Desmoplastic fibroma of the mandible: a rare gnathic bone tumor with a review of the literature

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ABSTRACT

Desmoplastic fibroma (DF) is a rare bone tumor, which is known to involve mostly the gnathic bones. In this setting, the clinical presentation is usually represented by a bulging tumor of the face. Radiologically, the tumor is usually characterized by an expansile lytic bone lesion. The histopathology of the tumor shows a poorly circumscribed hypocellular lesion rich in collagen fibers with interspersed spindle cells having bland nuclear chromatin. Despite the lack of mitoses and nuclear pleomorphism, DF has an aggressive nature, presenting as a destructive growth causing entrapment of neuro-vascular bundles, sinusitis, or trismus. Some cases of DF show mutations in the adenomatous polyposis coli pathway shown by nuclear localization of the $\beta$-catenin protein. Few reports showed an association with tuberous sclerosis, though most of these cases were sporadic. We discuss a rare case of desmoplastic fibroma involving the mandible, and a review of the literature of the DF cases involving the gnathic bones.

Keywords
Bone Neoplasms; Fibroma, Desmoplastic; Mandible; Maxilla; Histology

INTRODUCTION

Desmoplastic fibroma (DF) is an unusual bone tumor having a myofibroblastic origin, akin to the desmoid tumor seen in the soft tissue.\textsuperscript{1} Jaffe\textsuperscript{2} is credited to have described DF as a separate entity in 1958 and gave it the present nomenclature. As per the WHO classification of soft tissue and bone tumors of 2013; DF is classified as a benign tumor;\textsuperscript{3} however, it is reported to present aggressive behavior.\textsuperscript{4} In this article, we discuss a case of DF affecting the mandible and review the available literature data on DF affecting the gnathic bones, in an attempt to better understand the clinical and pathological characteristics of this rare tumor.

CASE REPORT

A 5-year-old girl was reported to the Head and Neck Surgery Department with the complaint of progressive right facial swelling over the last 2 years that reached the size of 7 × 6 cm at the initial evaluation. The mass involved the right side of the mandible with regular margins, but did not reduce the mouth opening. A contrast-enhanced computed tomography (CT) showed a 6.5 × 6 × 4.5 cm lytic lesion involving the right ramus and body of the mandible (Figure 1).

The child was taken up for the excision of the tumor followed by reconstruction of the mandible with a costochondral graft and plating. The excised

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The specimen (hemimandibulectomy) had an expansile lesion with an intact cortex (Figure 2A). At the tumor’s cut surface, a poorly circumscribed light-greyish firm lesion was seen (Figure 2B). The histology showed an infiltrative hypocellular collagenized stroma with interspersed thin bone trabeculae. The bone trabeculae lacked osteoblastic rimming. The spindle cells had bland nuclear chromatin and indistinct cell borders, which appeared to merge with the surrounding fibrous stroma (Figure 3A).

These spindle cells showed a dense and diffuse cytoplasmic positivity for vimentin (Figure 3B) and cytoplasmic positivity for smooth muscle actin (SMA) (Figure 3C). β-catenin immunohistochemistry was negative (Figure 3D). At the end of 5 months of follow-up, the girl is asymptomatic without any evidence of recurrence.

DISCUSSION

DF is a rare benign neoplasm of the bone with the incidence of 0.1% of all bone tumors. In a Mayo Clinic study, nine cases of DF were retrieved out of a total of 9,000 bone tumors. Of these, the mandible was the most common site of involvement, indicating the predilection of DF for the gnathic bones. The first case of DF to involve the gnathic bones was reported in 1965 by Griffith and Irby, in their description of an 8-year-old girl who presented with a moon-like facies secondary to a palpable expansile mass in the left side of the mandible.

A literature search was made using MESH terms “Desmoplastic fibroma,” “mandible,” and “maxilla” using the PubMed database. A total of 54 cases of DF involving the gnathic bones were found (Table 1). 42 cases (77%) involved the mandible, while the remaining showed the involvement of the maxilla. Most of the cases presented in childhood and adolescence, with 34 cases occurring between the age of 2 years and 16 years. However, DF has also been reported in adults, including a 60-year-old woman. There appears to be a female preponderance with a female to male ratio of 2.25:1. The mean tumor size was approximately 40 mm. Radiologically, most
Figure 3. Photomicrographs of the tumor. A – Hypocellular collagenized stroma with thin bony trabeculae (H&E, 400X); B – Diffuse cytoplasmic positivity for vimentin in the tumor cells and the endothelial cells (400X); C – Cytoplasmic positivity for SMA in the tumor cells (400X); D – Absence of staining by ß-catenin in the tumor cells with positive internal control (endothelial cells) (400X).

Table 1. Comparison of the reported cases of gnathic desmoplastic fibroma

| Author            | Age | Sex | Site | Size (mm) | Imaging | ß-catenin (+) | Complication/Association               |
|-------------------|-----|-----|------|-----------|---------|---------------|----------------------------------------|
| Griffith & Irby⁵  | 8   | F   | Md   | 40        | LET     | Na            | na                                    |
| Sleeman et al.¹²  | na  | na  | Mll  | na        | na      | Na            | na                                    |
| Miyamoto et al.¹¹ | 29  | F   | Md   | 71        | LET     | Na            | Associated with tuberous sclerosis    |
| Cranin et al.⁷    | 30  | M   | Md   | na        | na      | Na            | na                                    |
|                   | 9   | M   | Md   | na        | na      | Na            | na                                    |
| Iwai et al.¹⁰     | 3   | F   | Md   | na        | MLET    | Na            | na                                    |
| Hopkins et al.⁹   | 13  | M   | Md   | 50        | LET     | na            | na                                    |
|                   | 19  | F   | Md   | 80        | LET     | na            | na                                    |
| Templeton et al.¹⁴| 6   | F   | Md   | 40        | LET     | na            | Difficulty in opening mouth           |
| Bakaeen & Rajab¹⁵ | 4   | F   | Md   | 20        | LET     | na            | na                                    |
| Cupero et al.¹⁶   | 14  | F   | Mll  | 60        | LET     | na            | na                                    |
| Smith et al.¹⁷    | na  | na  | Mll  | na        | na      | na            | na                                    |

F = female; LET-lytic expansile tumor; Lsba = lytic soap bubble appearance; M = male; Md = mandible; Mll = maxilla; mm: millimeter; MLET = multilocular lytic expansile tumor; na = not available; sbpr = sunburst periosteal reaction; Zy= zygoma.
Table 1. Continued...

| Author                  | Age | Sex | Site | Size (mm) | Imaging | β-catenin (+) | Complication/Association                      |
|-------------------------|-----|-----|------|-----------|---------|--------------|-----------------------------------------------|
| Herford et al.          | 11  | F   | Md   | 40,20     | MLET    | na           | Multiple asynchronous                         |
| Kaplan & Torske         | 3   | M   | Md   | 40        | LET     | na           | Extension into soft tissue                    |
| Hauben et al.           | 44  | F   | Md   | na        | na      | Nuclear      | na                                            |
| Vargas-Gonzalez         | 14  | M   | Mill | 80        | Lsba    | na           | Associated with tuberous sclerosis            |
| Ikeshima & Utsunomiya   | 35  | M   | Md   | 82        | MLET    | na           | na                                            |
| Wippold et al.          | 6   | F   | Md   | 44        | LET     | na           | Soft tissue extension                         |
| Moorjani & , Stockton   | 6   | F   | Md   | na        | LET     | na           | Perineural extension/recurrence               |
| Said-Al-Naief et al.    | 8   | M   | Md   | na        | LET     | na           | na                                            |
| Rius Perisa et al       | 5   | M   | Md   | 50        | LET     | na           | Loose teeth                                   |
| Chen et al.             | 4   | M   | Md   | na        | LET     | na           | na                                            |
| Iatrou et al.           | 10  | M   | Md   | na        | LET     | na           | Temporomandibular dysfunction                 |
| Shi et al.              | 15  | na  | Md   | na        | LET     | na           | Soft tissue extension                         |
| Salah et al.            | 2   | F   | Mill | 25        | LET     | na           | na                                            |
| Chemli et al.           | 16  | F   | Md   | na        | LET     | na           | na                                            |
| Reid et al.             | 60  | F   | Md   | 15        | LET     | na           | na                                            |
| Schneider et al.        | 23  | M   | Md   | 13        | LET     | na           | na                                            |
| Boedeker et al.         | 44  | F   | Md   | 25        | LET     | na           | Loose teeth                                   |
| Averna et al.           | 3   | F   | Md   | na        | MLET    | na           | na                                            |
| Shekhar et al.          | 10  | M   | Md   | na        | na      | na           | na                                            |
| Mir-Mari et al.         | 34  | M   | Mill | 60        | LET     | na           | na                                            |
| Azola et al.            | 18  | M   | Mill | 26        | LET     | Nuclear      | Nasal obstruction                             |
| Tandon & Garg           | 8   | F   | Mill | 64        | LET     | na           | Associated with tuberous sclerosis            |
| Bontemps et al.         | 23  | F   | Zy   | 20        | MLET    | na           | na                                            |
| Jamali et al.           | na  | na  | Mill | na        | LET     | na           | na                                            |
| Ferri et al.            | 3   | F   | Md   | 45        | na      | na           | na                                            |
| 2                       | F   | Md   | 40    | na        | na      | na           | na                                            |
| 2                       | F   | Md   | na    | na        | na      | na           | na                                            |
| Gondak et al.           | 49  | M   | Md   | 30        | na      | Nuclear      | Sinusitis                                     |
| Flucke et al.           | 8   | F   | Md   | 60        | na      | Nuclear      | Soft tissue extension                         |
| 2                       | M   | Md   | 3     | na        | na      | Nuclear      | na                                            |
| Guerrero et al.         | na  | na  | Md   | na        | na      | na           | na                                            |
| Woods et al.            | 13  | F   | Md   | 25        | MLET    | Negative     | na                                            |
| 57                      | F   | Md   | 12    | LET       | Negative  | na           | na                                            |
| 20                      | F   | Md   | na    | LET       | Nuclear   | na           | na                                            |
| Gersak et al.           | 3   | M   | Md   | 34        | LET, sbpr| na           | Soft tissue extension                         |
| Khatib & Pogrel        | 8   | F   | Md   | 26        | LET     | na           | na                                            |
| 9                       | F   | Md   | 25    | LET       | na        | na           | na                                            |
| 2                       | F   | Md   | 25    | LET       | na        | Soft tissue extension                         |
| 2                       | F   | Md   | na    | LET       | na        | Soft tissue extension                         |
| Khan et al.             | 23  | F   | Md   | 5         | LET     |equivocal    | na                                            |
| Skinner et al.          | 3   | M   | Md   | 50        | LET     | na           | na                                            |

F = female; LET-lytic expansile tumor; Lsba = lytic soap bubble appearance; M = male; Md = mandible; Mill = maxilla; mm: millimeter; MLET = multilocular lytic expansile tumor; na = not available; sbpr = sunburst periosteal reaction; Zy = zygoma.
of the cases were characterized by an osteolytic expansile lesion with cortical thinning. Similarly, multilocular lytic lesions were reported in a few cases, and a sunburst appearance in those tumors with soft tissue extension.3,6-12 Frick et al., 13 in a retrospective study comprising 95 DF cases showed that osteolytic lesions with prominent T2 shortening in the magnetic resonance imaging (MRI) study makes the diagnosis of intraosseous DF plausible.

Grossly, the tumor is poorly circumscribed within the bone having a rubbery fibrous appearance.3 Only one case of multiple asynchronous DF involving the gnathic bones was reported.18 Histologically, the lesion is poorly demarcated and characterized by the presence of hypocellular collagen-rich stroma with few remnants of thin bony trabeculae.4 The sparse fibroblasts have uniform nuclei with a paucity of mitosis.1 The spindle cells stain for antibodies to muscle-specific markers, such as SMA (53%-77%).3,19 The differential diagnosis on histology included low grade fibrosarcoma (LGF), fibrous dysplasia (FD) and low-grade osteosarcoma (LGO).3 LGF may not show the characteristic herring-bone pattern with low to moderate cellularity.47 However, in addition to the similar low cellularity, DF shows cells with indistinct cell borders with an absence of nuclear atypia, and these cells are seen to encase boy trabecular spicules. FD is characterized by numerous irregularly shaped curvilinear woven bone, intervening hypocellular connective tissue composed of bland fibroblastic cells, and the presence of retraction of the bone from adjacent connective tissue.48 LGO shows focal chondro-osseous differentiation or myxoid areas with the cells showing anisocytosis. LGO has a high Ki67 proliferative index and is positive for P53.49 The involvement of adenomatous polyposis coli (APC)/β-catenin pathway is well established in desmoid fibromatosis.50 The morphological similarity has led some researchers to look for involvement of the APC/β-catenin pathway in cases of DF. However, the poor yield of DNA from decalcified sections has always been a hindrance.19,42 Flucke et al.42 showed the presence of a classic hot spot mutation 121 A>G in exon 3 of the CTNNB1 gene, which is also seen in cases of desmoid fibromatosis.41 The expression of β-catenin by immunohistochemistry in DF specimens led to conflicting results, with approximately six cases reporting a nuclear expression, while the others showed equivocal or absent staining for β-catenin.3,19,36,41,42,45 None of the reported cases had an associated familial adenomatous polyposis syndrome. Thus, the role of APC/β-catenin pathway cannot be excluded as part of the tumorigenesis; however, in the same breath, the findings point towards a far less essential role when compared to cases of desmoid fibromatosis. Though no definite etiological factor has been found, the literature data showed three cases to be associated with underlying tuberous sclerosis.11,20,37 A possible explanation is the tendency to form intra-oral hamartomas composed of proliferating fibroblasts and hemangioblasts.51 The treatment of choice is the en-bloc resection with a wide margin followed by reconstruction. Inadequately surgical margins are associated with higher rates of recurrence.30 Aggressive curettage also has been suggested as an alternative therapeutic approach by some authors.52 Anecdotal reports of successful use of radiotherapy in patients with DF are available, though these cases were of DF involving the lower limbs and not the gnathic bones.53,54 A wide range of complications have been described in cases of DF ranging from difficulty in mouth opening, extension into the adjacent soft tissue, perineural encasement, loosening of the overlying tooth, dysfunction of the temporomandibular joint, sinusitis, and nasal obstruction.1,8,13,22,23,25,27,28,32,36,41,42,44 All the complications are secondary to the aggressive nature of the tumor and the mass effect.

CONCLUSION

We describe a rare case of DF affecting the mandible. Although a benign, rare, bone tumor, DF involves the gnathic bones, mostly the mandible, with relative frequency. It usually presents in childhood as an osteolytic bony lesion. The morphology is similar to desmoid fibromatosis with approximately half the cases showing nuclear positivity for β-catenin immunohistochemistry. The APC/β-catenin pathway may play a role in tumorigenesis, though it may not be exclusive. Cases of tuberous sclerosis also may present with DF as part of the tendency to form proliferative fibroblastic hamartomas.
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The authors retain an informed written consent for publication by the father of the patient, and the manuscript is in accordance with the Institutional Ethics committee requirements.

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