Progressively enlarging hard swelling of the mandible

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CLINICAL PRESENTATION

A 53-year-old man presented to our unit for evaluation of a nonpainful swelling of the right side of the mandible. The patient claimed that the swelling had first appeared ~1 year earlier and was initially managed with antibiotics without improvement. His medical history included vascular hypertension and hypothyroidism, both controlled by medication.

Intraoral examination showed a 4.5 × 2.0 cm hard tissue swelling occupying the labial and buccal vestibule of the right mandible, extending from the right central incisor to the right second premolar area (Fig. 1). The swelling was covered by normal-appearing mucosal surface and was not tender on palpation. All involved teeth were vital. The canine and first premolar appeared to be displaced. No pain or numbness was reported.

A panoramic radiograph was exposed, revealing a 4.5 × 4.5 cm lesion of the right mandible (Fig. 2). The lesion appeared primarily as a radiopacity with diffusely admixed less opaque areas with ill defined margins, extending from the midline to the second premolar area. Other significant radiographic findings were the diversion of the roots of the canine and first premolar, as well as the widening of the periodontal ligament on the mesial surface of the first and second premolars. Recurrent decay of

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the second right premolar was also noted. Computerized tomography (CT) imaging of the mandible was performed, revealing a somewhat nondescript ill-defined mixed-density lesion of the medullary bone around the canine area of the right mandible associated with periosteal deposition of new bone (Fig. 3, A and B). In addition,

Fig. 3. Computerized tomography imaging of the mandible. A, Axial view showing a vague ill-defined mixed-density intramedullary lesion associated with periosteal deposition of new bone (arrow) in the canine-premolar area of the right mandible. B, C, Vertical views demonstrating periosteal reaction (B, arrows) and widening of the periodontal ligament on the buccal surface of the right canine in continuity with the intrabony lesion (C, arrow).
DIFFERENTIAL DIAGNOSIS

The differential diagnosis, taking into account the history, clinical presentation, and imaging findings, included an inflammatory or infectious process, such as chronic sclerosing osteomyelitis, because this can produce an ill-defined radiopaque lesion with cortical expansion and/or periosteal reaction. Notably, the recurrent decay on the second right premolar and the evident earlier extractions of the ipsilateral molars could theoretically serve as possible sources of infection. However, all involved teeth were vital, and although chronic osteomyelitis can occasionally extend to occupy a sizable portion of the mandible, it would be expected to involve and expand around the hypothesized central zone of infection (i.e., the second premolar-molar area). In addition, there were neither local nor systemic signs or symptoms, such as pain, paresthesia, fever, or lymphadenopathy.

Regarding benign but locally aggressive lesions, the diffuse ill-defined mixed to mostly radiopaque appearance excluded the majority of odontogenic lesions. Cementoblastoma may cause a radiopaque presentation in addition to cortical expansion, but it is characteristically well defined and typically merges with the roots of the involved tooth. A calcifying epithelial odontogenic tumor may be locally aggressive and may also produce radiopacities, but it usually presents as a mixed radiographic lesion with well defined borders. Similarly, desmoplastic ameloblastoma, besides being rare, should show a mixed pattern. Nonodontogenic benign entities that should be considered include the benign fibro-osseous lesions (BFOLs), such as fibrous dysplasia, ossifying fibroma, osteoblastoma, and cemento-osseous dysplasia. Fibrous dysplasia usually presents with poorly defined margins, but its mixed radiolucent-radiopaque appearance frequently assumes a typical ground glass presentation. In addition, fibrous dysplasia has a predilection for the maxilla and appears at a younger age. Ossifying fibroma and osteoblastoma more commonly affect the mandible and may cause bone swelling, but they have well defined, frequently sclerotic, margins typically separated from the surrounding normal bone by a radiolucent space, as well as a more limited growth potential. The aggressive BFOL variants, i.e., aggressive osteoblastoma and juvenile ossifying fibroma, are expected to be painful and to show a predilection for younger patients, respectively. Focal cemento-osseous dysplasia would typically be limited in size without causing cortical expansion, and its florid variant would show a more diffuse involvement of multiple quadrants. In addition,
none of the aforementioned benign conditions is typically associated with a periosteal reaction.

Certain malignant tumors could generate the clinical, radiographic, and imaging findings of the presented case. Considering primary tumors of bone, osteosarcoma and chondrosarcoma are consistent with the observed findings, especially the ill-defined radiopaque presentation. Moreover, the observed periosteal reaction in the form of surface bone deposition and the localized widening of the periodontal ligament (Garrington sign) are compatible with a malignant process.11-14 The patient’s age was also reasonable, considering the occurrence of jaw osteosarcomas at a later age compared with their extragnathic counterparts.11 On the other hand, the lack of characteristic clinical symptoms, such as paresthesia/dysesthesia, and the absence of typical radiographic findings, such as spiking root resorption, structural changes in the mandibular canal, and “sun ray” appearance, reduced the likelihood of a malignant process.11-14 In addition, tooth root diversion is suggestive of a benign process. Metastatic tumors to the jaws usually appear as ill-defined radiolucent lesions, although bone production has been associated with certain primary origins, particularly those of prostate and breast origin. However, as mentioned above, the lack of a pertinent history and the absence of any systemic manifestations during 1 year of progressive jaw expansion, weaken this possibility.15

**DIAGNOSIS AND MANAGEMENT**

Surgical exploration was performed, revealing a solid mass. Histopathologic examination (Fig. 4) revealed a cellular mass composed of pleomorphic malignant mesenchymal cells with variable round to spindle-shaped morphology. Extensive areas of chondroid differentiation exhibiting atypical cellular features with lobular arrangement were observed. Chondrocytes appeared pleomorphic, hyperchromatic, and occasionally binucleated and mitotically active. In addition, areas of direct osteoid production by malignant cells were discerned.

The final histopathologic diagnosis was chondroblastic osteosarcoma, grade III.

Computerized tomography of the head, neck, and chest and whole-body 99m-technetium methyl diphosphonate (99mTc-MDP) bone scintigraphy (Fig. 5) were performed to stage the patient’s tumor, with no findings suggesting metastatic disease. Under general anesthesia, the tumor was radically removed by partial osteotomy of the mandible, followed by reconstruction with a titanium plate.

Postoperatively, the patient received 4 rounds of chemotherapy consisting of cisplatin and adriamycin over a period of 3 months (at 3-week intervals) as well as radiotherapy (30 sessions of 2 Gy, total dose 60 Gy) to the primary site. CT scans of the mandible, chest, and abdomen performed 6 and 12 months after surgery found no sign of recurrence or metastatic spread. One year later, surgical intervention was performed to replace the reconstruction plate with a block of autoge-
DISCUSSION

Excluding multiple myeloma, osteosarcoma is the most common primary bone malignancy. It is most often detected in the long bones, with a predilection for the distal femur, proximal tibia and humerus. Paget’s disease, retinoblastoma, Li-Fraumeni syndrome, and previous radiation therapy have been found to be associated with increased prevalence of osteosarcomas. Similarly, its osteoblastoma, fibrous dysplasia, central giant cell osteomyelitis, ossifying fibroma, desmoplastic fibroma, benign, or other malignant neoplastic disease, e.g., osteof gnathic osteosarcomas may resemble inflammatory, represent the head and neck area, osteosarcomas are rare and approximately equal distribution appears to be likely. There is controversy on the frequency distribution between the 2 jaws, although an approximately equal distribution appears to be likely. Maxillary osteosarcomas are found mainly in the posterior alveolar processes, the palate, and the sinuses. In the mandible, they appear more commonly in the posterior body and the horizontal ramus followed by the angle, symphysis, and ascending ramus. Typically, jaw osteosarcomas appear as rapidly growing hard swellings of the buccal and lingual cortices, which are accompanied by no or only slight pain. However, clinical signs and symptoms can vary from swelling, pain, trismus, nonhealing of extraction socket, hypoesthesia or paresthesia of the lower lip (mandibular tumors), loosening of teeth, and nasal obstruction (maxillary tumors). Generally, the clinical manifestation of gnathic osteosarcomas may resemble inflammatory, benign, or other malignant neoplastic disease, e.g., osteomyelitis, ossifying fibroma, desmoplastic fibroma, osteoblastoma, fibrous dysplasia, central giant cell granuloma, and chondrosarcoma. Similarly, its radiographic image is not pathognomonic. Nonetheless, a thorough radiologic examination, including periapical, occlusal, and panoramic radiography, as well as CT, may provide clues to the diagnosis.

The main histopathologic feature of an osteosarcoma is the direct production of osteoid by atypical neoplastic mesenchymal cells. Other materials that can be found in the matrix are cartilage and fibrous connective tissue. The relative amounts of these products can vary. Accordingly, osteosarcomas are subclassified into 3 main histopathologic subtypes: osteoblastic, chondroblastic, and fibroblastic. Chondroblastic osteosarcoma is the prevailing subtype found in the jaws. In the present case, the final diagnosis was chondroblastic osteosarcoma, because of the presence of malignant mesenchymal cells of osteoblastic differentiation, which directly produced osteoid, along with deposits of malignant cartilage growing in lobules. It should be emphasized that the presence of any degree of malignant osteoid formation rules out a diagnosis of chondrosarcoma. Regarding tumor grade in the head and neck region, the literature does not suggest a clear preponderance of low- or high-grade osteosarcomas.

Osteosarcomas of the jaws should be treated with radical surgery as a primary modality. Surgical resection is considered to be successful when the bony margins of the resection are ≥ 3 cm and the soft tissue margins are ≥ 2 cm from the histologic edge of the tumor. More recent data highlight the benefits of a protocol consisting of preoperative chemotherapy, followed by surgical resection and then postoperative chemotherapy. The preoperative chemotherapy has the purpose of sterilizing micrometastatic deposits, testing the tumor’s responsiveness to chemotherapeutic agents, and decreasing tumor size. The role of postoperative chemotherapy is to sterilize any residual disease and improve the rates of survival and the patient’s quality of life. Regarding radiation therapy, some investigators suggest that it improves the outcome; however, it is not still widely used for the treatment of osteosarcoma.

The prognosis of osteosarcomas of the jaws, a 50% 5-year survival rate, is better than osteosarcomas of the long bones, which averages a 20% 5-year survival rate. Although in most cases, osteosarcoma of the jaws is identified as local disease, almost one-third of patients present with metastasis, the lungs being the predominant metastatic site. Although some studies indicate that tumor site, grade, and subtype do not correlate with poor prognosis, other studies have shown contradictory results suggesting that age > 60 years, tumor size > 6 cm, maxillary involvement, and advanced grade are poor prognostic factors. Additionally, clear surgical margins have been found to correlate with improved survival. Finally, patients who received chemotherapy in addition to initial radical surgery seem to have the best prognosis.

REFERENCES


