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REVIEW ARTICLE

Odontogenic myxoma: A review with report of an uncommon case with recurrence in the mandible of a teenage male

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Abstract We describe a 13-year-old boy with recurrence of an odontogenic myxoma of the mandible. We review the existing published literature on the lesion, emphasizing the similarities and differences among lesions in the differential diagnosis. Odontogenic myxoma is an uncommon benign tumor that mainly affects the mandible, with a peak incidence in the second to fourth decades of life and predilection for the female sex. Clinical, radiological, and histopathological features should be considered when making a diagnosis. Several of these characteristics overlap with those of other benign and some malignant tumors. Odontogenic myxoma is known for recurrence. The treatment plan should consider the age and sex of the patient and the site and size of the lesion. Reconstructive surgery may be required, but should be delayed until after an adequate follow-up to rule out recurrence.

Contents

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1. Introduction

Myxomas are rare tumors of the hard sclerous and soft tissues in the body. Odontogenic myxomas comprise only a small fraction of myxomas. Clinical and radiological features of odontogenic myxomas are variable and mimic those of other tumors of the region. The tumor may be an incidental finding or may cause symptoms, including pain, paresthesia, and tooth mobility (Gonzalez-Garcia et al., 2006; Li et al., 2006). Virchow has been credited with the coining of the word "myxoma" (Melo et al., 2008; Moore et al., 2008). Myxomas of odontogenic origin were first described by Thoma and Goldman (1947), on the basis of site of occurrence, age at occurrence, association with missing teeth, and histopathological examination, which showed structural resemblance with dental mesenchyme and the sporadic presence of islands of odontogenic epithelium.

Odontogenic myxoma is a benign but invasive tumor that has a high rate of recurrence after surgical removal (Speight, 2013). We describe the case of a 13-year-old boy who developed recurrence of an odontogenic myxoma of the mandible. We review the literature on the features, differential diagnosis, and treatment modalities of this lesion.

2. Case report

2.1. History and clinical examination

A 13-year-old boy reported to the outpatient clinic with complaints of a painless, gradually progressive firm swelling on the lower left side of the jaw of 9 months' duration. He gave a history of a similar swelling in the same location 2 years before, for which he was treated intraorally at a dental clinic under local anesthesia 15 months prior. The patient had no documents pertaining to the previous treatment.

Clinical examination revealed a diffuse swelling, measuring about 2 × 4 cm with no clear borders, over the left angle of the mandible. Skin over the swelling was normal with no local rise of temperature, ulceration, or redness (Fig. 1). Intraoral examination did not show any swelling or breach in the mucosa on the left posterior region. On palpation, the swelling was diffuse, nontender, firm, and resilient to touch. Superoinferiorly, the swelling extended from near the left ear lobule to the angle of the mandible. Anteroposteriorly, it extended 4 cm anteriorly from the posterior border of ramus of the mandible. Expansion of the buccal and lingual cortical plate was palpable near the ramus of mandible.

2.2. Investigations and differential diagnosis

Orthopantomography (OPG) showed a poorly defined, multilocular, radiolucent lesion of 2.0 × 4.5 cm involving the left angle of the mandible, with a thickened bony rim (Fig. 2). Routine laboratory investigations (hematological and serological) were normal. Differential diagnosis included keratocystic odontogenic tumor, ameloblastoma, central giant cell granuloma, and odontogenic myxoma.

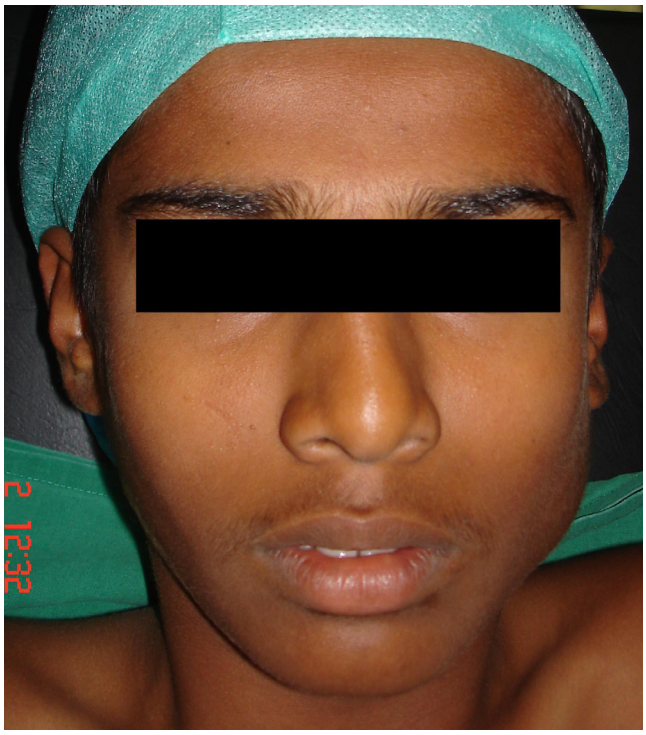

Fig. 1 Gross appearance of swelling-pre-operative clinical photograph. Showing swelling of the left angle of the mandible.

2.3. Surgical management

Given the patient's age, the recurrent and progressive nature of the lesion, and the observed buccal cortical expansion, we recommended radical surgery, which was rejected by the patient's parents due to domestic circumstances. After obtaining written informed consent from the patient and his parents, conservative surgical excision of the tumor with curettage was performed. Under general anesthesia, the lesion was exposed, together with the coronoid process, sigmoid notch, and condylar neck, through a submandibular approach. The lesion was completely excised and properly curetted. Scarification of the cavity was done with an acrylic bur. The surgical wound was irrigated with normal saline, povidone-iodine, and hydrogen peroxide solutions. The patient's parents were counseled and

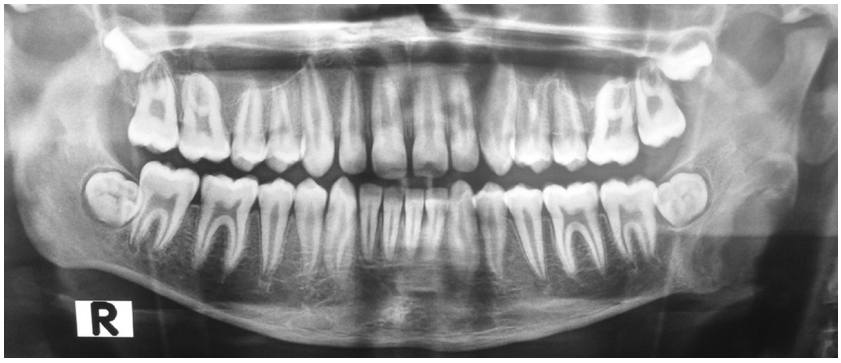

Fig. 2 Orthopantomogram. Shows an ill defined, multilocular, radiolucent lesion with fine trabeculations near the margins involving the angle of mandible on the left side.

advised to consider radical surgery with later reconstruction in the case of a further recurrence.

Excised tissues were gel-like pieces with a mucinous appearance and a gray-white color. The tissue was sent for histopathological examination. A capsule was not evident on gross examination of the tissue (Figs. 3 and 4).

2.4. Histopathology

Histopathological examination of the resected specimen with hematoxylin and eosin staining revealed spindle-shaped cells dispersed in a background of loose and abundant mesenchyme. Cells had long cytoplasmic processes at either end. Inflammatory cells were occasionally seen. All cells were uninucleate. Nuclei did not show any abnormality or variation in number or structure. Collagen fibers were loosely arranged. Vascularity was sparse, mainly of fine capillaries. Nests or islands of odontogenic epithelium were not seen. Cellular atypia or mitotic cells were not seen (Fig. 5). Considering the clinical, radiological, and histopathological findings, we made a final diagnosis of odontogenic myxoma.

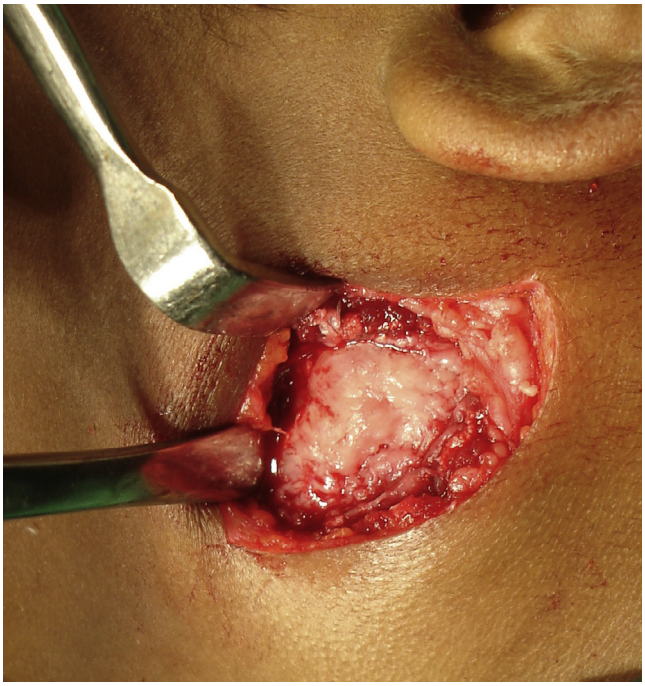

Fig. 3 Intraoperative image of odontogenic myxoma. Grayish-white appearance.

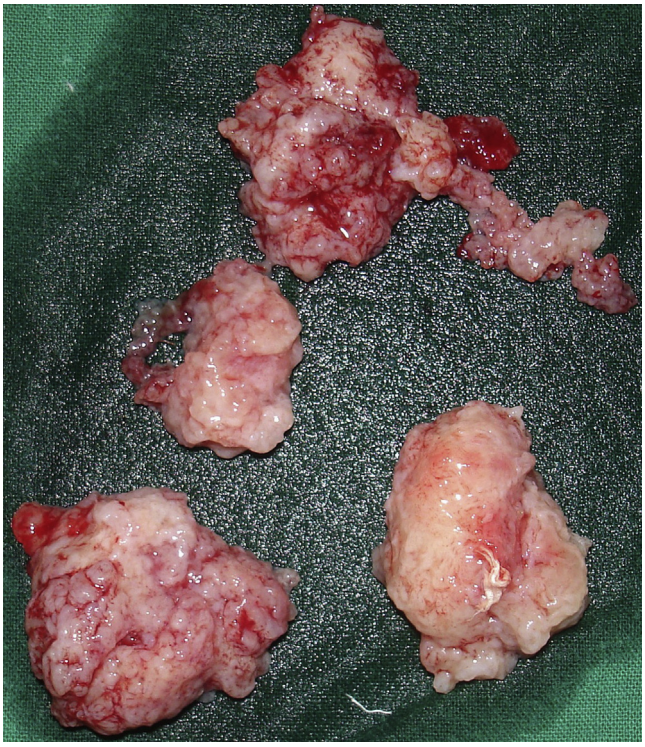

Fig. 4 Gross appearance of the tumor. Several grayish white tissue bits with jelly like appearance having lobulations.

2.5. Follow-up

The patient's 1-year follow-up clinical examination was uneventful and revealed no evidence of recurrence.

3. Discussion and review of related literature

Myxomas are very rare benign tumors of mesenchymal origin. These tumors are locally invasive (McFarland et al., 1996; Simon et al., 2004; Martinez-Mata et al., 2008; Zarbo, 2010; Speight, 2013) and occur in various tissues, such as the heart,

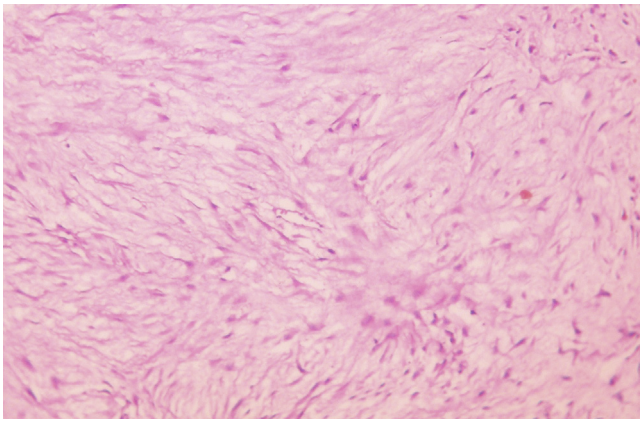

Fig. 5 Microscopic appearance. Hematoxylin and eosin stained tissue showing several spindle shaped cells with long cytoplasmic processes distributed evenly in loose and abundant mucoid tissue. Magnification 40×.

bones, skin, subcutaneous tissue, aponeuroses, genitourinary tract, and skeletal muscle (Kyriakos, 1990). Myxomas of the head and neck region occur mainly in the jaw bones, with a very small minority occurring in the pharynx, larynx, paranasal sinuses, and other soft tissues (Moore et al., 2008). We use the term "uncommon" to describe the present report of recurrence of odontogenic myxoma in a 13-year-old boy because these lesions are most prevalent in adult women (Shafer et al., 2003).

Odontogenic myxoma, also termed as odontogenic fibromyxoma or myxofibroma, is a subtype of myxoma occurring mainly in the hard, bony tissues of the face (Shafer et al., 2003), although the lesion may also occur in the surrounding soft tissues (Chrcanovic et al., 2010). Reported incidence rates of odontogenic myxoma range from 0.5% to 19% (Simon et al., 2004; Gonzalez-Garcia et al., 2006). In one large retrospective study, odontogenic myxoma constituted about 3% of 706 odontogenic tumors (Regezi, 2002). This wide variation in incidence may be attributed to the rarity of the lesion.

A few studies with large sample sizes are compared in Table 1 with respect to the demographic features of patients and the common sites and radiological features of the lesion. The usual age of occurrence of odontogenic myxoma is between 10 and 40 years of age, with a peak incidence in the third decade of life (Simon et al., 2004). Cases in children as young as 3 and 17 months have been reported (Fenton et al., 2003; Simon et al., 2004). Researchers do not agree with the reported sex bias. Simon et al. (2004) report a marked bias toward female sex, with a male: female ratio of 1:2, whereas other researchers have reported ratios ranging from 1:1.5 to 1:4. Shafer et al. (2003) stated that there is no sex predilection, whereas Zhang et al. (2007) reported a slight predominance in males.

The exact predilection of odontogenic myxoma to either the upper or lower jaw is also a matter of discussion. Some authors stated that the lesion is more common in the mandible (Shafer et al., 2003; Simon et al., 2004; Moore et al., 2008), whereas others found equal incidence in both jaws (Keszler et al., 1995). Regardless of the jaw, odontogenic myxoma is usually found in relation to a tooth, typically a premolar or molar (Li et al., 2006). Some researchers reported that the lesion is most often found in the mandibular premolar area (Speight, 2013). In the present case, the lesion was in the region of the posterior border of the ramus of the mandible not involving any teeth. There have been reports of odontogenic myxomas of the mandibular condyle, of the neck of the condyle (Halfpenny et al., 2000; Shafer et al., 2003), and, very rarely, of the gingiva (Shimoyama et al., 2000; Perrotti et al., 2006; Rius et al., 2013). Raubenheimer and Noffke (2012) proposed the name "peripheral odontogenic myxoma" for these very rare variants of odontogenic myxoma.

Myxomas of bones are found almost exclusively in the jaw bones, leading researchers to presume that the origin is the mesenchymal portion of the tooth germ (Halfpenny et al., 2000; Shafer et al., 2003). There is no consensus on the histogenesis of odontogenic myxoma (Martinez-Mata et al., 2008; Raubenheimer and Noffke, 2012). Immunohistochemistry and ultrastructural studies suggest that the cells of odontogenic myxoma have a myofibroblastic origin (Moshiri et al., 1992).

Although benign, odontogenic myxoma is invasive into surrounding normal bone, sometimes breaking through its boundaries (Chrcanovic et al., 2010). This invasiveness has been attributed to the expression of matrix metalloproteinases 2 and 9, which degrade the extracellular matrix (ECM). These enzymes purportedly cause tumor cells to penetrate the bony trabeculae by acting on the ECM, thus aiding tumor growth (Miyagi et al., 2008; Mauro et al., 2013).

Odontogenic myxoma is usually a slow-growing mass with late-appearing symptoms, primarily due to the mass effect. Symptoms include pain, paresthesia, ulceration, and tooth mobility (Gonzalez-Garcia et al., 2006), although none of these symptoms were found in the present case. Odontogenic myxomas crossing the midline are rare (Simon et al., 2004; Li et al., 2006) probably because the symptoms cause the patient to present to a clinician before the tumor is too large. Myxomas crossing the midline are usually found in the mandible (Landa et al., 2002).

On gross examination, odontogenic myxoma appears as a grayish white, nodular heterogeneous mass of variable consistency (Canalis et al., 1976), with a glistening gelatinous cut surface (Landa et al., 2002). The tumor may have a minimal true capsule (Li et al., 2006) or may be uncapsulated and poorly demarcated from surrounding tissues (Rius et al., 2013). In the present case, there was no capsule.

The lesion mimics dental pulp in its histological features (Regezi, 2002). Microscopically, the tumor has a mucoid-rich ECM, with scattered cells, connective tissue fibers, bony trabeculae, irregular calcifications, scant blood vessels, and sparse capillaries. Nests of odontogenic epithelium are occasionally seen but not essential for diagnosis (Simon et al., 2004; Li et al., 2006; Melo et al., 2008; Chrcanovic et al., 2010). The ECM comprises eosinophilic mucoid tissue, which resembles connective tissue of the umbilical cord. Spindle-shaped or stellate cells with small hyperchromatic nuclei and cytoplasmic processes are interspersed in collagen or reticulin fibers (Stout, 1948; Lo Muzio et al., 1996). Cellular atypia is rare, and the presence of mast cells has been reported (Martinez-Mata et al., 2008). Fibers are oriented toward the tumor periphery. All of these classical features were seen in our case. Immunohistochemistry studies of odontogenic myxomas are thought to be of little value in differentiating these lesions from other nonodontogenic cell tumors (Raubenheimer and Noffke, 2012).

Table 1 Comparison of a few earlier studies on odontogenic myxoma.

Researcher	Type of study	Sample size			Range of age in yrs (peak incidence in brackets)	Peak in_decade	Sites		Tooth displacement	Root resorption
		Total	Male	Female			Maxilla	Mandible		
Kaffe et al.	Systematic review with two case reports	164 (96-radiological)	64	100	01–73 (most cases in 2nd to 5th decade)	2nd	55 (33.5%)	109 (66.5%)	26%	9.5%
Martinez-Mata et al.	Retrospective	62	19	43	09–71 (most in 2nd to 4th decade)	3rd	25 (40.3%)	37 (59.7%)	12 (19.3%)	Not mentioned
Zhang et al.	Retrospective-radiological	41	22	19	04–63 (most cases in 1st to 5th decades)	3rd	17 (41%)	24 (59%)	21[a]	10[a]
Simon et al.	Prospective	33	12	21	03 months–64 years (majority in 2nd to 4th decade)	3rd	08 (25%)	24 (75%)	Number not mentioned	10 out of 21 avlbl cases
Noffke et al.	Retrospective	30	09	21	11–70 (most cases in 2nd to 3rd decade)	3rd	11 (36.7%)	19 (63.3%)	22 (73%)	13 (43%)
Ajike et al.	Retrospective	27	8	19	11–70 (peak in 4th decade)	4th	13 (48%)	14 (52%)	Not mentioned	Not seen
Li et al.	Retrospective	25	13	12	06–66 (peak between 2nd and 5th decade)	3rd	13 (52%)	12 (48%)	11	03
Friedrich et al.	Retrospective-radiological	14	3	11	08–45	–	5 (35.7%)	9 (64.3%)	8	2
Lo Muzio et al.	Retrospective	10	3	7	15–65	4th	4 (40%)	6 (60%)	2 of 10	2 of 10
Abiose et al.	Retrospective	10	2	8	10–40 (All between 2nd and 5th decade)	3rd	4 (40%)	6 (60%)	Number not mentioned	Number not mentioned

Sex predilection-mainly female predominance. One study – almost equal (Li et al.): Very slight male predominance-(Zhang).
Age range – 03 months to 73 years. Site predilection-Mandible more affected than maxilla in all studies except one (Li et al.).
[a] In six cases-no information. Also excludes missing teeth in relation to the lesion.

Table 2 Comparative features of some lesions which may be considered as differential diagnoses of odontogenic myxoma. (Shafer et al., 2003; Altug et al., 2011; Soames and Southam, 2005; Neville et al., 2002; Whaites, 2002).

		Odontogenic myxoma	Radicular cyst	Odontogenic keratocyst	Ameloblastoma	Central giant cell granuloma	Aneurysmal bone cyst	Osteosarcoma
Usual age of incidence		2nd–4th decade	2nd–5th decade	2nd–4th decade	3rd–4th decade	Adolescents; usually below 30 yrs	Adolescents; usually below 20 yrs	Young. under 30 years
Usual site of lesion		More in the mandible than the maxilla.	Apex of any non vital tooth. Especially upper lateral incisors	Posterior mandible/canine region of maxilla	Mainly the mandible. Maxilla-very occasional	Mandible. Often crosses the midline	Mandible. Occasionally in maxilla	Usually the mandible
Sex predilection		Female predominance	Not significant	Slight male predilection	Not significant	Equal. Slight female predilection	Not significant	Male predominance
Radiological appearance	Margins of the lesion	Not well defined	Smooth, well defined, well corticated if long-standing & if not infected	Smooth, well defined. Little mediolateral expansion	Smooth, scalloped, well corticated	Smooth, rarely perforates the cortical bone	Smooth, well defined. Cortex usually retained even when large. Buccal and Lingual expansion of cortex	Poorly defined-'moth eaten' appearance. Unilocular, widening of periodontal ligament space. Classical but rare is sunray appearance
	Loculation	May or may not be seen	Unilocular	Pseudo/multilocular	Multilocular. May be unilocular in initial stages	Multilocular. May be unilocular in early stages	Uni/multi locular	Usually unilocular
	Trabeculae/ septae	Occasional. If present, very fine. Calcification is seen occasionally	Not seen. Calcification may be present	Not described	Seen	Seen	Faint	Sclerosing form shows irregular spicules and trabeculae-Sunray appearance
	Root resorption	Usually not	Common	Rare	Common	Sometimes	Rare	Spiking resorption
	Tooth displacement	Very common	Rare	Rare/minimal	Common	Often	Often	(Widening of periodontal ligament space is very characteristic)
Histopathology	Matrix/cavity	Bland appearance	Inflammatory infiltrate in the connective tissue just adjacent to the wall is a characteristic feature. Cavity usually contains fluid with low protein content	Cavity filled with cheesy material or with clear fluid	Cystic changes & Squamous metaplasia is seen	Characteristic is few to many multinucleate giant cells. In a loose fibrillar connective tissue stroma	Blood-filled spaces of varying sizes separated by fibrous tissue	Irregular new osteoid formation seen. Widely variable atypical osteoblasts are seen

	Capsule	–	Fibrous CT wall lined by stratified squamous epithelium. Hyaline/rushton bodies may be present	Thin, fibrous. Lined by stratified squamous epithelium. Palisading of basal layer is characteristic. Satellite cysts within the fibrous wall are seen	–	–	–	–
	Cellular atypia	Not seen	Not seen	Occasional dysplasia present	Not seen	Multinucleated giant cells	Multinucleated giant cells	Atypical neoplastic osteoblasts arranged irregularly around bony trabeculae
	Nucleus	Single. Occasionally hyperchromatic	Single	Single	Single	Few or several dozen nuclei in each giant cell	Single	Large deeply staining
	Fibers	Few. collagen/ reticulin	Not present in lumen	Not seen	Varying amount seen	Collagen fibers not usually in bundles	Not seen	Anaplastic fibroblasts are seen in the Fibroblastic variety of the tumor
Recurrence		More than 25%	No. But a follow-up for a minimum of two years is strongly advised	30%. Most recurrences are in mandibular lesions	50–90%. Five year disease free period is not indicative of cure	15–20%. But recurrence rates of 50% have also been reported	Very variable. 8–60%	Known. More often in maxillary tumors

In our case, the radiological appearance was of a unilocular, mixed radiolucent-radiopaque type with corticated margins. The radiological appearance of odontogenic myxoma has been variably described as always radiolucent, usually radiolucent, or mixed radiolucent-radiopaque (Kaffe et al., 1997; Li et al., 2006; Melo et al., 2008; Altug et al., 2011). Margins of the lesion are classified as corticated, noncorticated, poorly defined, or diffuse (Noffke et al., 2007). The tumor may be uni- or multilocular on radiographs (Lo Muzio et al., 1996; Altug et al., 2011), with multiloculated lesions being larger than unilocular ones (Kaffe et al., 1997). The appearance is variably described as mottled, soap-bubble (Zarbo, 2010), tennis racquet (Noffke et al., 2007), or honeycombed (Shafer et al., 2003). The honeycomb appearance seems to be restricted to mandibular lesions (Friedrich et al., 2012). The lesion shows "wispy" bony trabeculae within radiolucent areas (Li et al., 2006). Zhang et al. (2007) classified the radiological appearance of odontogenic myxoma into six groups.

The tumor will usually displace adjacent teeth, and root resorption has been infrequently reported (Shafer et al., 2003; Noffke et al., 2007; Chrcanovic et al., 2010). Accurate diagnosis is difficult based on routine radiographs alone, as the features of odontogenic myxomas overlap with those of other lesions. Differential diagnoses suggested based on radiological appearance of odontogenic myxoma include ameloblastoma, intraosseous hemangioma, aneurysmal bone cyst, glandular odontogenic cyst, central giant cell granuloma, cherubism, metastatic tumor, simple cysts, odontogenic keratocyst, and osteosarcoma (Abiose et al., 1987; Li et al., 2006; Chrcanovic et al., 2010). Fibromyxoid sarcoma, myxoid chondrosarcoma, and rhabdomyosarcoma should also be ruled out (Speight, 2013). Some differentiating features of the lesions are described in Table 2. Diagnosis is made on the basis of clinical features, radiographic appearance, and histopathology. Computerized tomography, magnetic resonance imaging, immunohistochemistry, and ultrastructural studies can aid in the correct diagnosis. PET scans may help rule out metastasis (Guo et al., 2014).

Surgery is the treatment of choice, with the treatment protocol depending on the site and size of the tumor. Complete extirpation of the tumor is difficult because infiltration may be more extensive than that observed clinically. Surgery types vary from enucleation and curettage, wide excision, and resection, to radical surgeries involving resection of adjacent tissues (Halfpenny et al., 2000). Allphin et al. (1993) recommended an initially conservative approach, followed by radical surgery if required. When radical surgery is performed, delayed reconstruction has been advised because of the high recurrence rate (Leiser et al., 2009). Odontogenic myxoma is radioresistant (Shafer et al., 2003). Although a few researchers advised pre- or postoperative radiotherapy (Attie et al., 1966; Cuestas-Carneiro et al., 1988), the present consensus is that radiotherapy has no role in the management of odontogenic myxoma. In the present case study, an excisional biopsy was preferred over incisional biopsy to give the patient the best possible treatment under conditions beyond our control. The tumor was situated on the posterior-most part of ramus; therefore, an extraoral approach was chosen for reasons of accessibility and extension of exposure if required.

Odontogenic myxoma is notorious for a high recurrence rate of up to 25% after curettage (McFarland et al., 1996; Speight, 2013). A minimum follow-up period of 5 years without recurrence is recommended by some researchers before performing reconstructive surgeries. (Leiser et al., 2009). Rocha et al. (2009) reported a case of recurrent odontogenic myxoma 30 years after surgical treatment, which they treated by combining excision and curettage with cryotherapy.

4. Conclusion

Odontogenic myxoma is an uncommon entity occurring mainly in the bones of the face and jaws. Its clinical, radiological, and histopathological features mimic those of several other tumors and cysts. A high index of suspicion is to be maintained for accurate diagnosis and to rule out potentially malignant lesions. There is no consensus on the treatment protocol to be followed. In the present case of a growing patient, conservative surgery with strict clinical follow-up was recommended because the lesion has a significant chance of recurrence. Wider surgical excision should be employed in the case of recurrence. We recommend that large multicenter studies and systematic reviews of odontogenic myxoma be performed.

Conflict of interest

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors and none of the authors have any conflict of interest.

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