CASE REPORT

Osteoid osteoma transformation into osteoblastoma: Fact or fiction?

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Summary
Background: Osteoid osteoma and osteoblastoma are rare, benign, bone-forming tumours. The clinical presentation, imaging study findings, and course indicate clearly that these two tumours are distinct entities.
Clinical reports: We report two cases suggesting transformation of osteoid osteoma into osteoblastoma and therefore inviting a discussion of the links between these two tumours. An 11-year-old girl with a small metaphyseal lesion of the proximal tibia was given a diagnosis of osteoid osteoma. Over the next few weeks, worsening pain and marked tumour growth prompted a biopsy, which was consistent with an aggressive osteoblastoma. A review of the case suggested primary osteoblastoma at the earliest stage of development. In a 14-year-old boy, en-bloc excision was performed to remove a 1 cm defect located within the femoral shaft cortex and typical for osteoid osteoma. An asymptomatic recurrence measuring 20 mm along the long axis was removed 18 months later. Reassessment of the histological slides indicated recurrence of an incompletely excised osteoid osteoma.
Discussion: The histological similarities between osteoid osteoma and osteoblastoma, together with the lesion size criterion, may result in confusion. Collaboration between the clinician and pathologist is crucial and should take the tempo of evolution into account.
Conclusion: The histopathological differences between these two tumour types deserve to be emphasized. The data reported here challenge the concept that osteoid osteoma can transform into osteoblastoma. These two tumours are distinct entities that should no longer be differentiated based on size, as was long done in the past.
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Introduction

Osteoid osteoma and osteoblastoma are rare, benign, bone-forming tumours that account for about 12% and 3%, respectively, of all benign bone tumours [1,2]. In the past,
these two tumours were classified as variants of a single tumour type, based on a number of shared histological features [3–5]. Lesion size was long used as a discriminating criterion, with osteoid osteomas believed to reach 15–20 mm in diameter at the most and osteoblastomas to have the potential to become considerably larger.

The current consensus is that osteoid osteoma and osteoblastoma are two distinct entities that differ regarding their topographic distribution, clinical and radiological presentation and, above all, potential for progression [6–9]. However, reports of borderline forms that are difficult to classify and descriptions of a few cases of osteoid osteoma believed to have transformed into osteoblastoma have given new impetus to the old single-tumour concept [10–12].

Here, we present a detailed analysis of two cases that seemed consistent with transformation of osteoid osteoma into osteoblastoma. Whether these two tumour types are of the same lineage is discussed.

Case report #1

An 11-year-old girl experienced gradual onset of pain at the lateral aspect of her left knee, with no precipitating factor. The pain was mechanical initially then became continuous (without nocturnal awakenings). Radiographs obtained 2 weeks after symptom onset showed a lucency measuring 12 mm along its long axis and located in the anterolateral cortex of the proximal metaphysis of the left tibia (Fig. 1). By computed tomography (CT), the lucency measured 9 mm and exhibited a sclerotic rim and a calcification suggestive of a nidus (Fig. 2).

Under the hypothesis of an osteoid osteoma, a radionuclide bone scan was performed. Marked uptake predominating in the early phases and persisting in the late phases was seen at the site of the lesion (Fig. 2). These findings were consistent with osteoid osteoma. Given the location of the tumour, open excision surgery was scheduled. The pain became more severe and continuous, with a lancinating quality and loss of the response to paracetamol. Aspirin was introduced and alleviated the pain for several weeks. Aspirin therapy was stopped 2 weeks before the scheduled date of surgery, and the pain recurred gradually during this period.

The patient was admitted 5 months after symptom onset for surgical removal of the tumour. Intraoperative fluoroscopy to identify the lesion showed considerable expansion of the lucent defect, which measured 30 mm along its long axis. Consequently, a biopsy was performed instead of tumour excision. Findings during the biopsy were disappearance of the lateral cortex in contact with the lesion and thickening of the periosteum. The biopsy specimen was soft, fleshy, friable, and reddish in colour, with small foci of white granulations. It was sent to the laboratory for routine histological and bacteriological studies.

Radiographs and CT were performed immediately after the bone biopsy (Fig. 3). The bacteriological studies were negative. Histology showed an aggressive lesion, about which the advice of external experts was sought (Timone Marseille Teaching Hospital, France; and Mayo Clinic, Rochester, MN, USA). The final diagnosis was aggressive osteoblastoma rather than low-grade osteosarcoma (or osteoblastoma-like osteosarcoma) (Fig. 4 and 5). The surgical treatment consisted of painstaking curettage and filling of the defect with autologous bone. Histological examination of the residual tumour tissue removed during this procedure indicated osteoblastoma, with a less aggressive behaviour than in the biopsy specimen.

The pain resolved completely after surgery. At reevaluation 6 months later, the patient was symptom-free despite having resumed normal sporting activities, and her radiographs showed bone remodelling at the surgical site.

**Figure 1** Case #1: radiograph of the knee showing a 1 cm defect in the lateral cortex of the proximal tibia, with minimal rim sclerosis.
Case report #2

This 14-year-old boy was referred for a painful swelling in the left thigh that had appeared 1 month earlier. He reported loss of appetite and continuous pain that was worse at night. The initial radiograph showed thickening of the diaphyseal cortex due to a lamellar periosteal reaction around a central lucency measuring 1 cm in diameter (Fig. 6).

Magnetic resonance imaging (MRI) showed marked peritumoural and marrow oedema with an image suggesting a nidus (Fig. 6). An en-bloc open surgical biopsy provided immediate pain relief. The patient rapidly regained his appetite and was able to resume his sporting activities after a postoperative recovery period of 3 months. The surgeon described a raspberry-like appearance of the lesion around the edges of the bone flap that was consistent with osteoid osteoma. Bacteriological studies were negative. The pathologist confirmed the diagnosis of osteoid osteoma with, however, an atypical appearance that was also consistent with intra-osseous hemangioma (slide review by the French Bone Diseases Group, GFPO) and borderline excision margins. Given the immediate pain relief after tumour excision...
and the histological findings, a diagnosis of osteoid osteoma was given.

At re-evaluation 6 months later, the patient was free of symptoms and had normal physical findings (with no muscle wasting). The radiographs indicated good bone remodelling with gradual disappearance of the cortical thickening (Fig. 7). During the routine visit 1 year later, wasting of the thigh muscles was noted. The patient reported no symptoms. On the radiograph, at the site of previous excision, an intracortical lucency measuring 19 mm along its long axis was seen within the lateral femoral cortex, which was thickened (Fig. 7). Bone scanning showed a marked increase in radionuclide uptake at both the early and the late phases. By CT, a lucent defect in an eccentric position within the cortex was seen to be almost open into the medullary canal; the defect contained a nidus. On MRI T2-weighted images, signal intensity was markedly increased from the marrow and peripheral bone about the lesion (Fig. 8).

These findings suggested a recurrence with transformation into osteoblastoma, based on the size of the lesion (with a diameter of 20 mm along the long axis of the defect). Over the next year, the patient remained asymptomatic and there was no evidence of tumour growth. En-bloc surgical excision was then performed. Friable, fleshy, raspberry-like tissue was seen in contact with the deep aspect of the lateral femoral cortical flap. By gross examination, the lesion measured 18 mm along its long axis within the previous excision site. The initial histological diagnosis was osteoblastoma,
Discussion

We report two clinical cases that raise the issue of the connection between osteoid osteoma and osteoblastoma. Both tumours typically arise in the second decade of life. The histological features are very similar, with a vascular stroma and a network of anastomosed osteoid trabeculae. In osteoblastoma, however, the appearance is less organoid and the osteoblastic proliferation is more abundant, with cell clusters at different maturation stages within the stroma. A vascular pedicle is very often visible at the periphery of osteoid osteoma surgical specimens, as in our case #2.

Depending on the quality of the specimens, the histological distinction between osteoid osteoma and osteoblastoma may be challenging. A size criterion was widely used in the past: tumours larger than 2–3 cm in diameter were classified as osteoblastomas [7]. A lower cut-off of 1.5 cm was advocated by some authors, who suggested the term ‘‘giant osteoid osteoma’’ for larger lesions [13]. Clearly, size alone is of limited relevance for distinguishing these two tumours.
A large acquired lesion was necessarily small at some point of its development.

The current consensus is that osteoid osteoma and osteoblastoma are two distinct entities regarding not only their histology, but also their clinical and radiological presentation [6,9], rather than two modes of expression of a single tumour [3–5]. Clinically, osteoid osteomas arise in the long bones. The pain rapidly predominates at night, causing insomnia and responding to non-steroidal anti-inflammatory drugs. The pain is related to prostaglandin secretion by the nidus [14] and abates with aspirin therapy, which inhibits prostaglandin synthesis. Another source of pain may be the rich nerve supply to the tumour, with a number of similarities having been pointed out between osteoid osteomas and glomus tumours [15]. Osteoblastoma more often affects the axial bones. The pain does not increase at night initially, although this characteristic may appear later on, and is less responsive to anti-inflammatory medications. Osteoid osteoma has no potential for progression; thus, pain is the only problem raised by this tumour, and tumour regression may occur either spontaneously or with non-operative management [16,17]. Osteoblastoma, in contrast, has a greater potential for growth with destruction of bone tissue or even malignant transformation [18,19]. The sclerotic reaction is often milder in osteoblastoma than in osteoid osteoma. Osteoblastoma may exhibit a locally aggressive behaviour that may mistakenly suggest low-grade osteosarcoma [20] and is more likely than osteoid osteoma to recur after surgical excision.

Our first case report initially suggested direct transformation of an osteoid osteoma to an osteoblastoma in the space of only a few months. However, a primary osteoblastoma caught very early in its development is another possibility that is supported by the initial absence of nocturnal pain and the initial radiographs showing virtually no sclerotic rim and an atypical appearance of the nidus (calcification within the lesion in an eccentric position in the defect upon revision surgery). None of these suggestive features is sufficient to establish the diagnosis. In contrast, the final size of the lesion and, above all, the progression to a destructive lesion with rapidly worsening and poorly controlled pain strongly support a diagnosis of osteoblastoma. In 2005, Bruneau et al. described the case of a 25-year-old man with a cervical spine tumour initially felt to be an osteoid osteoma [21]. The patient declined surgery and was given non-steroidal anti-inflammatory drugs. After 7 years, exacerbation of the pain prompted surgery. Examination of the operative specimen established the diagnosis of osteoblastoma. The authors suggested transformation of an osteoid osteoma into an osteoblastoma in this patient [21]. The long symptom-free interval makes this hypothesis more plausible than in our case #1.

Our second case report describes the more classical situation of transformation into osteoblastoma during recurrence of a surgically-treated osteoid osteoma. Similar cases have been reported previously [10–12]. However, a review of this case led to a different interpretation consisting in recurrence of an incompletely removed osteoid osteoma. The marked sclerotic rim, histological features and, above all, stability of the lesion over 1 year argue in favour of recurrent osteoid osteoma, rather than osteoblastoma, despite the borderline lesion size (20 mm). The long time before repeat surgery was warranted by the absence of symptoms from the recurrence. To our knowledge, asymptomatic recurrence has not been previously described. The lack of symptoms may be ascribable to development of the tumour in a bone segment whose nerve supply was not restored after the initial surgical procedure. Asymptomatic osteoid osteomas may account for only 1.5% to 2% of all cases [7,18]; in a literature review, Jackson et al. identified 14 cases [18]. We believe that one source of difficulties in interpreting the histological features may lie in fragmentation or alteration of the biopsy specimen. In 1970, Dunlop et al. reported a case of metacarpal osteoid osteoma that recurred twice after en-bloc resection [22]. In 1989, after 11 surgical excisions over 21 years, these authors challenged their initial diagnosis, suggesting that the patient had locally aggressive osteoblastoma rather than osteoid osteoma [23]. This case illustrates the considerable challenges raised by the differentiation of osteoid osteoma and osteoblastoma and the often crucial information supplied by the time-course of the tumour.

**Conclusion**

Our first patient, whose case may have initially suggested transformation of a tibial osteoid osteoma into an aggressive osteoblastoma within a few weeks, was reclassified based on a review of the features as a primary osteoblastoma caught very early in its development. The second patient probably experienced a recurrence of an osteoid osteoma after incomplete excision of the initial tumour. We provide a detailed description of the histological differences between osteoid osteoma and osteoblastoma, which are different entities that should no longer be differentiated based on size alone. We challenge the ability of osteoid osteoma to transform into osteoblastoma. Recently introduced percutaneous methods of osteoid osteoma treatment do not provide histological specimens, which may hinder the differential diagnosis [24–26]. Further
work on the compounds released by osteoid osteomas into the bloodstream (e.g., osteocalcin) may help to differentiate these tumors from other lesions in the future [27].

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References