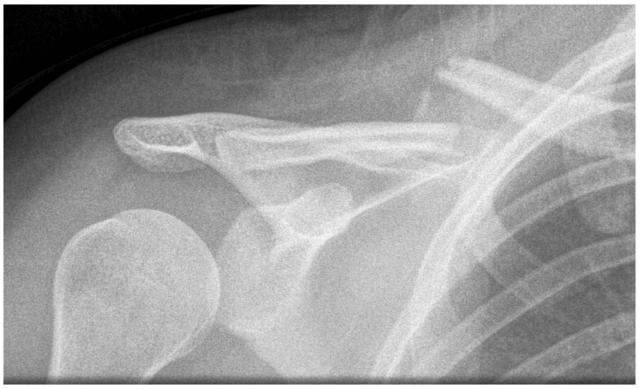

Fig. 1 Anteroposterior (AP) radiograph demonstrating a fracture of the right clavicle middle third. There is no radiographic evidence of an underlying lesion or other evidence to suggest that this is a pathologic fracture

obtained after hardware removal again demonstrated a healed fracture without evidence of an underlying osseous lesion (Fig. 3).

Despite plate removal, the patients' symptoms persisted and progressively worsened over time. She developed pain radiating to her neck and right arm. Five years after the initial trauma, she also began to develop weakness in her right arm, and therefore she was referred to thoracic surgery to evaluate for thoracic outlet syndrome. At the time of the consultation, she had also noticed a bulge in the soft tissues about the midportion of her right clavicle. She did not have fever, chills, or drainage from the area and had otherwise excellent health. On the physical exam, there was good healing of incisions. Physical examination confirmed "fullness" of the right midclavicle, which was also exquisitely tender to light palpation. The overlying skin appeared normal and there was no frank neurovascular or neuromotor deficit in the right upper extremity.

Computerized tomography of the chest showed a solitary lucent lesion at the site of the previous right clavicle fracture (Fig. 4). The lesion expanded the contours of the bone. It

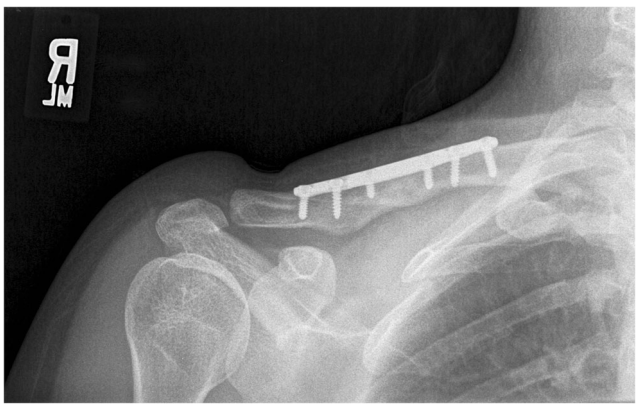

Fig. 2 Anteroposterior (AP) radiograph of the right clavicle two and a half years after internal fixation shows healing of the fracture without evidence of an underlying osseous lesion. The hardware is intact

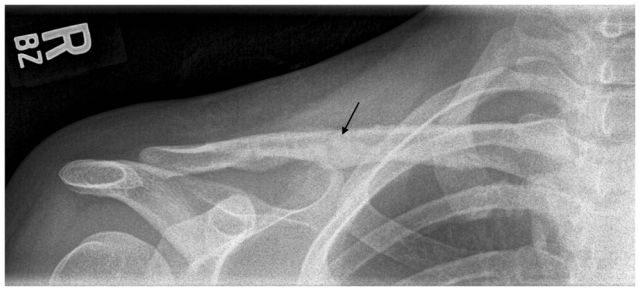

Fig. 3 Anteroposterior (AP) radiograph of the right clavicle after removal of the hardware, 3 years after the fracture. The site of the previous fracture (*arrow*) is healed and no osseous lesion is seen

measured 3.4 (AP) × 3.0 (TV) × 2.8 (SI) cm, and was well defined with a thin sclerotic rim. It contained small foci of internal ossification. MRI demonstrated a lobulated lesion centered in the mid portion of the right clavicle with heterogeneous hypointense signal on T1-weighted images and hyperintense signal on T2-weighted images (Fig. 5). Small foci of hypointensity were seen in all sequences, corresponding to the ossified matrix noted on CT. In addition, there was diffuse enhancement after administration of intravenous contrast. There was mild surrounding fat stranding but no extraosseous soft tissue mass. The surrounding bone did not show significant edema or periostitis.

The patient underwent CT-guided needle biopsy. Histopathologic examination showed features of a benign bone-forming tumor with haphazard arrangements of woven bone rimmed by plump osteoblasts and occasional multinucleated osteoclasts. By immunohistochemistry the tumor cells were strongly positive for SATB2, consistent with osteogenic differentiation (Fig. 6). These findings were compatible with osteoblastoma.

Subsequently, the patient underwent right clavicular curettage and allograft packing (Fig. 7). The surgical pathology once again showed a benign bone forming tumor exhibiting prominent woven bone formation and intertrabecular spaces filled with a loose fibrovascular connective tissue. There was no cytologic atypia, tumor necrosis, or infiltrating growth pattern, confirming the diagnosis of osteoblastoma (Fig. 8).

After the surgical procedure, the patient reported complete relief of the symptoms and was able to return to her normal activities, including physical training.

Discussion

To the best of our knowledge, this is the first report of an osteoblastoma arising at the site of a previous fracture.

Although the development of a rare tumor directly at the site of a previous fracture may be coincidental, several unusual features of this case may suggest that there is more than a chance association.

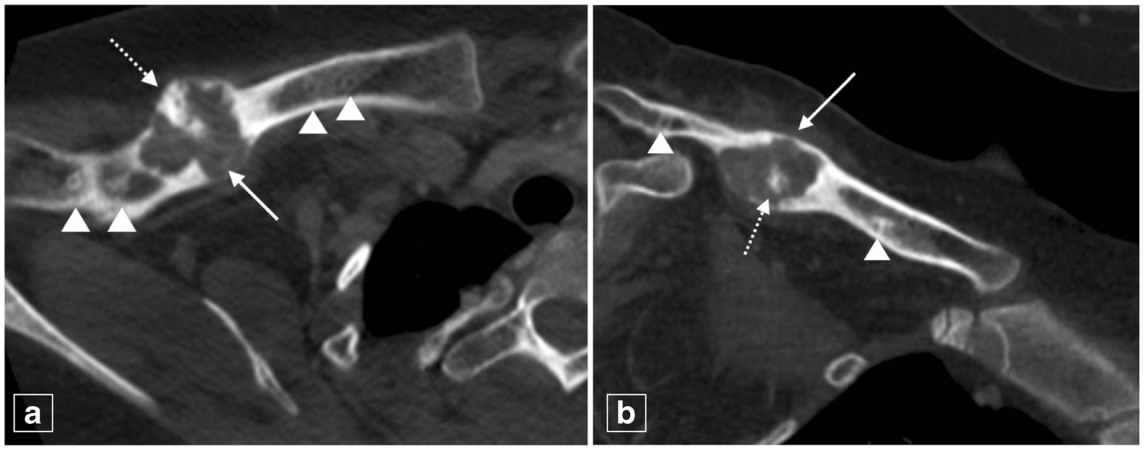

Fig. 4 Axial (**a**) and coronal (**b**) reformats of a chest CT, which included the clavicle 5 years after the initial trauma showing a well-defined expansile lytic lesion (*solid arrows*) with small foci of internal osteoid matrix (*dashed arrows*) in the middle third of the right clavicle, corresponding to the site of the previous fracture. The location of the screws for fixation of the fracture is also seen (*arrowheads*)

Osteoblastomas are rare tumors, accounting for < 1% of all bone tumors [19]. Although our patient was female, males are significantly more likely to develop osteoblastomas than females (ratio of 2:1). Most patients with osteoblastoma are diagnosed in the second decade of life [20], while our patient was 27 at the time the tumor was diagnosed. Most osteoblastomas affect the spine (33%), particularly the posterior elements of the vertebral column. The next most common site is the metaphysis of the long bones of the extremities [21]. The mid clavicle is a distinctly unusual location for the development of an osteoblastoma.

Histologic differentiation between osteoid osteoma and osteoblastoma can be very difficult or even impossible. This is because both lesions are composed of reactive-appearing woven bone with intermixed benign-appearing osteoblasts [18, 22]. Although histologically similar, the two types of

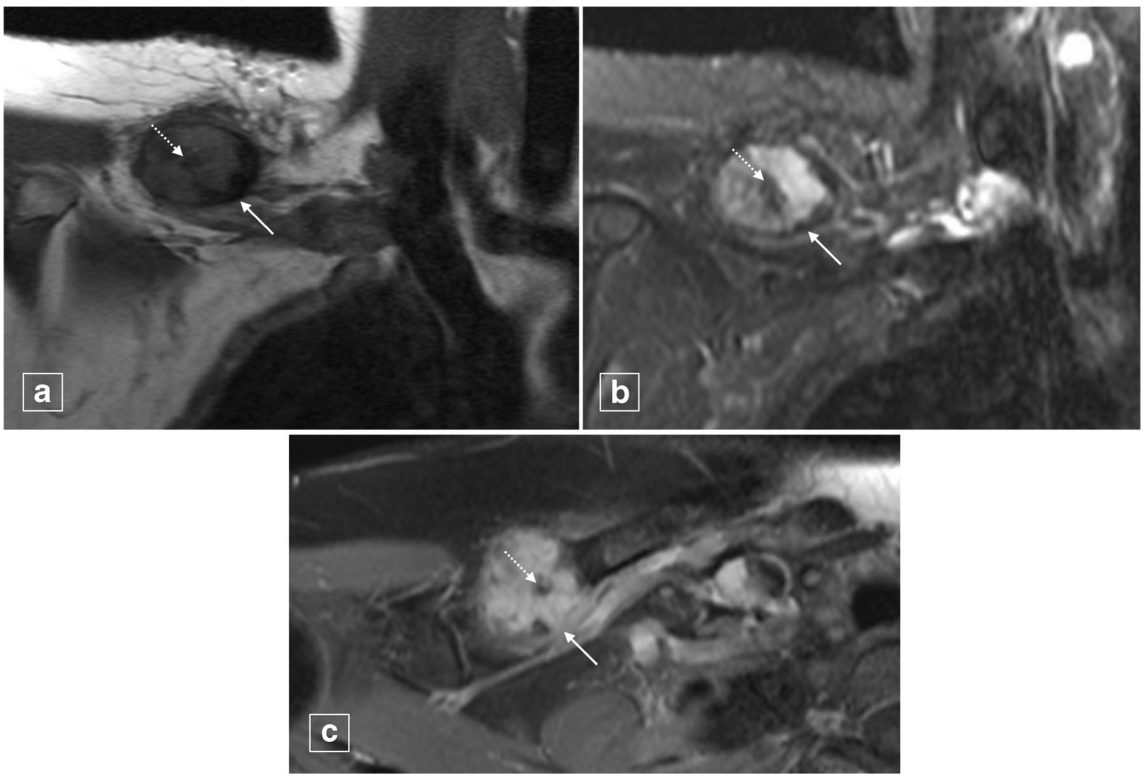

Fig. 5 MRI demonstrating an expansile and lobulated lesion (*solid arrows*) centered in the right mid clavicle with heterogeneous hypointense signal on T1-weighted images (**a**) and hyperintense signal T2-weighted images (**b**). After intravenous gadolinium administration (**c**), diffuse enhancement is seen. Small rounded foci that were hypointense on all sequences (*dashed arrows*) corresponding to the ossified matrix seen on CT

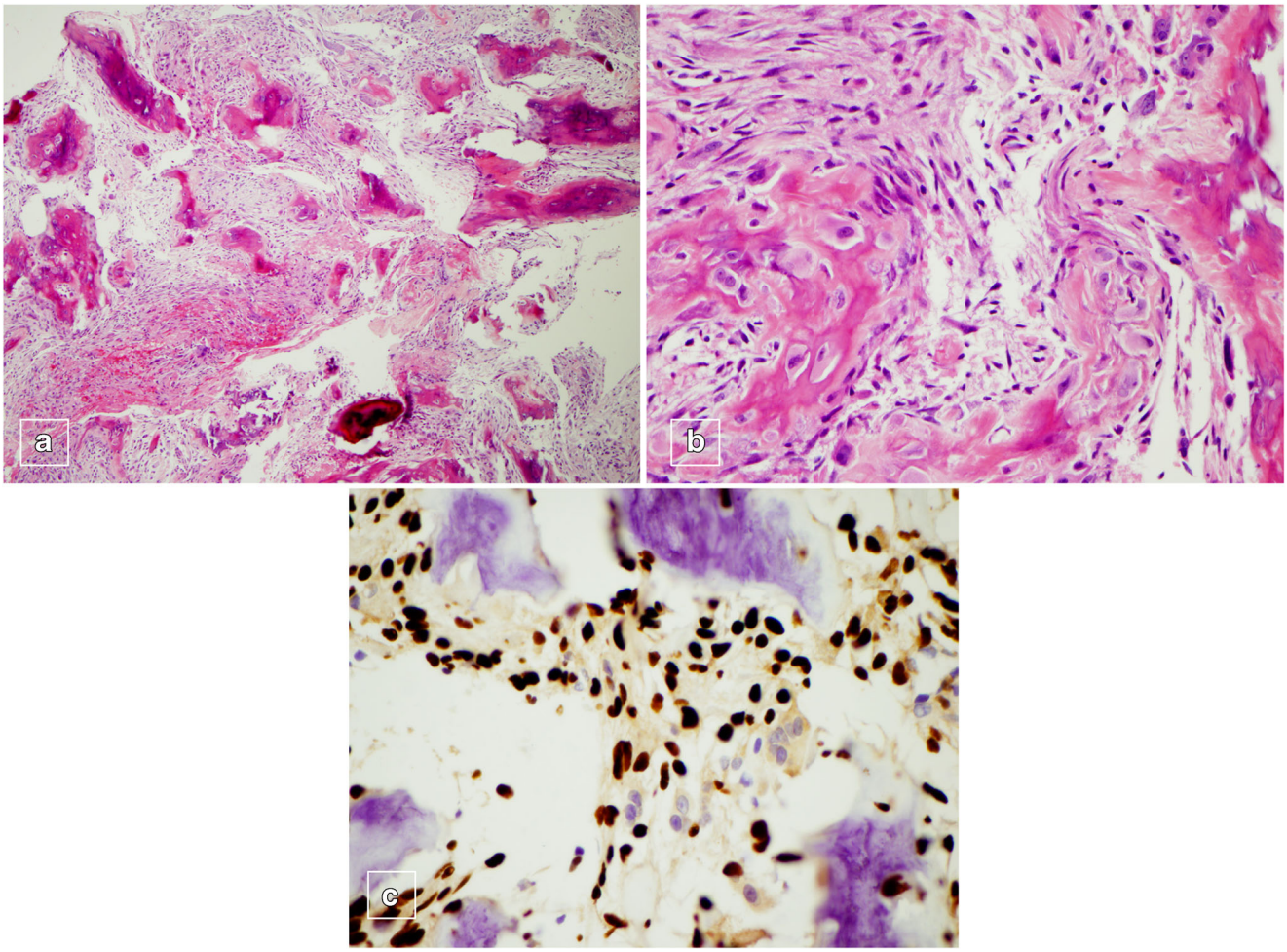

Fig. 6 Core needle biopsy (**a**) showing fragments of reactive appearing woven bone with intervening fibrous stroma (20× magnification). High-power view of core needle biopsy (**b**) showing reactive bone embedded in a fibrous stroma with admixed plump epithelioid osteoblasts and rare osteoclast (40× magnification). Osteoblast nuclei stained strongly for SATB2 immunohistochemistry within osteoblastic cells (**c**). These findings were consistent with osteoblastoma

lesions are usually distinguished by clinicopathological criteria, symptoms, skeletal location, and radiographic features [18].

Clinically, osteoblastomas do not cause the intense night pain associated with osteoid osteomas, which usually respond to aspirin to various degrees. However, osteoblastoma of the spine may have symptoms and signs similar to those of osteoid osteomas, including back pain and scoliosis [18, 23, 24].

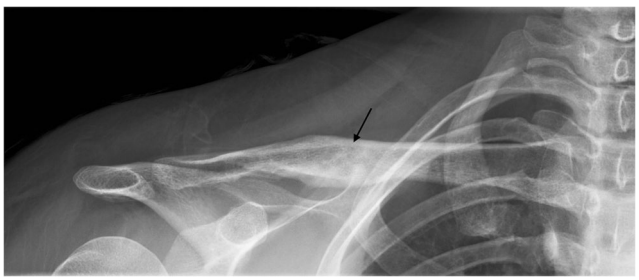

Fig. 7 AP radiograph of the right clavicle showing the result of the curettage and allograft packing (*arrow*)

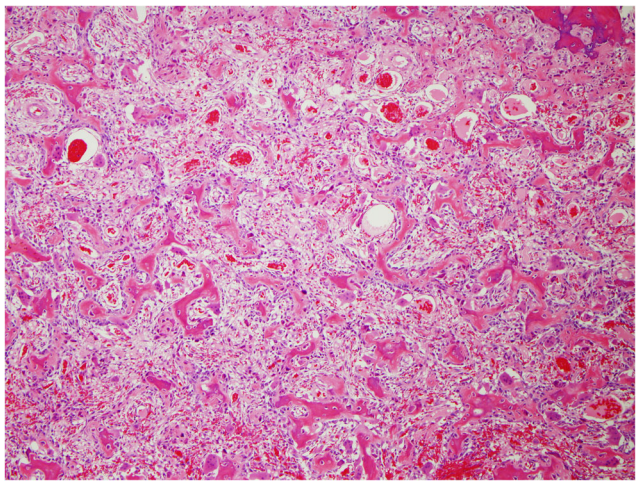

Fig. 8 Low-power view of the curettage material showing prominent reactive-appearing woven bone embedded rimmed by osteoblastic cells with a prominent loose fibrovascular stroma, consistent with osteoblastoma

Radiographically, osteoblastoma often presents as a well-defined, mixed lytic and blastic mass with sclerotic margins, and may cause bone expansion. CT and MRI imaging usually show a well-circumscribed heterogeneous mass that may have cystic components and is surrounded by edema and reactive bone. Some osteoblastomas are large and have poorly defined margins, resembling a more aggressive tumor. Osteoid osteomas are usually round to oval and have a targetoid appearance. CT shows a well-circumscribed, lucent mass with central mineralization (nidus) that is usually surrounded by a zone of sclerosis. Important surrounding bone marrow edema can be seen on fluid-sensitive MRI sequences [25].

Because of the histological similarities, osteoid osteoma and osteoblastoma are sometimes distinguished by size, with tumors larger than 15–20 mm classified as osteoblastomas and tumors smaller than that classified as osteoid osteomas [26]. These size criteria, however, are merely guidelines for trying to predict the biological behavior of these lesions; with smaller lesions having a lower chance of progression. Reports exist in which the behavior of the lesions does not conform to expectations based upon size [27, 28]. The recent finding of *FOS* and *FOSB* rearrangements in both of these tumors suggests that they are similar at a molecular level and may represent a spectrum of the same biologic process [26].

We have found nine cases of histology-proven osteoid osteomas occurring in a previous fracture site. The time between the occurrence of the fracture and the diagnosis of the tumor ranged between 2 and 12 years [8–16]. Two cases occurred following non-operative treatment [8, 9] and seven cases followed internal fixation [10–16].

All the cases followed a clinical course similar to our patient, with recurrent or persistent pain after the initial trauma and complete recovery after removal of the osteoid osteoma. Adil et al. suggested that perhaps the osteoid osteoma was caused by a periosteal invagination at the time of reduction and fixation of the fracture [15], although such a mechanism cannot be implicated in the great majority of osteoid osteomas.

Most current thinking concerning the pathogenesis of neoplasia expects a genetic basis. It is highly likely that osteoblastoma will be found to fit this pattern. Until very recently, no consistent genetic aberrations were known to be associated with osteoblastoma. However, recent work has shown that deletions from chromosome 22 may be seen in the aggressive variants of osteoblastoma [29]. Even more recently, recurrent rearrangements of *FOS* and *FOSB* oncogenes have been implicated in the development of both osteoblastomas and osteoid osteomas and a subset of vascular tumors, suggesting possible shared developmental pathways [26].

However, the presence of a genetic alteration does not necessarily completely eliminate the possibility that trauma could play a supporting role in pathogenesis. Given the number of reported cases of osteoid osteoma, and now this case of osteoblastoma arising in association with a prior fracture site, we believe that it is possible that trauma may facilitate or potentiate the neoplastic transformation.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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