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CASE REPORT

Intraosseous hibernoma of the appendicular skeleton

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Abstract
Hibernomas are rare lipomatous tumors composed of brown adipocytes. The relative paucity of reported cases involving the bones accounts for the poor understanding of this entity, which is known to affect almost exclusively the axial skeleton. We present a case of intraosseous hibernoma of the humerus, which was found incidentally in a 52-year-old woman and initially misinterpreted as a cartilaginous tumor on magnetic resonance imaging (MRI). The lesion was unchanged in size and morphology at short interval follow-up but increased in size during follow-up over 6 years with an 11 mm increase in the largest diameter. Given the patient's concerns and lesion growth, curettage was performed. Pathology analysis revealed brown fat in keeping with the diagnosis of intraosseous hibernoma. Radiological and pathological findings and pitfalls are herein highlighted to enforce knowledge on this lesion rarely affecting the long bones. Radiologists should think of intraosseous hibernoma if they come across a sclerotic lesion on X-ray or computed tomography, which contains macroscopic fat and shows enhancement on contrast-enhanced MRI. In addition, an intraosseous hibernoma may be picked up incidentally on positron emission tomography-computed tomography due to high fluorodeoxyglucose avidity.

Keywords Brown fat · Lipomatous lesion · Hibernoma · Magnetic resonance imaging

Introduction

Hibernomas are rare lipomatous tumors composed of brown adipocytes. They are uncommon in comparison with lipomas, which are composed of white adipocytes, and mainly found in soft-tissues with the thigh being the most common location [1]. Intraosseous hibernoma was first reported in 2008 and, to date, thirty-three cases have been described in case reports and case series [2]. This relative paucity of reported cases accounts for the poor understanding of this entity, which is known to affect almost exclusively the axial skeleton [2]. However, hibernoma may occur in the appendicular skeleton and very few cases involving the femur have been reported to date. We present a case of hibernoma located in the humerus, which was initially interpreted as a cartilaginous lesion based on location, patient's age, and magnetic resonance imaging (MRI) features. Imaging follow-up was performed and demonstrated that intraosseous hibernoma may grow slowly over time. Thus, radiological and pathological findings and pitfalls are herein highlighted to enforce knowledge on this lesion rarely affecting the long bones.

Case report

Consent for publication was obtained for the individual person's data included in the study. A 52-year-old woman was referred to our institution as an outside consult case after shoulder non-contrast MRI incidentally revealed an osseous lesion in the right proximal humerus (Fig. 1). According to the reported clinical information, the patient had shoulder pain which was attributed to rotator cuff degenerative disease and subacromial bursitis, confirmed on MRI. Her past medical history was unremarkable. The lesion was located intramedullary in the proximal diaphysis of the humerus, had lobulated morphology with well-defined margins, and

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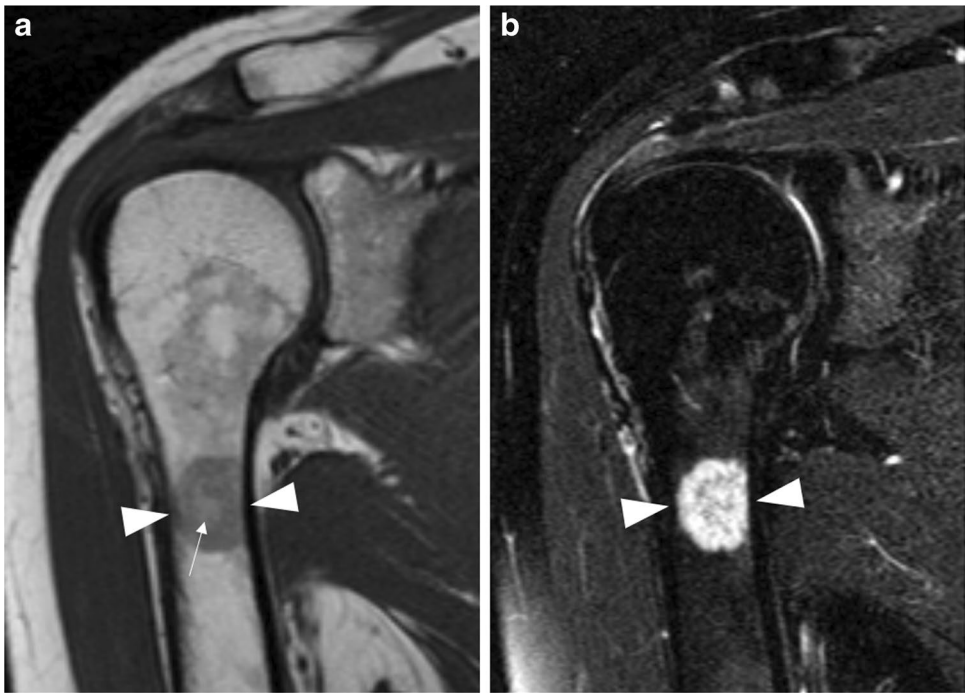

Fig. 1 Baseline non-contrast MRI. An intramedullary lesion (arrowheads) of the proximal humeral diaphysis shows hypo-to-isointense signal on T1-weighted sequence (**a**) with some foci of intralesional fat (arrow) and hyperintense signal on fat-suppressed T2-weighted sequence (**b**). At this stage the lesion was misinterpreted as an atypical cartilaginous tumor

measured 14 × 15 × 21 mm (AP × LL × CC). It showed high signal intensity on T2-weighted sequence and low-to-intermediate signal intensity on T1-weighted sequence with some foci of intralesional fat, which were thought to be intralesional fatty marrow. On the medial side, the lesion adhered to the inner layer of the cortex without determining any deep scalloping, cortical remodeling, or interruption. There was no evidence of perilesional edema, periostitis, or soft tissue involvement. Retrospectively, only mild osseous sclerosis could be noted in the area of the lesion on X-rays previously performed (Fig. 2). The lesion was interpreted as an atypical cartilaginous tumor and managed with imaging follow-up. No biopsy was performed as per our routine procedure in the case of cartilaginous bone lesions, which suffer from sample errors [3]. At 6-month follow-up, contrast-enhanced MRI was performed and showed unchanged size and shape and mainly peripheral enhancement of the lesion (Fig. 3). Longer interval follow-ups were undertaken given the morpho-dimensional stability of the lesion over time. At 3-year follow-up, the lesion was only slightly increased in size and measured 14 × 16 × 25 mm (AP × LL × CC). At 6-year follow-up (Fig. 4), a further increase in size was noted and the lesion measured 18 × 16 × 32 mm (AP × LR × CC). No other suspicious MRI findings or changes in imaging characteristics were seen. Because of the increase in size and patient's concerns, curettage was performed. Histologic examination showed aggregates of brown fat cells with multivacuolated cytoplasm in a background of hematopoietic tissue of bone marrow (Fig. 5), compatible with a diagnosis of intraosseous hibernoma. No cartilaginous tissue was present. Immunohistochemistry showed strong positive staining of brown fat cells with S100 (Fig. 6). The patient was discharged after surgery with no post-operative complications. Follow-up X-rays showed progressive integration of the spongiosaplasty after curettage (Fig. 7).

Discussion

Intraosseous hibernoma are rare benign entities mostly observed in the spine and pelvis [2]. To our knowledge, including the patient presented in this report, only four cases have been described in the appendicular skeleton. They include three hibernomas of the femur previously reported [2, 4] and our case which is the first described in the humerus. The mean age at presentation for hibernoma is 58.6 years (range 36–85 years) [2]. They can be either asymptomatic and incidentally discovered, or cause focal pain [2]. In our patient, as pain was localized in the shoulder rather than in the upper arm, it could be better explained by rotator cuff degenerative disease and subacromial bursitis.

On imaging, intraosseous hibernomas are described as sclerotic lesions in most cases [5], similar to ours where some degree of sclerosis was present on X-rays, and osteolytic lesions less frequently [2]. On MRI, hibernomas show hyperintensity on T2-weighted sequence, hypo-to-isointensity on T1-weighted sequence, and contrast enhancement, as seen in our case [5]. The presence of macroscopic intralesional fat signal has been variably reported [6, 7]. In our case, intralesional fat signal was misinterpreted as foci

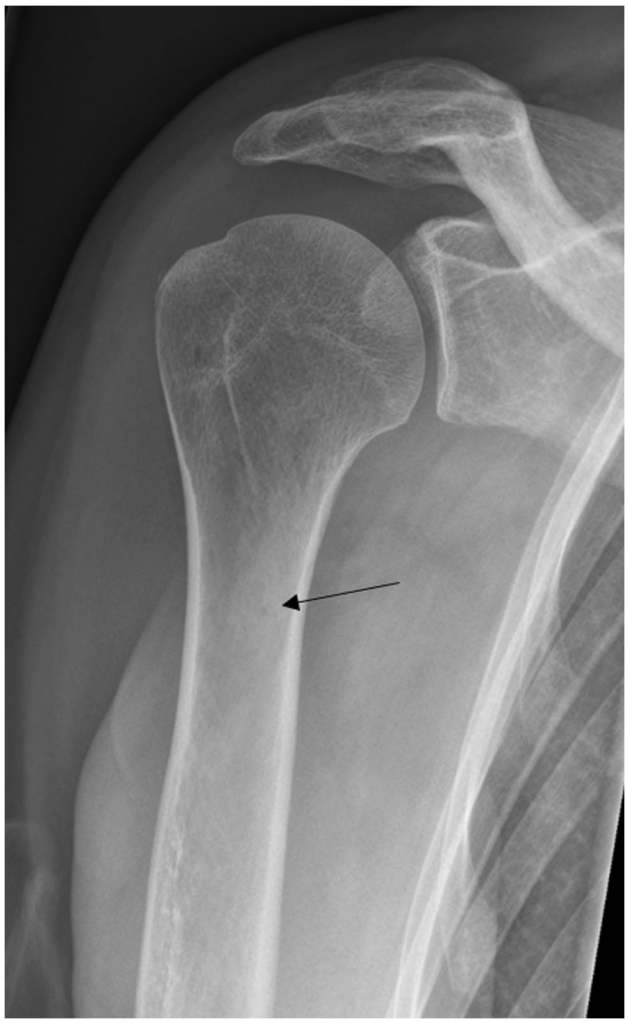

Fig. 2 Baseline X-rays. Retrospectively, mild sclerosis (arrow) can be noted in the region of the lesion known from MRI. No chondroid mineralization is present

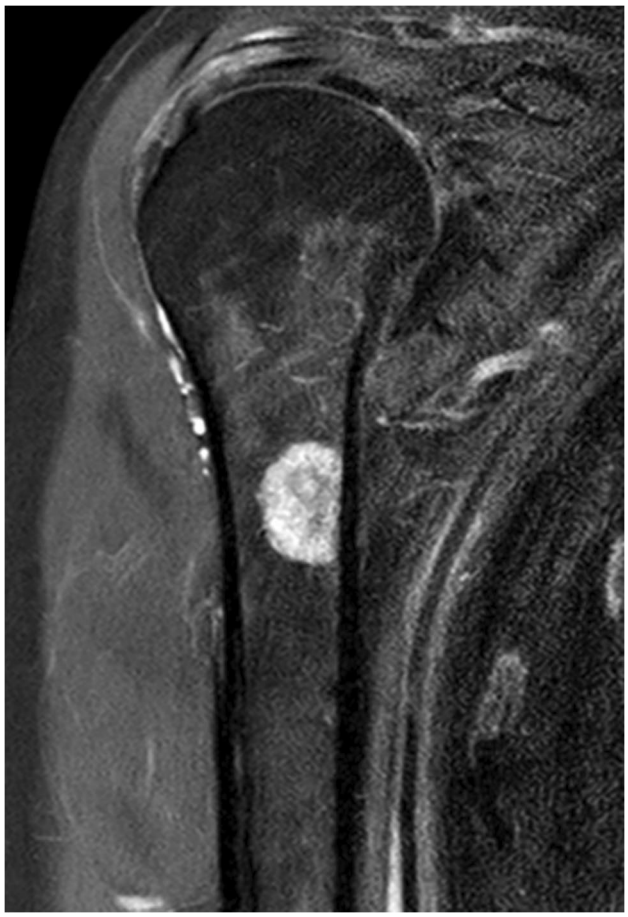

Fig. 3 6-month follow-up contrast-enhanced MRI. The known lesion of the humerus shows mainly peripheral enhancement pattern after contrast administration

of fatty marrow, which can be seen in cartilaginous bone lesions. Similar to soft tissue hibernomas which demonstrate high metabolic activity [8], elevated uptake has been described in intraosseous hibernoma when positron emission tomography-computed tomography was performed, with a maximum standardized uptake value of 4.1 [7]. This case illustrates that intraosseous hibernoma can exhibit slow growth over time, as also observed in its soft-tissue counterpart [1].

The radiological characteristics of intraosseous hibernoma are not pathognomonic and, in the humerus and other long bones, it can be a mimicker of several other entities. Metastasis is included in the differential diagnosis when the patient is known with primary cancer. Multiple myeloma in case of osteolytic hibernoma and lymphoma should be considered, as patients with hibernoma are typically middle-aged to elderly. Fat-containing primary benign tumors are also diagnostic considerations, particularly if macroscopic fat is visible on MRI, such as hemangioma and fibrous dysplasia. Cartilaginous tumors such as enchondroma and atypical cartilaginous tumors can contain foci of fatty marrow and should also be in the differential of hibernoma, although the septonodular enhancement pattern should help to differentiate them on contrast-enhanced MRI. However, given its unspecific features and the rarity of this entity in long bones, the diagnosis of intraosseous hibernoma is hardly considered on imaging alone and achieved only when biopsy is performed.

Definitive diagnosis of intraosseous hibernoma relies on pathology and biopsy is usually conclusive. In our case, the lesion was misinterpreted as an atypical cartilaginous tumor and biopsy was not performed as per routine procedure in the case of cartilaginous tumors, because of the risk for sample errors [3]. Thus, pathological assessment of the surgical specimen showed brown adipocytes admixed with hematopoietic elements [9] and provided the diagnosis.

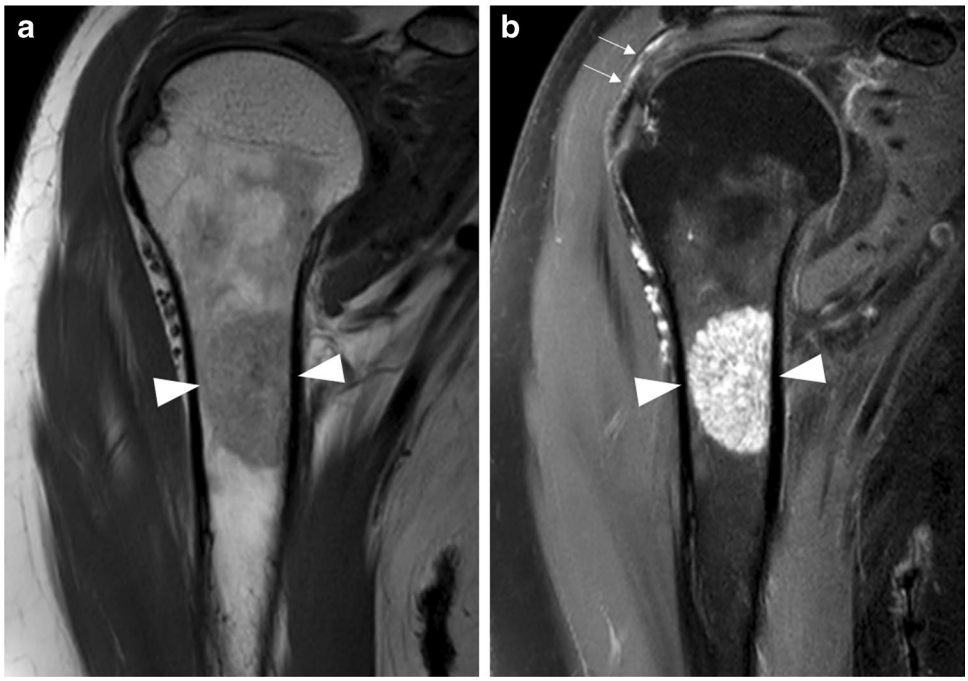

Fig. 4 6-year follow-up contrast-enhanced MRI. On pre-contrast (**a**) and post-contrast fat-suppressed (**b**) T1-weighted sequences, a substantial increase in size of the lesion (arrowheads) is noted without cortical scalloping or interruption. Cuff degenerative disease and subacromial bursitis (arrows) are still present

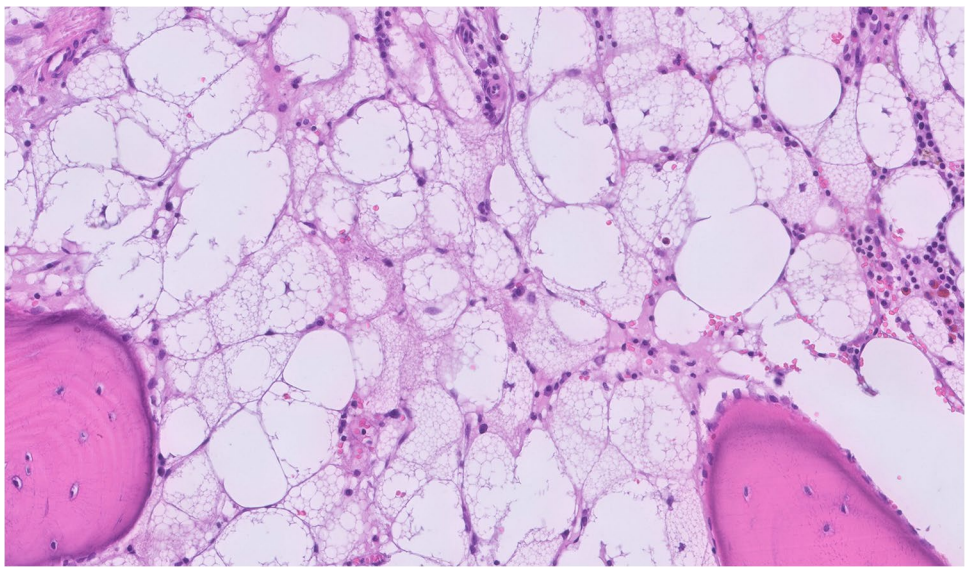

Fig. 5 Brown fat cells in hibernoma are large and show multivacuolated cytoplasm with scalloping of centrally placed nuclei

In conclusion, we presented a case of intraosseous hibernoma of the humerus highlighting new possible locations of this uncommon entity. Radiologists should be aware of and consider intraosseous hibernoma in the differential diagnosis of an appendicular bone lesion, particularly if it shows some degree of sclerosis on X-rays or computed tomography and macroscopic fat and contrast enhancement on MRI.

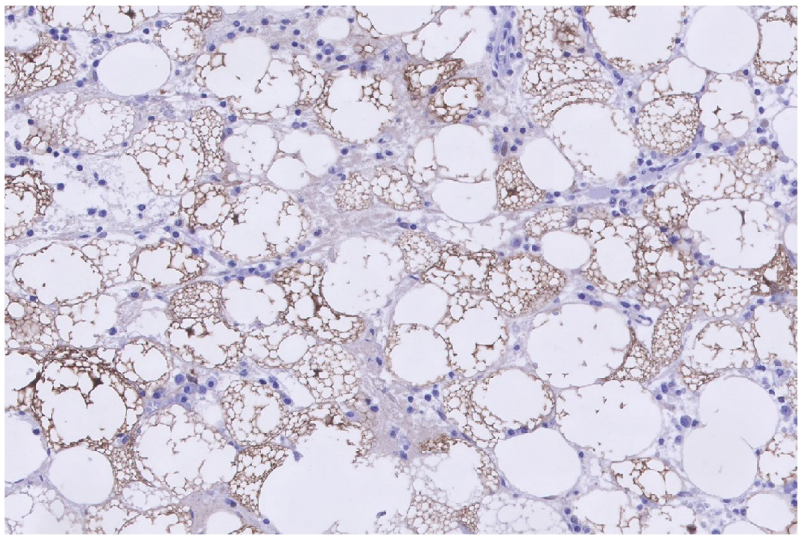

Fig. 6 Immunohistochemistry shows strong positive staining of brown fat cells with S100

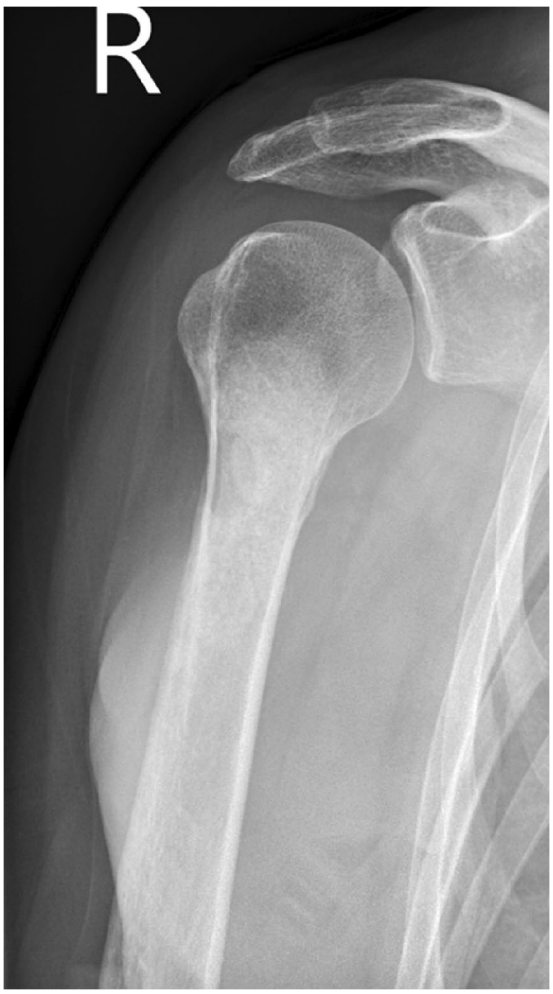

Fig. 7 X-rays shows progressive integration of the spongiosaplasty 7 weeks after surgery

Declarations

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from the subject described in this report.

Conflict of interest The authors declare no competing interests.

References

1. Furlong MA, Fanburg-Smith JC, Miettinen M. The morphologic spectrum of hibernoma. Am J Surg Pathol. 2001;25:809–14. https://doi.org/10.1097/00000478-200106000-00014.
2. Myslicki FA, Rosenberg AE, Chaitowitz I, Subhawong TK. Intraosseous hibernoma. J Comput Assist Tomogr. 2019;43:793–8. https://doi.org/10.1097/RCT.0000000000000912.
3. Hodel S, Laux C, Farei-Campagna J, Götschi T, Bode-Lesniewska B, Müller DA. The impact of biopsy sampling errors and the quality of surgical margins on local recurrence and survival in chondrosarcoma. Cancer Manag Res. 2018;10:3765–71. https://doi.org/10.2147/CMAR.S178768.
4. Song B, Ryu HJ, Lee C, Moon KC. Intraosseous hibernoma: a rare and unique intraosseous lesion. J Pathol Transl Med. 2017;51:499–504. https://doi.org/10.4132/jptm.2017.07.28.
5. Bonar SF, Watson G, Gragnaniello C, Seex K, Magnussen J, Earwaker J. Intraosseous hibernoma: characterization of five cases and literature review. Skeletal Radiol. 2014;43:939–46. https://doi.org/10.1007/s00256-014-1868-8.
6. Kumar R, Deaver MT, Czerniak BA, Madewell JE. Intraosseous hibernoma. Skeletal Radiol. 2011;40:641–5. https://doi.org/10.1007/s00256-010-1079-x.
7. Vlychou M, Teh J, Whitwell D, Athanasou NA. Intraosseous hibernoma: a rare adipocytic bone tumour. Skeletal Radiol. 2016;45:1565–9. https://doi.org/10.1007/s00256-016-2460-1.

8. Baffour FI, Wenger DE, Broski SM. 18F-FDG PET/CT imaging features of lipomatous tumors. Am J Nucl Med Mol Imaging. 2020;10:74–82.
9. WHO Classification of Tumours Editorial Board. WHO classification of tumours: soft tissue and bone tumours. Lyon: International Agency for Research on Cancer Press; 2020.