Fibromyxoma of the Jaw: Case Report and Review of the Literature

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Abstract We report a case of fibromyxoma of the mandible, a rare benign odontogenic tumor. Our patient presented in the first trimester of pregnancy with a large mass in the right body of the mandible exhibiting displacement of teeth and destruction of an extensive area of the mandibular bone. The mass was biopsied and diagnosed as a fibromyxoma. The large size of the tumor dictated a wide mandibular resection. We will review the clinical, radiographic, and histologic features of fibromyxoma and discuss its differential diagnoses. In addition, we will provide an overview of patient management. Fibromyxoma is a benign gnathic tumor that can be locally aggressive. To ensure appropriate treatment, it is important to distinguish this neoplasm from

other mimickers in which myxoid, spindle mesenchymal cell proliferation is prominent.

Keywords Fibromyxoma · Myxoma · Odontogenic · Mesenchymal tumor

Introduction

Rudolph Virchow first used the term “myxoma” in 1863 to describe abdominal and soft tissue lesions [1]. However, gnathic myxoma was not described until several decades later in 1947 by Thoma and Goldman as “a rare benign tumor of the tooth-bearing areas of the jaw bone” [2].

In 1964, Marcove et al. first used the term fibromyxoma in a report of 3 extragnathic lesions [3]. Fibromyxomas are similar to myxomas, as both myxomas and fibromyxomas exhibit a proliferation of primitive mesenchymal cells that produce an amorphous mucoid-rich intercellular matrix [4, 5]. While the world health organization (WHO) uses the terms “myxoma” and “fibromyxoma” interchangeably [6], some authors report that fibromyxomas tend to have more prominent collagen fibers than myxomas [4, 7].

Odontogenic fibromyxoma (also called odontogenic myxofibroma) is a relatively rare neoplasm and accounts for only 3–8% of all odontogenic tumors and cysts of the jaws [7]. This lesion is a benign tumor of mesenchymal origin that may contain odontogenic epithelium [8]. Fibromyxomas in the head and neck region originate either from the soft tissues or from the facial skeleton, albeit peripheral fibromyxomas are exceedingly rare [9, 10]. The clinical presentation is varied, although the majority of patients with odontogenic fibromyxomas present with a painless swelling [11]. However, patients may be symptomatic and may present with malocclusion, and loose or impacted

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teeth [11]. In severe cases, patients may present with parasesthesia of the mandibular nerve [12].

In this article, we report a case of a gnathic fibromyxoma in a female during her first trimester of pregnancy. We will review the clinical presentation, radiographic examination, histological features, differential diagnoses, and management of this rare neoplasm.

Case Report

A 22 year-old female in her first trimester of pregnancy presented to the Oral and Maxillofacial Surgery clinic, University at Buffalo, for evaluation of a right mandibular mass that had been gradually enlarging for the last 2–3 years. The patient reported discomfort when eating as she was biting on the mass during mastication. She denied any numbness or tingling in the lower lip or chin. She also denied fever, chills, night sweats or weight loss. Physical examination demonstrated an expansile mass involving the right mandible. The patient reported tenderness upon palpation of the mass. The tumor caused displacement of the right mandibular molar and premolar teeth. The mucosa overlying the neoplasm was intact and no gross ulceration or hemorrhage was observed. Head and neck exam was negative for any lymphadenopathy. Computed tomography (CT) scan revealed a septated, expansile mass in the body of the right mandible measuring 4.0×2.5 cm with displacement of the first and second right mandibular molars (Fig. 1 a–d). There were associated areas of multilocular radiolucency. An incisional biopsy was performed and the mass was as diagnosed as a fibromyxoma.

Given the diagnosis and extensive involvement of the body of the mandible, the patient underwent a segmental resection with approximately 1.0 cm margins. She was reconstructed with a 2.4 mm reconstruction bar. Because the patient was approximately 7 weeks pregnant, the decision was made to defer definitive reconstruction with a fibular free flap for a later time. The patient was admitted to the oral and maxillofacial surgery service postoperatively and managed concurrently with the obstetrics and gynecology service.

On resection, the tumor appeared as a white–pink multinodular, ill defined, partially encapsulated mass. Histologic examination revealed a partially circumscribed tumor extending to the anterior mandibular margin (Fig. 2 a–c). The tumor consisted of a proliferation of plumped, spindle mesenchymal cells with stellate cytoplasm in a background of interspersed collagen fibers amidst interstitial basophilic myxoid ground substance (Fig. 2b, c). Alcian blue staining highlighted the predominant myxoid nature of the neoplasm (Fig. 2d). Immunohistochemical staining for Ki-67 showed the tumor had a relatively low proliferative index of approximately 8% (Fig. 2e). Immunohistochemical stains were negative for

MUC4, p63, CD99, smooth muscle actin (SMA), Sox10, CD34 and S-100, supporting the diagnosis of fibromyxoma. A representative negative immunostaining for MUC4 is shown in Fig. 2f. The patient continues to be followed and remained free of disease 6 months post-surgery (Fig. 3).

Discussion

We report a rare case of gnathic fibromyxoma. We will review the clinical, radiographic, and histologic features of fibromyxoma. In addition, we will discuss differential diagnoses and patient management for this odontogenic neoplasm. Odontogenic fibromyxoma is a benign, aggressive neoplasm and it is important to distinguish it from less aggressive gnathic lesions and mesenchymal malignancies in order to ensure appropriate patient management.

Odontogenic Fibromyxoma Demographics and Clinical Presentation

The WHO uses the terms myxoma, odontogenic myxoma, and fibromyxoma interchangeably [6]. Therefore, since there are relatively few studies of fibromyxoma specifically, studies of the characteristics of odontogenic myxoma are likely relevant to fibromyxoma as well. In patients with odontogenic myxoma, the mean age at the time of diagnosis is 30 years (75% occur in the second to fourth decades), with a wide age range (1–73 years) [13]. These tumors display a female to male ratio of 1.5:1 and are twice as common in the mandible than the maxilla [13]. They can occur anywhere in the jaws but have a predilection for the molar and premolar regions [4]. Odontogenic myxomas are rarely observed in children under 10 years of age [14]. Consistent with our case, swelling is the most common clinical feature [10]. Fibromyxomas are generally asymptomatic and behave in a locally aggressive manner [4].

Imaging Characteristics of Fibromyxoma

The radiographic presentation of fibromyxoma is variable. Most fibromyxomas present as multilocular radiolucencies with well-defined borders, however it is not uncommon for these lesions to be unilocular [13]. The multilocular radiolucencies present different appearances including “soap bubble”, “honey comb”, “tennis racquet”, “wispy”, or “spiderweb” patterns [8, 10, 15]. While most odontogenic fibromyxomas present as radiolucencies, a small percentage are reported to be radiopaque or mixed radiolucent and radiopaque [13]. The most characteristic radiographic feature of fibromyxoma is the “tennis racquet” appearance. This is due to the fine straight bony trabeculation within the lesion that form

Fig. 1 Computed tomography reveals a mass in the body of the right mandible. **a** axial, **b** sagittal, and **c** coronal images are shown. **d** Three dimensional reconstruction reveals the extent of the tumor. **e** Pre-operative panoramic image is shown

square or triangular compartments [16]. The tumor may be scalloped between the roots of teeth and may cause expansion of the cortical plates. Additionally, displacement of teeth may be seen [10].

Gross and Histopathologic Characteristics of Fibromyxoma

Grossly, odontogenic fibromyxomas are generally gray-white to tan-yellow in color, unencapsulated,

well-delineated masses that may be rubbery, soft or gelatinous in texture [4, 9]. While formal histologic criteria to distinguish myxoma from fibromyxoma are lacking, microscopic examination of these lesions reveals a tumor composed of randomly oriented, morphologically bland stellate-to-spindle shaped cells embedded in a loose myxoid extracellular matrix with cells presenting with thin, long cytoplasmic prolongations that give the tissue characteristics of immature mesenchyme [17, 18]. Fibromyxomas exhibit a prominent hyalinized or collagenous background

Fig. 2 Histopathological findings are consistent with fibromyxoma. **a** Surgical specimen (low power view) showing the tumor mass and cortical bone (hematoxylin–eosin stain; original magnification $\times 10$). **b** Surgical specimen (medium power view). Hypocellular collagenized myxoid stroma exhibiting bland spindle mesenchymal cells organized in fascicles oriented in different directions (hematoxylin–eosin stain; original magnification $\times 200$). **c** Surgical specimen (high power view). Spindle to oval mesenchymal cells, some displaying a stellate cytoplasm. No cellular pleomorphism or mitotic figures are observed (hematoxylin–eosin stain; original magnification $\times 400$). **d** Alcian blue stain ($\times 400$) and immunohistochemical stains for **e** Ki-67 ($\times 400$) and **f** MUC4 are shown ($\times 400$)

Fig. 3 Post-operative panoramic image. The mandibular resection and reconstruction bar are shown. The patient remains free of disease 6 months post-surgery

[4, 7]. Islands of odontogenic epithelium are variably present, although these are thought to be a residual element rather than an integral part of the lesion [4]. Fibromyxomas express vimentin and are typically negative for S-100, CD34, SMA, and CD68 [19]. A summary of the reported demographics and histopathological characteristics of odontogenic fibromyxomas published within the last 10 years is provided in Table 1 [14, 18, 20–26].

The Histogenesis of Odontogenic Fibromyxoma is Uncertain

Under the WHO classification of odontogenic neoplasms, odontogenic myxomas and fibromyxomas are classified as mesenchymal odontogenic tumors (with limited or without odontogenic epithelium) [27]. These tumors are thought to be of odontogenic origin due to the fact that they arise in tooth-bearing areas of the maxillofacial bones and are reported almost exclusively in the jaws [4]. It is hypothesized that they may be derived from embryonic mesenchymal elements of dental origin including the dental follicle, dental papilla or periodontal ligament [28]. Additional support of an odontogenic origin is suggested by the fact that odontogenic myxoma may be associated with an unerupted tooth [13, 29].

However, other careful studies dispute an odontogenic origin for this neoplasm. Goldblatt conducted an ultrastructural study on an odontogenic myxoma and was unable to demonstrate conclusively that the tumor was of odontogenic origin. In this study, examination of an odontogenic myxoma by electron microscopy revealed that the principal tumor cells are fibroblast-like secretory cells that produce an acid mucopolysaccharide matrix. Thus, the myxoma cell is similar to the fibroblasts of the dental papilla, dental pulp, and odontogenic fibroma, a finding that suggests

an odontogenic origin for this tumor. However, an odontogenic origin cannot be proved on the basis of ultrastructural evidence alone, as the myxoma cell also resembles cells of the umbilical cord. Thus, it is possible that the myxoma may originate from primitive non-odontogenic pluripotent mesenchymal cells [30]. Similarly, in a study conducted on a mandibular myxoma, the matrix of the myxoma was found to be distinct from that of the dental pulp and the periodontal ligament [31]. A more recent study using a cell line derived from a human odontogenic myxoma found that the tumor cells have secretory capacity and are of mesenchymal origin [5]. Thus, while odontogenic myxomas (and fibromyxomas) resemble components of normal developing teeth, it is unclear at present as to whether they actually originate from these structures.

Differential Diagnosis: Clinical

The clinical presentation of odontogenic fibromyxoma is relatively non-specific, as patients with fibromyxoma typically present with a painless swelling of the posterior mandible [10]. On the basis of its clinical presentation, the differential diagnosis for fibromyxoma includes a variety of gnathic odontogenic lesions, including ameloblastoma, central odontogenic fibroma (COF), odontogenic keratocyst, vascular conditions (central hemangioma), and non-neoplastic lesions such as central giant cell granuloma. Malignant neoplasms that arise in bone may also be considered.

Differential Diagnosis: Radiographic

Fibromyxomas are not easily distinguished from other radiolucent lesions of the jaws. Typically, fibromyxomas

Table 1 Demographic and Histologic Features of Recently Reported Fibromyxomas

Case	Location	Age	Gender	Histopathology	Ref.
1	Mandible	12	M	Abundant fibrocollagenous tissue in a myxoid stroma. Stellate-shaped cells relatively uniform in size. Cells evenly spaced within relatively avascular, fibrillar, mucinous matrix	[25]
2	Mandible	8	M	Fibromyxomatous tissues with blood vessels and collagen fibers	[23]
3	Mandible	40	F	Spindle round or stellate cells with mild nuclear pleomorphism and myxoid stroma. Rare mitotic figures. Stroma mainly myxoid and contained reticulin and collagen fibers	[24]
4	Maxilla	46	M	Randomly arranged stellate, oval and spindle-shaped cells in a myxoid stroma	[18]
5	Maxilla	32	F	Abundantly myxoid connective stroma, areas of moderately dense collagen fibers, and strands of odontogenic epithelium within the connective tissue stroma	[22]
6	Maxilla	12	F	Spindle-shaped fibroblasts in loose myxoid tissue	[26]
7	Mandible/ Maxilla	13	F	Relatively hypocellular tumor tissues formed of spindle and stellate cells within a predominantly collagenous, focally myxoid background with intervening thin-walled vessels	[21]
8	Mandible	21	M	Hypocellular, loosely arranged spindle-shaped stellate cells with a loose myxoid intracellular matrix. Mildly to moderately collagenous fibromyxoid stroma with benign stromal cells	[20]
9	Mandible	6	M	Spindle to stellate cells in a variable myxoid and collagenized stroma. Bland cellular morphology with no significant nuclear pleomorphism or mitotic activity. Small rest of odontogenic epithelium seen	[14]

show a “tennis racquet” appearance, demonstrating angular or straight trabeculations, which frequently form square or triangular compartments [16]. However, they may also exhibit “soap bubble” or “honey-comb” features, and this presentation is also seen with ameloblastomas and odontogenic keratocysts [16]. Of note, ameloblastomas can be distinguished from fibromyxomas by magnetic resonance imaging (MRI) when a contrast agent is administered, as ameloblastomas show strong enhancement of the solid portion of the tumor whereas myxomas show homogenous high signal intensity [18].

Other lesions that appear radiolucent or mixed radiolucent/radiopaque should be considered, including central giant cell granuloma, ameloblastic fibroma, and calcifying epithelial odontogenic tumor [13]. Since approximately one-third of fibromyxomas have poorly defined borders, malignant lesions should also be included in the radiographic differential diagnosis [13].

Differential Diagnosis: Histopathology

Histopathologically, fibromyxomas can mimic normal developing teeth, and both benign and malignant lesions. It is important to distinguish myxomas and fibromyxomas from dental follicles and dental papillae. In contrast to odontogenic fibromyxoma, the dental papilla is bordered by odontoblasts [4]. In addition, myxomas lack odontogenic epithelia (cords and islands) that are typically seen in dental follicles and odontogenic fibromas [4]. Of note, a study conducted by the Armed Forces Institute of Pathology found that dental papilla was the most common developing dental tissue to be misdiagnosed as odontogenic myxoma [32].

Fibromyxomas should also be differentiated from chondromyxoid fibroma, odontogenic fibroma, desmoplastic fibroma, and myxoid neurofibroma (MNF). Although chondromyxoid fibroma rarely involves the jaws, this lesion should be considered as it consists of nodular myxoid tissue with scattered giant cells along with areas of cartilaginous differentiation [33]. The pseudolobules of myxomatous tissue that are found in chondromyxoid fibroma are separated by septae of small, darkly staining spindle to stellate cells with hyperchromatic nuclei that concentrate at the periphery of the lobules [34]. Dystrophic calcification or mineralization resembling osteoid may be seen [35]. However, this lesion can readily be distinguished from fibromyxoma by the presence of chondroid and calcified elements. Moreover, septae or pseudolobules are not observed in fibromyxomas [36]. Furthermore, fibromyxomas express vimentin and are typically negative for S-100, while chondromyxoid fibromas are S-100 positive [36].

COF should also be considered in the differential diagnosis of fibromyxoma. This lesion is composed of mature

collagenous fibrous tissue that may contain odontogenic epithelium and cementum-like or dentinoid calcified material [34, 37]. The odontogenic epithelium is arranged in nests or long strands that are present throughout the lesion [37]. This is in contradistinction to fibromyxomas, which typically display a prominent myxoid component and lack calcifications [4]. COF can be readily distinguished from fibromyxoma on routine H&E staining and immunohistochemical studies are not required to confirm the diagnosis.

In addition, desmoplastic fibroma may mimic fibromyxoma histologically. Desmoplastic fibromas are rare aggressive intraosseous lesions that are seen more commonly in the mandible [38]. This neoplasm is comprised of proliferative spindle cells within a bland collagenous stroma. The spindle cells are uniform in appearance and few mitoses are seen [39]. Spindle cells often exhibit short fascicles and bundles with mild swirling. This lesion is of myofibroblastic origin, so focal SMA positivity may be useful to distinguish it from fibromyxoma [39].

MNF may also resemble fibromyxomas microscopically. MNF contains elongated spindle cells with wavy nuclei, intralesional neurites, and has “wire-like” collagen fibrils [36, 40]. The MNF is usually well-demarcated but is not encapsulated [40]. MNF can be distinguished from fibromyxoma because the latter lacks neurites and is usually poorly circumscribed [4]. S-100 staining is rarely seen in fibromyxoma, while this marker is usually positive in MNF [36].

Finally, myxomatous components can be seen in several malignant neoplasms, such as low-grade fibromyxoid sarcoma (LGFMS), myxoid leiomyosarcoma, myxoid liposarcoma, extraskeletal myxoid chondrosarcoma, and the embryonal and botryoid variants of rhabdomyosarcoma [36, 40]. These tumors typically exhibit increased cellularity and pleomorphism [9]. In addition, high mitotic activity is suggestive of malignancy [34].

LGFMS has both myxoid and fibrous components. LGFMS typically occurs in the proximal extremities, but also is reported in the craniofacial complex [41]. Although it is classified as malignant, this lesion has minimal nuclear atypia and rare mitoses. Prominent arching vasculature and collagen rosettes are also seen in these tumors [41]. LGFMS may be difficult to distinguish from other bland fibrous and myxoid neoplasms, so adjunctive tests are needed when it is suspected. LGFMS typically displays the *FUS/CREB3L2* gene fusion [t(7;16)(q34;p11)] [41]. In addition, immunohistochemistry for MUC4 may be helpful in establishing the diagnosis. MUC4 shows strong cytoplasmic staining and was positive in all head and neck tumors examined in one study [41]. Therefore, gene rearrangement studies and immunohistochemistry are warranted when LGFMS is suspected.

Table 2 Pattern of immunostaining that aids in the differential diagnosis of fibromyxoma

	S-100	Desmin	p63	EMA	Caldesmon	CD34	MUC4	CK	SMA	MyoD1	Myogenin
Odontogenic fibromyxoma	–	–	–	–	–	–	–	–	–	–	–
Desmoplastic fibroma	–	–	–	–	–	–	–	–	+	–	–
Chondromyxoid fibroma	+	–	–	–	–	–	–	–	+	–	–
MNF	+	–	–	+/-	–	–	–	–	–	–	–
LGFMS	–	–	+/-	–	–	–	+	–	–	–	–
Leiomyosarcoma	–	+	–	+/-	+	–	–	+/-	+	–	–
Embryonal rhabdomyosarcoma	–	+	+	–	–	–	–	–	+/-	+	+

Genetic and immunohistochemical studies are of value in identifying other sarcomatous lesions with myxoid components. Specifically, the *FUS-DDIT3* rearrangement is seen in myxoid liposarcoma [t(7;16)(q34;p11)], and the *EWSR1-NR4A3* fusion has diagnostic utility for identification of extraskeletal myxoid chondrosarcoma [t(9;22)(q31;q12)] [42]. Muscle markers may be helpful in distinguishing leiomyosarcoma and rhabdomyosarcoma from fibromyxoma, as these tend to be negative in the latter. Leiomyosarcomas stain with antibodies to SMA, desmin, and caldesmon [43], while embryonal rhabdomyosarcoma shows positivity for MyoD and myogenin [44]. A summary of immunohistochemical stains that can be used to distinguish fibromyxoma is provided in Table 2 [40, 45–54].

Management and Prognosis

While there are no universally accepted treatment recommendations for the management of fibromyxoma, is important to consider the aggressive nature of this neoplasm in patient management decisions. Although the recommended treatment is usually surgical excision, approaches differ depending on the size of tumor and include conservative surgical excision, enucleation and curettage, curettage with and without electrical or chemical cautery, en bloc resection and wide resection with and without bone grafting [4, 55, 56].

Recurrence rates between 25% and as high as 43% are reported for gnathic fibromyxomas [55, 57]. In some studies, a high rate of recurrence is documented after conservative therapy. This is attributed to the incomplete removal of the lesion rather than the intrinsic biological behavior of the lesion [58]. Due to the tumor's local aggressive biological behavior and high potential for recurrence, wide surgical resection is recommended [59, 60]. Radiotherapy is generally agreed to be ineffective in the treatment of fibromyxoma [4]. Resection with 1.0–1.5 cm bony margins and one uninvolved anatomic barrier margin is suggested [4]. Follow-up of the patient is warranted due to the high recurrence potential of this tumor.

Conclusion

In conclusion, odontogenic fibromyxoma is a rare, aggressive neoplasm that occurs most commonly in the posterior mandible of females. Histopathologic examination is essential to distinguish this lesion from other benign processes and malignancies to ensure proper patient management.

Compliance with Ethical Standards

Conflict of interest The authors do not have any relevant conflict of interests.

Research Involving Human and Animal Participants This article does not contain any studies with human participants or animals performed by any of the authors.

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