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Chondromyxoid fibroma of the mandible in an older adult: A case report

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ABSTRACT

Chondromyxoid fibroma (CMF) is a rare benign neoplasm of cartilaginous origin and represents less than 1% of all primary tumors of bone. The craniofacial region is affected in only 2% of cases. CMF of the jaw is exceedingly rare, with no significant sex predilection and an average age at diagnosis of 28 (range 9–67 years). A 50 year old woman was referred by her general dentist to our department in June 2017 with a swelling in the vestibular area of the left mandible. She had first noticed this painless, slow-growing, palpable mass 6 months earlier, but had not any difficulties in everyday functioning. Extra-oral examination revealed an oval, firm, and immobile mass, measuring approximately 3.0 x 2.0 cm that was attached to the lower border of the left mandible. An incisional biopsy of the mass was performed under local infiltration anesthesia and sent for histopathologic examination, and was reported as CMF. Given that the lesion was relatively small, it was treated by conservative local enucleation via an intraoral approach. CMF is rarely located in the maxillofacial region, but should be included in the differential diagnosis in patients with a tumor affecting the skull bones because it could be misdiagnosed as one of the more aggressive tumors found in this area. A preoperative radiologic diagnosis that is concordant with the histopathologic examination is very important for surgical planning and prognostication. Using an adequate treatment modality a better outcome can be achieved with detailed knowledge of this lesion.

1. Introduction

Chondromyxoid fibroma (CMF) is a rare benign cartilaginous neoplasm that accounts for less than 1% of all primary tumors of bone. The first case was decribed in 1948. by Jaffe and Lichtenstein [1]. CMF can localize in any part of the skeleton, although it appears most often in the metaphyseal region of long bones, specifically in the proximal tibia and distal femur. The craniofacial region is affected in only 2% of cases. Reviewing the 76 reports of CMF in the literature, only one of 189 cases was localized in the skull, while in one study the facial bones or skull were reported to be affected in 15 of 278 cases [2–4].

When the whole skeleton is considered, CMF has a slight male sex predilection in a ratio of 1.28:1 [5]. CMF of the jaw is exceedingly rare, with no sex predilections and an average age at diagnosis of 28 (9–67 years). In the majority of cases, CMF is discovered in the second or third decade of life. Comparing the incidence of CMF between the maxilla and mandible, approximately three quarters (76%) of cases occur in the mandible [6].

A long standing history of non-specific symptoms and signs, such as pain, cortical ballooning and expansion helps to secure the diagnosis. Some cases are asymptomatic and are detected as incidental radiographic findings [4,6]. The radiographic features of CMF almost always suggest a benign lesion, with only a few reported cases of malignant transformation [7]. CMF of the jaw is seen radiographically as a well-circumscribed radiolucent lesions with scalloped or sclerotic margins and internal trabeculations. A purely lucent matrix is sometimes present within the lesion [5,6]. Radiographic diagnose can be made with conventional radiography (CR), computer tomography (CT) or with magnetic resonance imaging (MRI). CMF is very similar to other types of cartilage tumors which are characterized with decreases signal on T1 images and heterogeneous increased signal on T2 images, while CMF is presented with calcified chondroid matrix on standard radiography and CT [8–10]. Cystic changes are observed on T1 and T2 sequences because they are weakly visible on soft tissue images in CT. Perilesional sclerosis is equally sensitive with CT or CR, but widening of the tumor is best analyzed with MRI. Changes of cortical bone as cortical thinning,destruction of the cortex and breakthrough are best seen and evaluated on CT scan [7]. Although the periosteum often remains intact, destruction of cortical bone is common. The size of a CMF may vary from 1.0 cm to 6.5 cm.

The differential diagnosis includes chondrosarcoma, chondroblastoma, giant cell tumor, aneurysmal bone cyst, non-ossifying fibroma and enchondroma [7,11]. Cytogenetic analysis has shown that clonal nonrandom abnormalities of chromosome 6 affect the

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development of cartilage, and analysis of these chromosomal abnormalities may be helpful in distinguishing between CMF and chondrosarcoma which are very similar histopathologically [12,13].

A multidiciplinary (radiological, clinical and pathological) approach is needed to diagnose this bone tumor and guide the treatment options.

In this report, we describe the case of a 50-year old woman with CMF of the mandible.

2. Case report

A 50-year old woman was referred by her general dentist to the Department of Oral Surgery, School of Dental Medicine, University of Zagreb on June 2017 because of a swelling in the left vestibular region of the mandible. She reported having first noticed this painless, slow-growing palpable mass 6 months earliers, but had no difficulties in everyday functioning. There were no enlarged lymph nodes in the head and neck area.

On questioning the patient denied any systemic disease or condition and reported no previous surgeries. She did not have any deleterious habits such as smoking or alcohol consumption. A general physical examination was unremarkable. There was no history of swelling or trauma in the jaw area. Extra-oral examination revealed an oval, firm and immobile mass attached to the lower border of the left mandible that was measured to be approximately 3.0 x 2.0 cm using a digital caliper (Mitutoyo Corp., Kawasaki, Japan). There was no redness or discharge from the swelling and the skin was not fixed to the underlying lesion. Intra-oral inspection showed a solitary lobulated swelling in the vestibular part of the left mandible between the first left premolar and the distal edentulous area. There was no change in color or in the appearance of the surrounding mucosa. There was no bruit, pulsation, crepitus or fluctuation, the first left premolar was not mobile without any evidence of dental caries and a percussion test was negative.

Cone-beam computed tomography (CBCT) of the affected area revealed an expansive mass measuring about 2.5 × 1.5 x 1 cm with mixed density and clear boundaries. A swelling affecting the lower border of the left mandible was visible underneath the foramen mentalis on a projection of the apical part of the root of the first left premolar and the edentulous area distal to this tooth. Soft tissue was also seen to be surrounding small calcified foci suggestive of a chondroid neoplasm (Fig. 1). An incisional biopsy of the mass performed under local infiltration anesthesia (4% articaine with epinephrine 1:200 000; 1.8 mL) and sent for histopathologic examination was reported as CMF.

In accordance with the ethical protocol of the School of Dental Medicine, University of Zagreb, Croatia, written consent was obtained from the patient before surgery. Given the relatively small size of this jaw lesion it was treated by conservative local enucleation via an intraoral approach. First, regional nerve block anesthesia (4% articaine with epinephrine 1:200 000; 3.6 mL) was administered. After carefully raising the mucoperiosteal flap and isolating the mental nerve, the cortical bone surrounding the lesion was removed using a round bur at 40 000 rpm so that the base of the CMF could be approached. The lesion was removed completely (Fig. 2) using a surgical mallet and chisel with curettage of the underlying bone, and defect was closed primary. The surgical specimen was sent for histologic analysis. Microscopic examination of the resected, oval, firm, encapsulated specimen showed that it contained hard tissue resembling cartilage in the center and fibrous tissue with small amount of adipose tissue on the periphery. The tumor tissue was arranged in lobules of varying size within a myxoid matrix, and were separated by zones of more cellular tissue composed of fibroblast like spindle cells with hyperchromatic nuclei. The center of each lobule was hypocellular with a myxochondroid appearance and was surrounded by peripheral hypercellular areas. Cellular atypia and mitotic figures were not reported. These histopathologic findings were consistent with diagnosis of CMF (Figs. 3 and 4).

The sutures were removed on the 10th post-operative day at which time the surgical site was healing as expected. The patient recovered completely, with no postoperative left mental nerve paresthesia. She continues to be followed up and remains well. (Fig. 5)

3. Discussion

Lichtenstein and Jaffe [1] were the first to recognize CMF. They reviewed 358 patients in whom different bones of the body were affected, and showed that CMF can be localized in any part of the skeleton. According to the literature CMF rarely occurs in the maxillofacial region, which includes the maxilla, mandible, frontal bone, orbital floor and pterygopalatine fossa, as well as the ethmoid, parietal, petrous, sphenoid, mastoid, occipital and zygomatic bones of the skull, and suggests that the mandible is the most commonly affected skull bone [1,2]. Although two thirds of the published reports are for patients aged younger than 30 years and with a slight male predominance, the present case involves a 50-year old woman with localization of CMF in the mandible. The lesion in this woman had a diameter of 2.5 cm, which is smaller than the average diameter of 3.3 cm reported by Hammad et al. [6].

The diagnosis of CMF is difficult and is often one of exclusion. Patients with this lesion usually present with a long history of nonspecific symptoms typically edema with mild, intermittent, and dull pain over a period of 6 months to 2 years [14]. In most cases CMF is slow growing and detected incidentally on routine radiography in patients with a long history of chronic localized pain (85%), swelling and edema (65%), and palpable soft tissue. Macroscopically, it is a well circumscribed, firm and lobulated mass that is rubbery to soft in consistency. The specimen shows multiple, firm, irregular and reddish areas of tissue with white semi-translucent glistening areas that are soft and gelatinous, while the peripheral areas have a fibrous appearance. Opalescent gray-blue areas resembling fibrocartilage may be noticed when the surface of the lesion is cut [14]. CMF can restrict movement and cause eating problems when the tumor protrudes from the mouth or, in rare instances, is associated with a pathologic fracture [14,15]. The lesion was asymptomatic in our patient, who had only noticed it as an unattractive protrusion near the inferior border of the left mandible that had grown slowly during the previous 6 months. On macroscopic examination the specimen was an ovoid-shaped, firm, encapsulated, reddish-yellow nodule that was measured to be 2.5 × 1.9 × 1.0 cm using a digital caliper and had an appearance similar to that of fibrocartilaginous tissue.

The precise etiology of CMF is unknown, as is the case with most bone tumors, although some authors have reported an association with certain chromosomal abnormalities. Smith et al. [12] found that 11 of the 14 subjects had nonrandom, clonal abnormalities of chromosome 6, involving band 6p25q13, which has not been associated with other bone tumors. It is important to point up that chromosome 6 has been involved normal cartilaginous development, carrying genes BMP6 (bone morphogenetic protein 6), COL9A1 (collagen type 9 α 1), COL10A1 (collagen type 10 α 1), and IGF2 (insulin-like growth factor 2) [16]. The patient declined the offer of genetic testing for these clonal abnormalities because of the benign nature of her lesion. There is a case in the literature where patient had symptoms and subsequent diagnosis of CMF during pregnancy, so it shows that this kind of bone tumor may be hormonally sensitive and a hormonal influence is potentially associated with its formation and growth [17]. Analyzing the cases in the literature, their medical history showed no systemic diseases or conditions that could cause this type of bone tumor [7,18,19].

Zustin et al. in their study [20] revealed that CMF is a tumor, that is mimicking or originating the fetal cartilage canals in the immature Meckel's cartilage, from which is mandible developing by intramembraneous ossification. Cartilage canals are developed according to angiogenesis, apoptosis of resident cells, mineralization and degradation of cartilage. Remodeling the cartilaginous matrix, nutrition of the growing cartilage and elimination of waste products is achieved by this cartilage canals, which regression is in correlation with age and

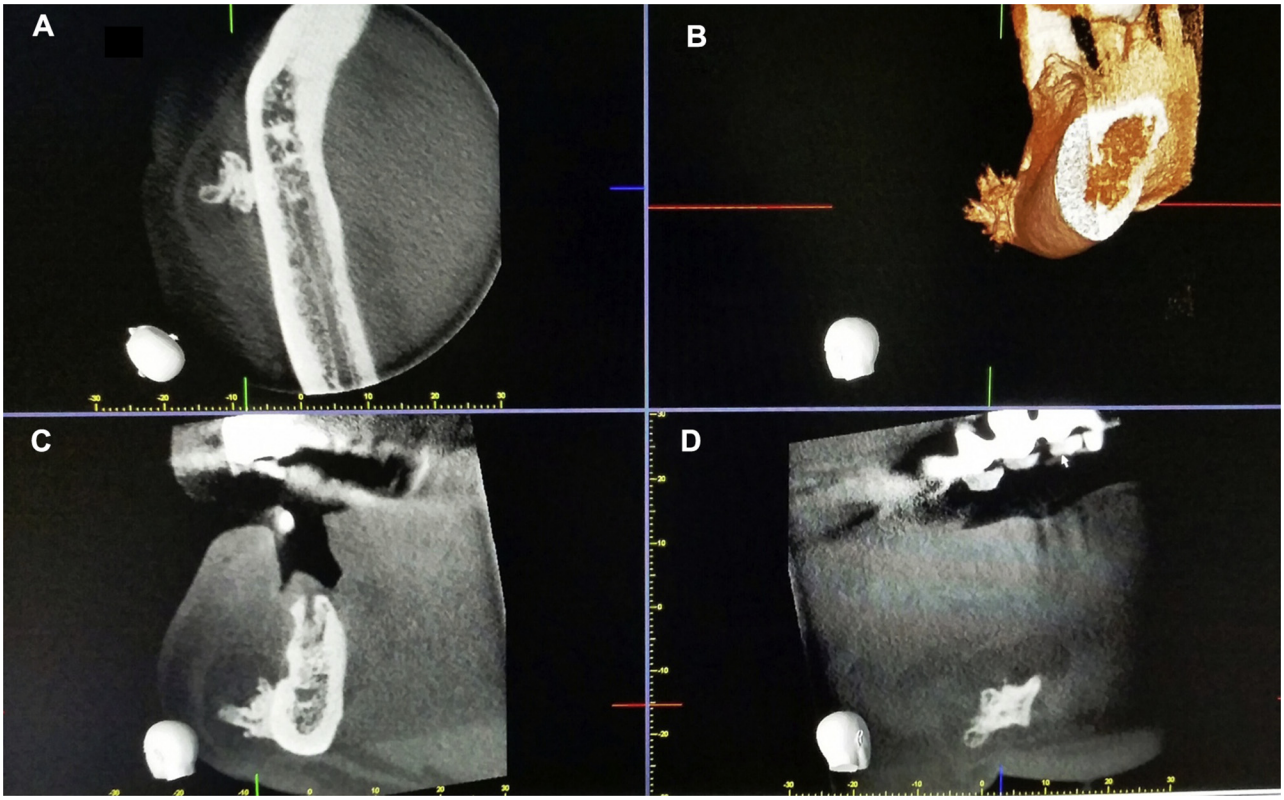

Fig. 1. CBCT of CMF shown from different angles.
A – axial section, B – 3D picture, C – sagittal section and D – coronal section.

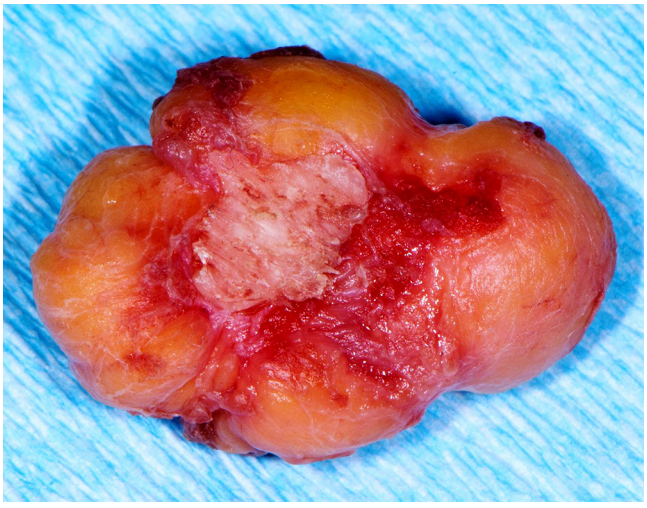

Fig. 2. Removed specimen sent for histologic analysis.

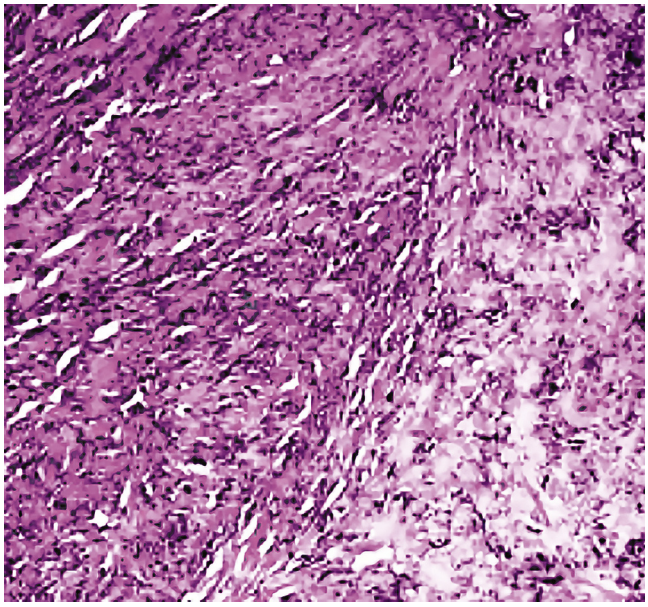

Fig. 3. Histopathological image of CMF-high magnification.

starts at blind end [21]. Immunohistochemistry with non-cartilaginous and non-osseous markers and histopathological analysis supported possible histogenetic coherence between the CMF and cartilage canals [20].

CMF is not easy to diagnose radiologically because of the variation seen on imaging. The lesion is described as expansile, lobulated and lytic with complete or partial erosion of cortical bone, but the integrity of the periosteum is often preserved. The cortical bone is usually expanded and thin, and is absent in 50% of cases. In almost one third of the cases reported there was radiographic evidence of extension of CMF into the soft tissue. The lobulated periphery of the lesion has an effect on growth of surrounding bone, so the tumor may have a trabeculated appearance [15,22]. The radiographic description in our patient was of a radiolucent and lobulated lesion with inner calcification and defined scalloped edges.

For the diagnosis of CMF imaging studies are very important. Conventional radiographs may not show calcification within the tumor, but this is visible on computed tomography (CT) scans, which may raise suspicion that a lesion is osteolytic and cartilaginous with sclerotic margin [23]. On magnetic resonance imaging (MRI) the center of the tumor may be hyperintense on T2-weighted spin-echo images and short tau inversion recovery sequences, depending on the amounts of

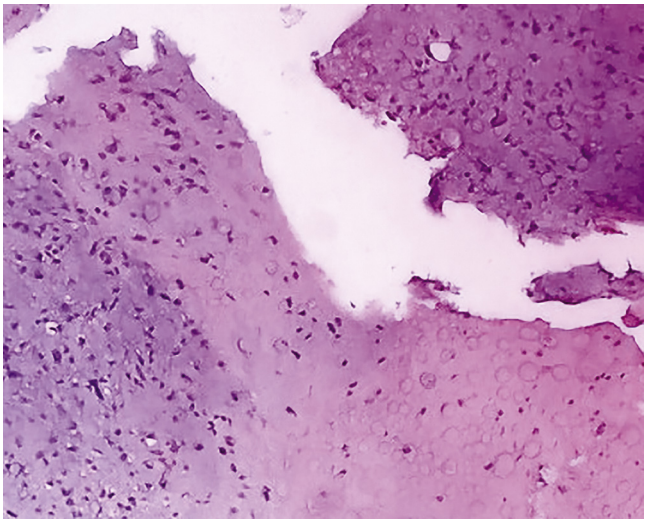

Fig. 4. Histopathological image of CMF-low magnification.

cartilage and myxoid tissue. The highly vascularized connective tissue at the border of the lesion accounts for the rim of moderate to high signal enhancement seen on T1-weighted images [24]. Hypointense T1-weighted and hyperintense T2-weighted images indicate the presence of cartilage and myxoid tissue. A fibrous tissue is confirmed with inhomogeneous contrast enhancement. Shen et al. [25] presented CT result as cluster of mild to high density shadows with mineralized parts at the margin, while MRI showed a hybrid signal on T2-weighted image and hypointensity on the T1-weighted image with inhomogeneous contrast enhancement. The isointensity on the T2 image and high density shadow on CT revealed foci of calcifications as an uncommon feature in this type of bone tumor [2,23]. CBCT in our patient revealed soft tissue infiltration and that the cortical outline was not destroyed by the expansive mass.

According to the literature, CMF microscopically has lobulated areas of spindle-shaped or stellate cells with an abundance of myxoid or chondroid intercellular substances that are separated by zones of more cellular tissue composed of round or spindle-shaped cells with varying numbers of multinucleated giant cells. The lobules have a hypocellular center and a hypercellular periphery. The myxoid areas become more fibrotic during maturation of the tumor. Within the tumor, spicules of residual bone and focal areas of calcification may be present.

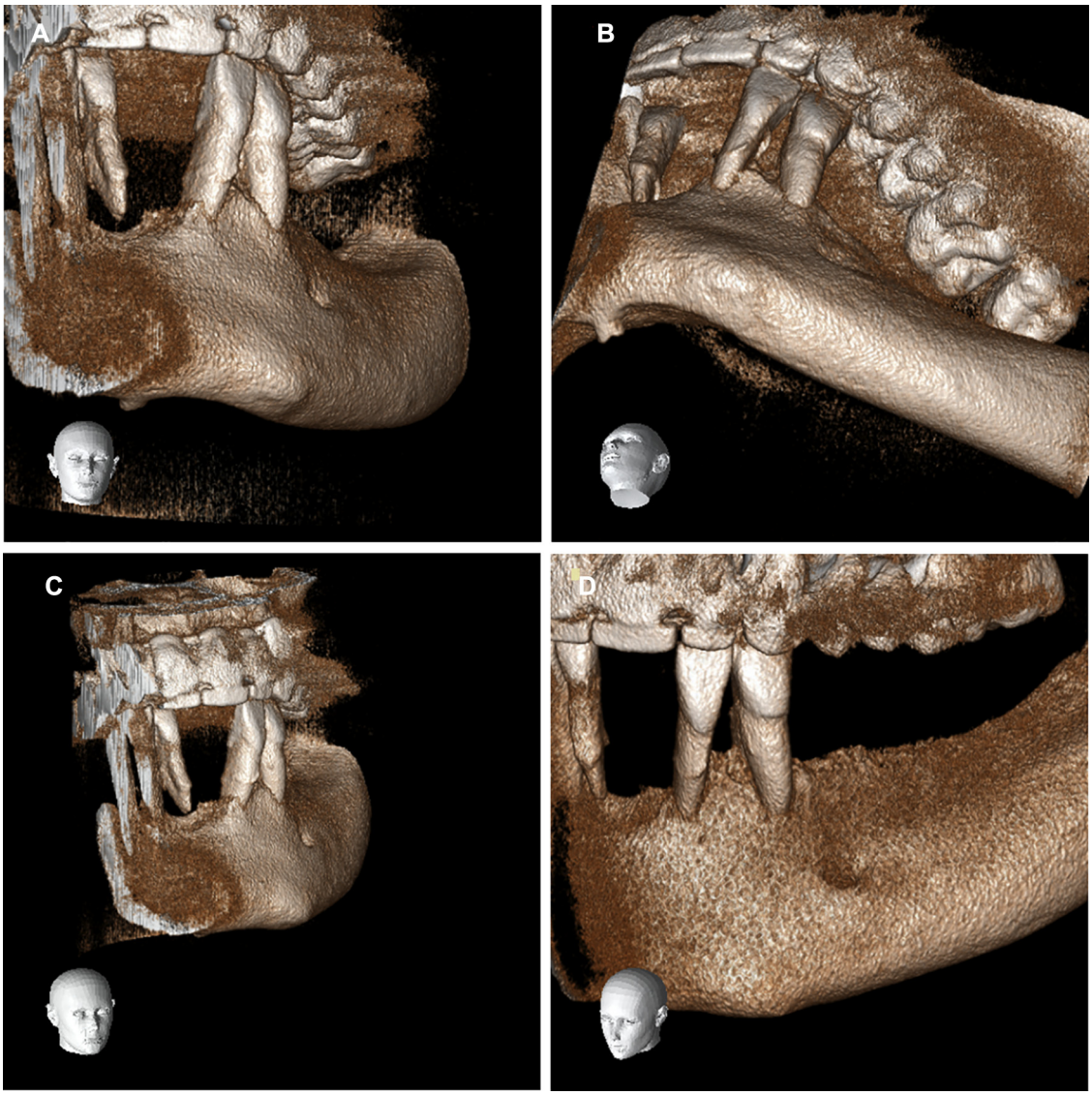

Fig. 5. CBCT finding made 5 months after surgery.
A,B,C,D –3D picture from different angles.

Ultrastructurally, these tumors are reported to contain two types of cells with fibrocytic and chondrocytic morphology [2,12,15]. The histologic description of our specimen was similar to that in previous reports.

The list of differential diagnoses includes chondrosarcoma, chondroblastoma, giant cell tumor, aneurysmal bone cyst, non-ossifying fibroma and enchondroma [7,11]. Cytologically, CMF is most similar to benign lesions such as chondroblastoma and myxoid chondrosarcoma, it is important to distinguish CMF from these two lesions, beacuse a wrong diagnosis can easily be made. Chondrosarcoma can be differentiated from CMF by the presence of mitosis, nuclear atypia and an invasive growth pattern. Large pleomorphic cells may cause confusion, but the absence of a fibrous component and the presence of a formed hyaline matrix in CMF are important features that distinguish these two entities. Radiographically chondrosarcoma presents as a radiolucent area with cortical destruction or erosion and several radiopaque regions in ring shapes or with pointed forms. Chondroma and chondroblastoma are benign tumors with cartilaginous differentiation that can be distinguished from CMF immunohistochemically because they only express protein S100 whereas CMF expresses cytokeratins antigens, epithelial membrane antigen and protein S100. Histologically, chondroblastoma consists of multinucleated giant cells, an eosinophilic chondroid matrix and sheets of stromal cells [15,26,27].

Depending on the size of the lesion there are two main treatment options for craniofacial CMF, i.e. curettage and en bloc resection, which have shown satisfactory outcomes [28] . Many authors now recommend conservative surgical removal by local enucleation or curettage, especially for relatively small lesions invloving the craniofacial bones. Patients can avoid the esthetic and functional side effects of total tumor removal but strict follow-up is necessary. Malignant transformation in this area is rare, but radiation therapy is indicated when the tumor is in a surgically inaccessible location. The definitive management of a large lesion is en-bloc surgical resection, particularly in cases affecting the long bones, and involves resection of part of the surrounding normal bone to prevent a recurrence [2,6,15,28]. In the present case, a mucoperiosteal flap was raised under local anesthesia and the whole lesion was removed by local enucleation and curettage with no cosmetic or functional sequelae.

CMF is an uncommon benign bone neoplasm of cartilaginous origin that is rarely located in the maxillofacial region. However, it should be kept in mind as one of the differential diagnoses in a patient with a tumor affecting a skull bone. It can be misdiagnosed and confused with more aggressive tumors. Preoperative radiologic diagnosis in concordance with histopathologic examination is very important during surgical planning and for further prognostication. A better outcome can be accomplished using an appropriate treatment modality and with a detailed knowledge about this lesion.

Conflict of interest

Author Marko Vuletić, Author Mato Sušić, and Author Dragana Gabrić declare that they have no conflict of interest.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Informed consent was obtained from all patients for being included in the study.

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