Collagenous Myofibroblastic Tumor of the Mandible: Case Report of a Unique Locally Aggressive Neoplasm

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Received: 13 February 2009 / Accepted: 18 November 2009 / Published online: 10 December 2009
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Abstract We report a locally aggressive collagenous myofibroblastic neoplasm of the mandible in an 18-year-old male. Clinically, the lesion presented with rapid growth and irregular mandibular bone destruction. Grossly, the tumor was 10 cm in greatest dimension, light-tan, firm, and involving the posterior one-thirds of the body and inferior half of the left mandibular ramus. Histologically, the lesion was composed of a loose spindle cell proliferation interspersed with periodic dense bands of collagen. The spindle cells reacted positively to smooth muscle actin, calponin, and focally to desmin and were negative for S-100, pancytokeratin, CD99, CD34 and caldesmon, supporting myofibroblastic derivation. At our 4 year follow-up, the patient remained free of local recurrence and surgery related complications. The clinicopathologic findings and the differential diagnosis of this lesion is presented and discussed.

Keywords Mandible · Myofibroblastic neoplasm · Mesenchymal tumors · Odontogenic tumors

Introduction

Intraosseous mandibular tumors comprise a wide range spectrum of clinicopathologic entities representing both odontogenic and non-odontogenic origins. Most of these tumors are of odontogenic derivation and classified based on their cellular composition into epithelial, mesenchymal, or mixed subtypes [1]. The gross, radiographic, and pathologic features and the natural history of these tumors are well documented [1]. We report a previously undescribed spindle cell collagenous tumor of myofibroblastic differentiation and discuss the histogenesis and the differential diagnosis.

Case Report

An 18-year-old African American male was referred to the Department of Head and Neck Surgery, M.D. Anderson Cancer Center for evaluation and treatment of a tumor involving his right posterior mandible. The patient reported that he underwent dental treatment of the 2nd molar approximately 6 months prior to the presentation. His dentist restored his mandibular 2nd molar which was affected by dental caries. Four weeks after his initial treatment, he returned to his dentist complaining of pain in his right posterior mandible. Radiographic examination performed at that time revealed a radiolucent lesion associated with his mandibular second molar which was interpreted by his dentist as a periapical abscess. The patient elected to have the tooth extracted but after weeks, the patient developed pain and swelling in the right posterior mandible. His dentist treated him with ibuprofen, amoxicillin and clindamycin without any significant clinical benefit. His mandibular swelling continued to enlarge

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which prompted his dentist to perform a panoramic radiographic examination which showed a large, ill-defined multilocular expansile radiolucency in his right posterior mandible producing “a soap-bubble” appearance. The patient was subsequently transferred to The University of Texas M.D. Anderson Cancer Center for comprehensive evaluation and treatment.

The patient’s medical history, review of systems and family history were unremarkable. Clinical examination revealed a firm, diffuse swelling involving the right sub-mandibular area extending into the facial aspect of the angle of the mandible. Intraorally, the lingual and facial surfaces of the mandibular swelling were covered by intact mucosa and the prior extraction site was healed and covered by alveolar mucosa. There were no signs of infection such as, erythema, purulent drainage, fluctuance or indurated swelling of the surrounding soft tissue. His right tonsil was displaced medially due to the expansion of the mandibular ramus. All remaining right mandibular teeth were vital with no evidence of increased mobility. The remainder of the physical examination was non-contributory and regional lymph nodes were non-palpable.

Radiologic Findings

A CT scan revealed a lytic expansile mass which completely replaced the posterior third of the body and inferior ramus of the mandible including the roots of the mandibular 3rd molar. This lesion measures about 5 cm in oblique anterior-posterior dimension and 4 cm in oblique lateral dimension. There was thinning of the lingual cortical plate but the cortical bone was intact without disruption (Fig. 1).

Surgery

At the time of initial presentation, a fine needle aspiration of the lesion was performed. Subsequent incisional biopsy was similarly non-diagnostic. At surgery, an intraoperative frozen biopsy was performed and a diagnosis of “myxoid neoplasm with collagen deposition of undetermined malignant potential” was rendered. Because of the uncertain malignant diagnosis and the insufficient functional mandibular bony segment after complete surgical removal of the mass, a wide en bloc resection of the mandibular tumor was performed. The posterior segment of the mandible and inferior ramus were resected 2 cm posterior to the mental foramen to the ramus, sparing the condyle. The margins of the resected specimen were confirmed to be free of tumor. The mandibular defect was reconstructed using vascularized free left fibular flap and the patient recovered with an uneventful post-operative course. The wound was completely healed and there have been no recurrences or surgery related complications during 4 years follow-up period.

Fig. 1 CT scan axial image at level of mandible showing an expansible, lytic mass within the right posterior mandibular body

Gross Pathology

The specimen is consisted of an en bloc resection of posterior third of the body and inferior ramus of the right mandible. Grossly, the lesion consisted of a homogenous, firm and fibrotic mass within the excised mandibular segment containing a fully erupted 3rd molar at the angle of the mandible. The tumor mass measured $5 \times 4 \times 3$ cm and was surrounded by a thin rim of mandibular cortical bone and composed of light tan and firm soft tissue mass (Fig. 2).

Fig. 2 A gross photograph of the resected right segment of the mandible revealing complete replacement of the bone with homogenous soft tissue mass

Microscopic Examination

Histopathologic examination of the resected mandibular segment revealed a non-encapsulated, locally invasive, spindle cell tumor (Fig. 3a). This tumor was composed of a diffuse proliferation of spindled and polygonal cells in a predominantly fibromyxoid stroma interspersed with dense bands of collagen (Fig. 3b). The collagen bands were organized in densely packed collagen fibers and regularly spaced within the tumor. In contrast to collagen depositions in other fibrous lesions, they were uniform in thickness (measures). Tumor cells were characterized by indistinct borders of pale cytoplasm with occasional vacuolation and centrally placed round or ovoid nuclei. Tumor cells exhibited rare mitoses with a mitotic index ranging from 0 to 1 mitotic figure per high-power field. Cellular pleomorphism, nuclear atypia and tumor necrosis are not apparent.

Immunohistochemistry

Immunohistochemical studies revealed that the tumor cells reacted strongly to smooth muscle actin (Fig. 3c), calponin and focally to desmin (Fig. 3d). Tumor cells were uniformly negative for pan-cytokeratin, CD99, CD34, S-100, and caldesmon [3–5]. Nuclear immunostaining for Ki-67, a cell proliferation marker, was rare and accounted for

less than 1% of tumor cells. Ki-67 labeling index was calculated as the percentage of Ki-67-positive tumor cells that showed nuclear staining among 1,000 cells counted in three randomly selected high-power ($\times 400$) fields [2].

Discussion

We report a previously undescribed, locally aggressive, myofibroblastic tumor with a distinctive, dense, collagenous deposition in the mandible. The tumor's locally aggressive growth and unique histopathologic features combined with the clinical presentations distinguish this lesion from other spindle cell tumors of the head and neck. The immunohistochemical studies support an origin from myofibroblastic or undifferentiated primitive ectomesenchymal cells with myofibroblastic transformation [3–6]. The differential diagnoses of this tumor include a spectrum of non-odontogenic and odontogenic neoplasia of mesenchymal origin. Non-odontogenic spindle cell lesions that should be considered are myofibroma, fibromatosis, solitary fibrous tumor, fibrous histiocytoma, inflammatory pseudotumor, neural and smooth muscle lesions. These tumors exhibit benign or locally aggressive growth with uncertain malignant potential. In contrast to these entities the clinical, radiographic, histopathologic and immunohistochemical

Fig. 3 Photomicrographs of the mandibular tumor displaying loose spindle cell proliferation with collagen bank (a and b). The tumor cells show positive cytoplasmic staining for smooth muscle actin (c) and calponin (d)

characteristics of the current case are at variance with these lesions.

Myofibroblastic tumors are composed of spindle mesenchymal cells which share myofibroblastic and smooth muscle cell phenotype may occur in both soft tissue and bone [7–12]. A subset of these myofibroblastic tumors has demonstrated a low malignant potential with a tendency for local recurrence and [6, 13–16] include myofibrosarcoma and low-grade myofibroblastic sarcoma [6, 14–16]. These lesions typically lack the inflammatory component of benign inflammatory myofibroblastic lesions [17, 18]. Although majority of the aggressive myofibroblastic tumors involve the deep soft tissues, several examples of myofibroblastic tumors involving the axial skeletal and facial bones have been documented [6, 19, 20]. The histopathologic and immunohistochemical features of the current case suggest that this case may represent a non-axial form of myofibroblastic tumor [6]. Similar to the current case, myofibroblastic tumors also express calponin, desmin and smooth muscle actin but are negative for caldesmon [6].

Myofibromas affect young adults with a predilection for the head and neck area including jaw bones and demonstrate a nodular biphasic pattern of spindle cells within a myxoid background and hemangiopericytoma-like vascular stromal pattern [21, 22]. Moreover, in contrast to the current case which is focally positive for desmin, myofibromas are negative for this marker [23]. Also, fibromatosis and nodular fasciitis which may exhibit collagen formation, should be considered in this setting. These lesions, however, are purely fibroblastic and are negative for smooth muscle specific actin and caldesmon. In addition, the lack of feathery spindle cell features, extravasated red blood cells, and an inflammatory infiltrate excludes nodular fasciitis [24]. Well differentiated osteo- and chondrosarcomas with predominantly myxoid and spindle cell components should also be differentiated from this tumor. Combined clinical, radiologic and histological analysis, readily excludes these entities. Similarly, low-grade leiomyosarcoma and neurogenic sarcoma which may occur in the mandible can be excluded from the differential diagnosis, based on the cytomorphologic features and negative reactivity of tumor cells to caldesmon and S-100 protein [25].

Mesenchymal tumors of odontogenic origin that should be differentiated from our case include odontogenic myxoma/fibromyxoma and simple type odontogenic fibroma [1, 26]. Intraosseous (central) odontogenic fibroma is derived from odontogenic ectomesenchyme, and is composed of dense cellular fibrous connective tissue with (WHO type) or without (simple type) scattered islands of odontogenic epithelium [1, 26]. Foci of calcified collagenous material resembling dysplastic cementum and tubular dentin are also frequently noted in central odontogenic

fibroma [1, 26]. Odontogenic fibroma (WHO type) typically has scattered nests of odontogenic epithelium that were not seen in this case. However, odontogenic fibromas are not positive for immunohistochemical markers of smooth muscle features. Odontogenic myxoma, a benign odontogenic tumor of ectomesenchymal origin, is locally invasive and its histologic findings are similar to that of dental papilla of the developing tooth [1, 26]. Odontogenic myxoma is characterized by stellate- and ovoid-shaped cells with variable amounts of fine collagen fibrils embedded within the myxoid stroma [1, 26]. Some of these lesions show extensive collagen deposition within the myxoid stroma and are described as odontogenic myxofibroma [1, 26]. The current tumor shares some of the phenotypic features manifested in both odontogenic fibroma and myxoma.

Based on the histomorphologic and immunophenotypic characteristics of this tumor, we postulate it's most likely the result of myofibroblastic transformation of an odontogenic mesenchymal cell progenitor [13]. The finding of collagen deposition in other myofibroblastic lesions including nodular fasciitis [24] and the experimental evidence, linking collagen formation in pulmonary myofibroblastic fibrosis to the elevation of TGF- β 1 lend further credence to this contention [27–30]. Of further interest, is the association of the FIZZ1-gene (found in inflammatory zone) up-regulation in myofibroblastic proliferative lesions [31]. In vitro studies using a FIZZ1-expressing plasmid induced myofibroblastic differentiation independent of TGF- β 1 expression. The role of this gene in myofibroblastic tumorigenesis, however, remains to be investigated.

On the basis of the phenotypic and the immunohistochemical findings, we contend that our case represents a unique myofibroblastic variant in the spectrum of fibromyxoid neoplasms of the mandible. From a histogenetic view, an ectomesenchymal origin is likely and this, in itself, does not exclude odontogenic elements.

Acknowledgments The authors thank Dr. John G. Batsakis for his review and constructive suggestions.

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