A mandibular swelling of long duration

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CASE PRESENTATION

A 45-year-old female presented to the Department of Oral Medicine and Radiology at our institute with dull, aching pain on the right side of her lower jaw for the past 2 months. There was no history of toothache, fever, pus discharge, or any trauma to the region. However, the patient did give a history of a swelling over the same region, which had been slowly but progressively increasing in size for the past 30 years but had not troubled her until 2 months previously. For this reason, she had not sought any treatment for the swelling other than local medicinal treatment at a rural center, the records for which had been lost. There was no history of similar swellings elsewhere in the body. The patient was a housewife, and her medical and personal histories were unremarkable. There was also no history of similar complaints or any chronic illness in her family.

Gross facial asymmetry was evident on extraoral clinical examination, and a diffuse, smooth, bony hard, tender swelling could be seen over the right hemimandible, extending from the symphyseal region up to the right preauricular area and inferiorly extending below the inferior border of mandible into the right submandibular region (Figure 1A). The overlying skin was normal in color, texture, and temperature, and no paresthesia was elicited.

The oral cavity reflected gross neglect of dental hygiene, with abundant deposits of calculus and generalized gingival recession. The right posterior mandibular arch was edentulous distal to the right mandibular first premolar, and a bony hard swelling involving the mandibular alveolus was apparent, extending from first premolar to the right retromolar region. The swelling obliterated the buccal vestibule and was palpable lingually, but tongue movements were unrestricted. Over the ridge crest, the lesion was firm on palpation, and faint indentations of the opposing dentition were visible (Figure 1B).

Orthopantomography showed an ill-defined, mixed radiolucent/radiopaque lesion involving the right body of the mandible, extending from the symphyseal region to the right coronoid process and the right subcondylar region and expanding posteriorly and inferiorly with intact cortical margins. Noncontrast computed tomography (CT) revealed a large, expansile, well-defined radiolucency involving the right ramus, right coronoid process, and right half of arch/body of the mandible up to the midline, showing few intervening ground-glass opacities and sclerotic areas with endosteal scalloping. No periosteal reaction was seen. The lesion was seen to slightly displace the contents of the oral cavity toward the left side; however, no obvious infiltration was seen into adjacent structures (Figures 2A-2C). Few subcentimeter-sized lymph nodes were seen in bilateral deep cervical regions.

DIFFERENTIAL DIAGNOSIS

The clinical and radiologic features in this patient presented a wide spectrum of possible diagnoses. However, the 30-year-long duration of illness suggested an extremely slow-growing lesion, implying a benign pathology. Also, because of the presence of pain, an inflammatory condition could not be ruled out. Consequently, our differential diagnosis included a fibro-osseous lesion; chronic osteomyelitis; benign odontogenic neoplasms, such as desmoplastic ameloblastoma and calcifying epithelial odontogenic tumor; and other benign nonodontogenic neoplastic processes.

Initially, an indolent mixed radiolucent/radiopaque mandibular lesion causing cortical expansion suggested the possibility of a fibro-osseous lesion. Fibro-osseous lesions of the craniofacial bones encompass a group of lesions composed of hypercellular fibrous elements as well as osseous elements.[1] Craniofacial fibrous dysplasia is a characteristically slow-growing fibro-osseous lesion, wherein normal bone is replaced by immature, haphazardly distributed fibrous and bony tissues.[2,3] It is essentially a tumor-like condition that results in a gradually developing painless expansion of bone in all directions, commonly presenting clinically as facial asymmetry,[3] features that could be well-correlated with the current lesion. Radiographically, fibrous dysplasia displays a range of mixed radiolucent/radiopaque presentations, varying from a ground-glass appearance to a predominantly sclerotic appearance of the affected bone. The margins of the lesion are diffuse, with the lesion blending gradually into the adjacent normal bone. The present lesion exhibited similar findings, with ill-defined margins and the body of the lesion displaying a ground-glass appearance among few sclerotic areas.

Cemento-ossifying fibroma (COF), another slow-growing lesion affecting the jaws, is a benign

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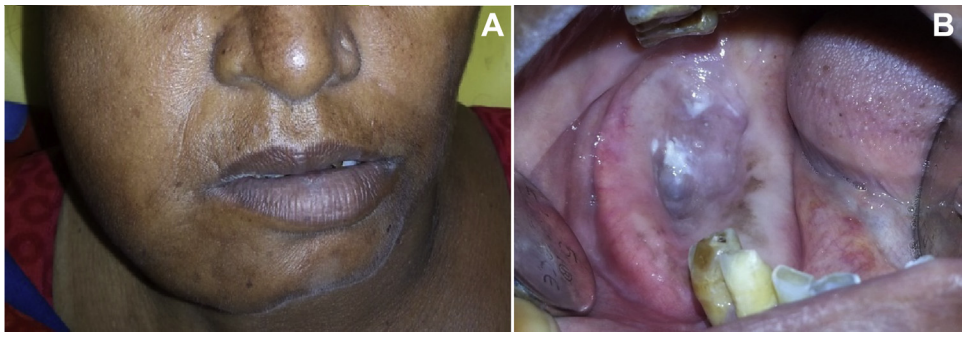

Fig. 1. Preoperative clinical presentation of the patient. **A,** Extraoral frontal view showing diffuse swelling on the right side of the face. **B,** Intraoral view showing buccolingual expansion of the right mandible and tooth indentations over the ridge crest.

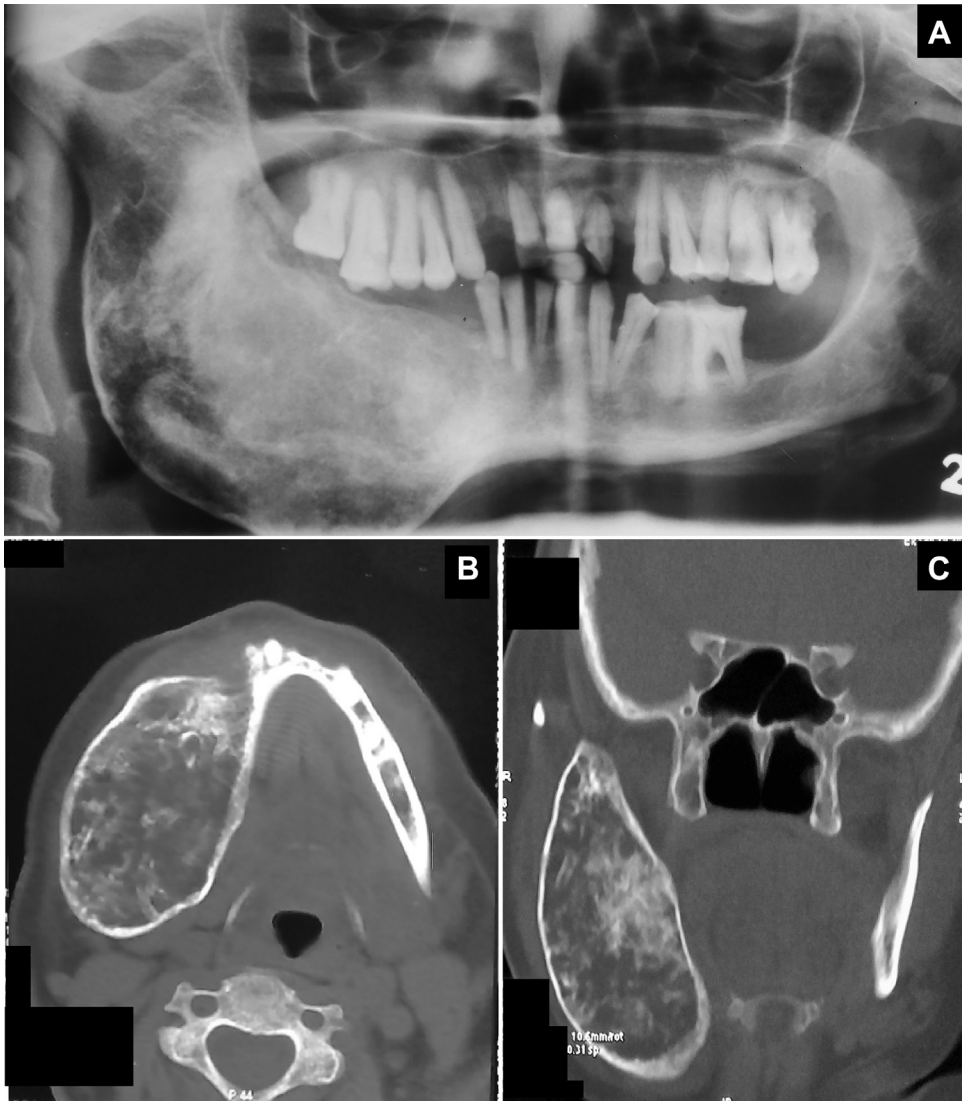

Fig. 2. Radiographic presentation of the lesion. **A,** Panoramic view showing expansile radiolucent/radiopaque mass with ill-defined borders involving the right hemimandible. **B,** Axial computed tomography (CT) section showing significant buccolingual expansion with intact cortices. **C,** Coronal CT section showing superoinferior extent and diffuse central radiopacities within the body of the lesion.

fibro-osseous neoplasm composed of proliferating fibroblasts and osseous tissues, including bone and cementum-like material. Clinically, COF usually presents as a spherical or ovoid mass, painless and expansile, with displacement or resorption of the roots of adjacent teeth.[1] Unlike fibrous dysplasia, however, the tumor is characteristically well defined, clearly demarcated from the adjacent healthy bone, and occasionally corticated. Radiographically, as the lesions enlarge and mature, they transition from a radiolucent lesion to a mixed radiolucent/radiopaque one and finally progress to a stage at which they become predominantly radiopaque.[1,4] COF was included in the differential diagnosis, as the clinical and radiographic presentation of the lesion in this case resembled that of a COF mature enough to be in a mixed radiolucent/radiopaque stage, as would be expected from such a longstanding lesion. However, orthopantomography of this lesion lacked the well-defined radiographic margins classically seen in a COF, although the same could be appreciated on the CT scan reasonably well.

Chronic nonsuppurative osteomyelitis is the sequel of a longstanding, low-grade, usually odontogenic or post-traumatic infection, primarily associated with the clinical expression of deep pain, malaise, fever, and anorexia. This is most often accompanied by an indurated swelling and lymphadenopathy, as well as other clinical features, such as loose teeth and trismus, although the condition may often remain clinically silent for years. Radiographic presentation is fairly similar to a fibro-osseous lesion, with plain radiographs demonstrating ill-defined, variably mixed, lucent, and sclerotic areas within the lesion and bony expansion caused by cortical thickening by appositional periosteal bone formation. CT patterns in chronic osteomyelitis range from a bone defect pattern, which histologically represents granulation tissue, to a ground-glass pattern relating to small osseous trabeculae formation, to a compact bone pattern corresponding to thickening of the osseous trabeculae.[5] A hard, painful swelling of long duration with associated lymphadenopathy, as appreciated in our patient, correlates well with the diagnosis of chronic nonsuppurative osteomyelitis. In fact, of all the suggested diagnoses, it provided the only plausible explanation for the enlarged deep cervical lymph nodes seen on CT. Additionally, the diffuse, ground-glass appearance seen radiographically made this the more likely diagnosis, although no periosteal reaction was appreciated on CT. Chronic nonsuppurative osteomyelitis was, thus, included as a differential diagnosis in this case.

Among the benign odontogenic neoplasms, two tumors bear a striking resemblance to the patient's lesion: desmoplastic ameloblastoma and calcifying epithelial odontogenic tumor (CEOT). Desmoplastic ameloblastoma is an uncommon variant of ameloblastoma with a known potential for recurrence. It usually presents as a painless swelling commonly associated with buccal expansion, with possible tooth displacement. Radiographically, the lesion appears dissimilar to the other histologic variants of ameloblastoma, appearing as a mixed radiolucent/radiopaque mass with ill-defined borders, difficult to distinguish from a fibro-osseous lesion. Expansion of the cortical plate, particularly the labial or buccal plate, is frequently observed.[6,7] Most of the clinical and radiologic features of this lesion correlate with the lesion in our case, making it a rational differential diagnosis.

The CEOT, popularly known as the *Pindborg tumor*, is yet another odontogenic neoplasm, presenting as a painless, slow-growing mass, most commonly occurring in the posterior mandible. Some lesions may remain asymptomatic and be incidentally discovered on routine radiography. As with COF, CEOTs exhibit variable radiographic appearances, depending on the stage of development. Characteristically, the lesions show an irregular, unilocular or multilocular, radiolucent area that may be poorly or clearly defined. Within this radiolucent area, multiple radiopaque masses of varying sizes and radiodensity develop. Often, extensive areas of calcification exist, making the lesion largely radiopaque.[8,9] Given the site affected and the heterogeneous radiographic presentation, the features of the current patient's lesion displayed resemblance to a CEOT, which therefore was included as a differential.

Keeping the above lesions in mind, a series of investigations were performed to arrive at a confirmatory diagnosis.

DIAGNOSIS

All routine laboratory investigations revealed values well within the normal range. Because of the presence of thick cortical plates, a needle aspiration could not be done, and we decided to proceed with an incisional biopsy. A 2.3 × 1.1 × 0.7 cm mass was incised intraorally with the patient under local anesthesia. Histopathologic examination revealed resorbing trabeculae of bone, with osteocytes within lacunae and prominent resting and reversal lines. Supporting stromal tissue was composed entirely of mature adipocytes having empty cytoplasm and signet-ring appearance of nucleus. Focal areas of increased vascularity and areas of hemorrhage were also observed. On the basis of these features, a diagnosis of mandibular intraosseous lipoma (IOL) was made, with infiltrating lipomatosis to be ruled out after excisional biopsy.

Facial congenital infiltrating lipomatosis is a rare congenital pathosis, exhibiting groups of unencapsulated, mature lipocytes infiltrating adjacent soft tissues

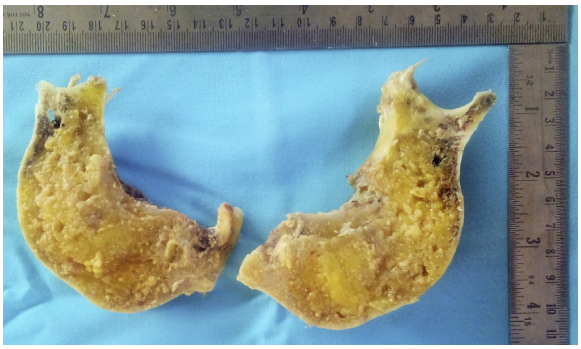

Fig. 3. Bisected gross specimen demonstrating extensive lipomatous-appearing mass occupying the body of the mandible.

and muscle. The lesion typically affects one side of the face and may be associated with enlargement of the underlying bone.[10] The disease contrasts in clinical and microscopic features with an IOL, as it shows no respect for anatomic boundaries. Lipomatosis is an unencapsulated adipose tissue proliferation that freely infiltrates its surrounding tissues. The uncircumscribed nature of the proliferation can be demonstrated on histopathologic examination of a completely excised specimen. Although the clinical and radiologic features of our patient's lesion suggested a more confined intraosseous process, we could not entirely exclude the possibility of infiltrating lipomatosis until all of the margins of the excised lesion were evaluated histopathologically.

MANAGEMENT

A thorough literature search on mandibular IOLs failed to describe a lesion as extensive as the one in our patient. Although conservative surgical excision has traditionally been advised for IOLs,[11] a segmental resection with a 1.5-cm healthy tissue margin was planned for this patient, bearing in mind the size of the lesion and its potential for malignant transformation. With the patient under general anesthesia, a right hemimandibulectomy was done, and a surgical specimen measuring 10 × 5 × 3 cm in size, with significant buccolingual cortical expansion, was removed. A pale, soft tissue mass measuring 1 × 1 cm in size was seen filling the cavity on the superior surface of the excised lesion in the retromolar region. A reconstruction plate was fixed in the surgical defect and the wound closed in layers.

Gross examination of the cut biopsy specimen revealed generalized infiltration of the mandibular marrow space with a soft, pale yellow mass, resembling fatty tissue (Figure 3). Microscopic examination revealed lesional tissue composed of mature adipocytes interspersed with numerous residual

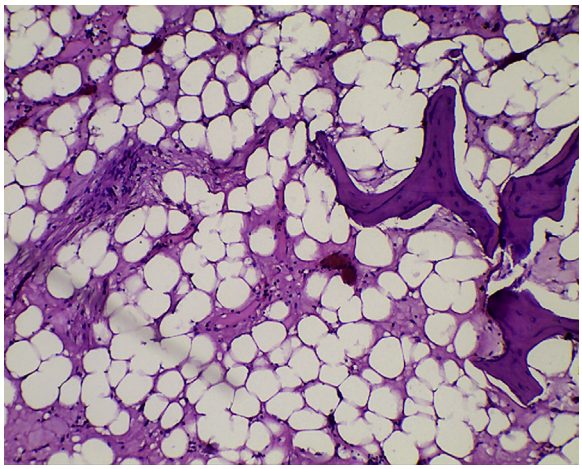

Fig. 4. Photomicrograph showing mature adipocytes interspersed with residual osseous trabeculae (×40). *A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM02794.*

osseous trabeculae, possibly representing resorbing native mandibular bone. The trabeculae were thin and irregularly shaped with osteocytes within the lacunae (Figure 4). The lesional tissue was limited by an intact cortical plate, and there was no evidence of infiltration by adipocytes. Consequently, a final diagnosis of IOL was established, and infiltrating lipomatosis was ruled out. The surgical margins were tumor-free. The recovery course was uneventful, and no evidence of recurrence was seen in the 6-month follow-up period.

DISCUSSION

Lipoma is a benign neoplastic lesion of the adipose tissue, fairly common in the soft tissues of the trunk and extremities, principally existing in a subcutaneous or an intramuscular location. IOL, which originates from the medullary adipose tissue, however, is a rare occurrence despite the ample fatty marrow present in the adult bones. Comprising less than 0.1% of all bone tumors, they are thought to be the rarest benign primary osseous neoplasms. IOL usually presents in the metaphysis of long bones and in the calcaneus.[11-13] The diaphysis or epiphysis of long bones, ilium, sacrum, vertebrae, and skull bones are other, less frequently affected osseous sites.[14] The occurrence of an IOL of the jaws is rare, with only 17 cases reported in the literature since 1948,[13,15] making IOL a highly unlikely diagnosis for a jaw swelling.

Although some authors have reported no gender predilection, others have described a slight female predilection, although the number of cases reviewed are too small to be of any significant value.[11] The age range for occurrence of IOL has been reported to be 20 to

65 years, with patients commonly presenting in the fourth or fifth decade.[11,12] The features are consistent with those seen in our patient, who was a female presenting in her fifth decade, although her ambiguous history suggested that the lesion had been present for over 30 years.

Most IOLs are asymptomatic lesions that seldom cause any pain or swelling and are discovered coincidentally on routine radiography.[12] The lesion in the current case, however, was associated with both swelling and pain. In fact, to the best of our knowledge, it is the largest reported IOL of the jaw, with significant buccolingual cortical expansion involving the entire right hemimandible up to the sigmoid notch. As evidenced by the patient's poor oral health, gross dental neglect spanning 3 decades can be assumed to be the cause of the severity of symptoms, rather than the lipomatous proliferative process itself.

Various theories have been proposed to elucidate the pathophysiology of this benign lesion. Most authors believe IOLs to be true benign neoplasms of the medullary adipose tissue, whereas others have suggested that they are, in fact, reactive lesions produced secondary to infarcts, trauma, or inflammation. Proponents of the latter theory claim that obliteration of the nutrient vessels arising from the inferior alveolar artery may result in areas of infarction within bone, wherein adipocytes from bone marrow may gather to produce a lipomatous mass, forming the lesion. Still others hypothesize that they are conglomerations of the fatty marrow, formed as a result of the normal aging process of bone.[12,14] In the present case, the lack of any signs of infection or trauma pointed to a neoplastic origin of the lesion. At our institution, we were unable to perform a cytogenetic analysis to identify possible genetic mutations or chromosomal aberrations that could unequivocally confirm our patient's lesion as a truly benign neoplasm. Furthermore, at this time, the literature on IOL lacks definitive cytogenetic data to confirm the neoplastic nature of an IOL.

Radiographically, long bone IOLs appear as well-defined osteolytic lesions, with a sclerotic margin and diffuse, central radiopacities, representing areas of fat necrosis and dystrophic calcification. The presence of radiopacities within the lesion, however, is rare in mandibular IOLs, with only two such previously reported cases.[14] The lesion in the present case distinctly exhibited sizable diffuse radiopacities within the body of the tumor. However, these were thought to represent the resorbing native osseous trabeculae, rather than dystrophic calcifications, as the latter could not be appreciated microscopically. In a series of 61 cases, Milgram classified IOLs into three stages based on his clinical, radiographic, and pathologic analyses.[16] On the basis of the aforementioned radiologic and microscopic findings, the present lesion could be categorized as Milgram's stage 1.

Histopathologically, IOL must be differentiated from a well-differentiated liposarcoma, an osteoporotic bone marrow defect, and normal fibrofatty bone marrow.[12] In our case, liposarcoma was excluded, since adipocytes with cellular atypia or giant cells were absent. Because of the presence of substantial cortical expansion and lack of hematopoietic tissue[12] microscopically, a diagnosis of normal bone marrow was ruled out. Furthermore, an osteoporotic bone marrow defect was excluded as a diagnosis because of the absence of a history of trauma to the site.[12]

Most authors recommend conservative surgical excision as the treatment for an IOL. Although no cases of recurrence or malignant transformation in the jaws have been reported so far in the literature,[11] the cases reported are too few to provide a definitive standard of care. Additionally, a lesion as extensive as the one in this case has not yet been documented, and an appropriate treatment strategy still needs to be developed for such lesions. Therefore, keeping in mind the recurrence rate and the malignant potential of IOLs elsewhere in the body (four cases),[17] hemimandibulectomy was performed and is recommended by the senior author for such longstanding cases.

CONCLUSIONS

IOLs are benign neoplasms of the medullary adipose tissue, rarely occurring in the jaws. Although the lesions are slow growing and usually asymptomatic, if left untreated they may produce significant swelling and dental problems, resulting in facial disfigurement and functional impairment. Therefore, they must be considered among the differential diagnoses while evaluating a patient with a jaw swelling of long duration and be distinguished from other similarly presenting diffuse, mixed radiolucent/radiopaque lesions. Smaller IOLs may be treated effectively with a conservative surgical excision; however, it is recommended that larger lesions be addressed more radically.

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