RECURRENT DESMOPLASTIC FIBROMA OF THE MAXILLA

Case report and review of the literature

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ABSTRACT

Desmoplastic fibroma (DF) of the maxilla is a rare, intraosseous, benign tumour which has high rates of recurrence. Signs, symptoms and imaging studies are generally non-specific. While histopathological diagnosis remains the gold standard, the lack of reliable immunohistochemical markers and overlap with malignant processes may lead to misdiagnosis. Management remains mainly surgical, with wide local resection with clear margins to reduce recurrence rates. The use of chemotherapy and radiotherapy in DF is not well established and data from their use in desmoid type fibromatosis may not be appropriate with emerging data separating these as pathologically distinct entities.

INTRODUCTION

Desmoplastic fibroma (DF) is a rare, benign, and locally aggressive intraosseous lesion. Long bone involvement was first described by Jaffe in 1958 and the first report of jaw DF was in 1965 by Griffith and Irby.[1,2] There have been several reports of involvement of the jaws with a predilection for the mandible over the maxilla.[3] Owing to its rarity, issues with diagnosis and management at all sites are reported, as well as high rates of recurrence particularly in the mandible[3]. We present a case of recurrent desmoplastic fibroma of the maxilla and review of the literature of desmoplastic fibroma at this site, which aims to highlight the difficulty in surgically treating a benign but locally aggressive tumour and investigate the current diagnostic and medical and surgical treatment algorithms.

Keywords:
desmoplastic | benign | fibroma | maxilla | recurrence

CASE REPORT

A 61-year-old Caucasian male was referred to the Oral & Maxillofacial Department following an incidental finding of a right maxillary lesion on cone beam tomography (CT) during investigation for seizures. He had a past medical history for mild dilated cardiopathy with previous myocardial infarction, progressive spinocerebellar ataxia, hypertension and alcohol abuse. On presentation, he denied any related symptoms but did complain of longstanding nasal obstruction. Examination revealed a palpable swelling with associated bone loss over the right anterior maxilla. There was no infra-orbital nerve paraesthesia.

The initial CT scan performed for investigation for seizures showed a soft tissue lesion in the anterior right maxilla continuous with the hard palate causing bone erosion and protruding into the anterior nasal cavity. Following this, a targeted maxillary cone beam CT showed a 2.6 x 1.5 x 1.1cm radiolucent lesion with irregular margins in the midline maxilla *(Figure 1)*. There was destruction of the anterior and central superior cortex, with a small breach in the mucoso of the right nasal floor, but without evidence of soft tissue mass beyond the margins of the maxilla.

Given concern of primary malignancy, he underwent initial incisional biopsy. Histologically, the lesion showed sclerotic hypocellular fibrous tissue with loss and infiltration of bone without significant cellular atypia or mitoses. Skeletal

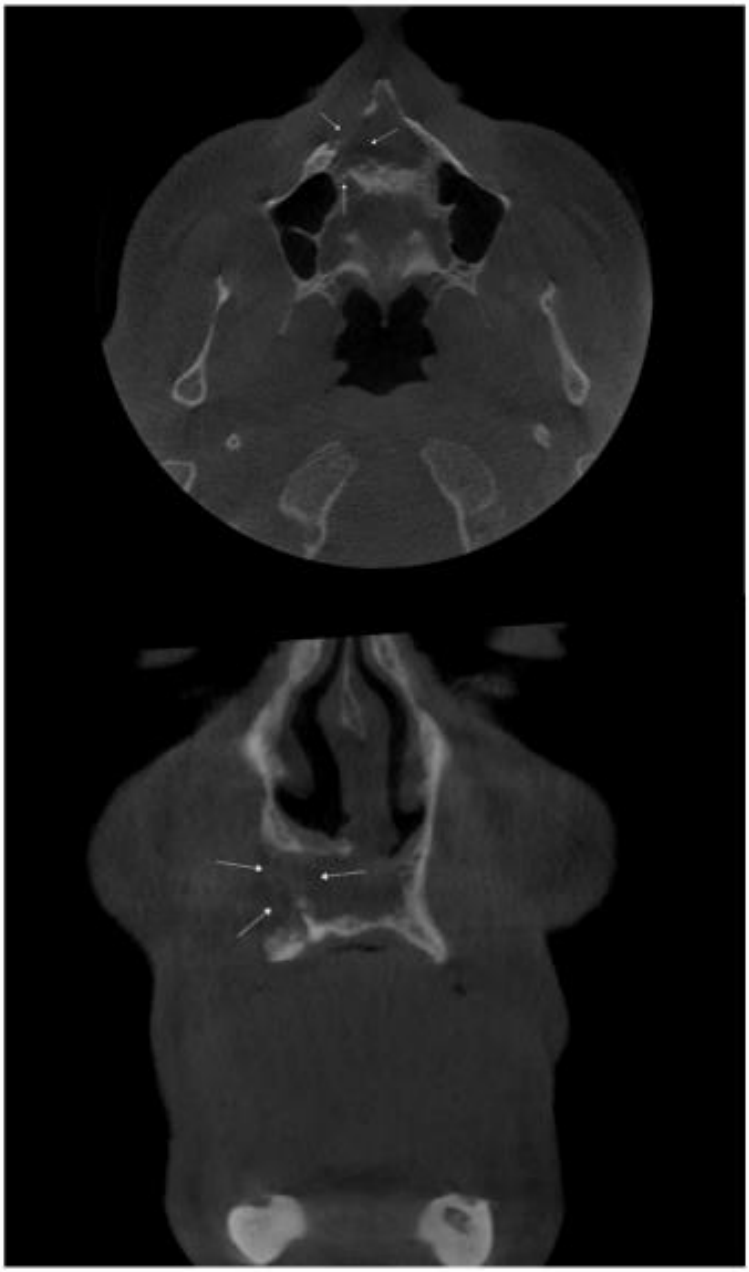

Figure 1 CT facial bones showing destruction of the anterior maxillary bone, as well as the central superior cortex and the hard palate. A) Coronal view, b) Axial view

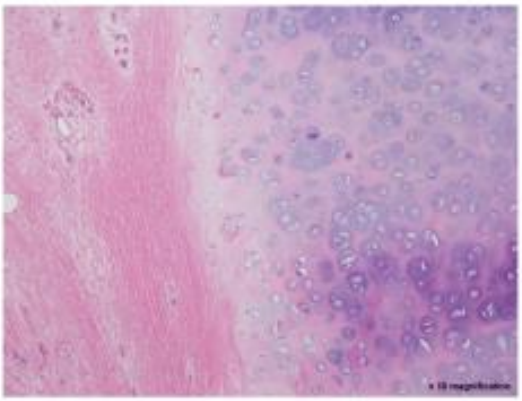

Figure 2 Histology of desmoplastic fibroma

muscle and respiratory mucosa were seen adjacent to the lesion confirming destruction of cortical bone. Immunohistochemistry was negative for S100, SMA, MDM2 and beta-catenin. This result was suggestive of desmoplastic fibroma *(Figure 2)*.

Given this result, the patient underwent an anterior subtotal maxillectomy via a bilateral Weber Ferguson approach and immediate free fibula osseomyocutaneous flap reconstruction *(Figure 3)*. This approach facilitated cutting guides and virtual surgical planning (VSP), as well as assisting with the free fibular reconstruction. Histology the surgical specimen revealed a 23 x 14mm mass, supporting the diagnosis of desmoplastic fibroma with positive posterior margins. There was no extension beyond cortical bone in this specimen. Given positive margins, radiotherapy was offered to reduce recurrence, but the patient failed to attend.

The patient was subsequently lost to follow-up for five months. On re-presentation, there was a firm bony prominence on the left side of the palate seen on examination. Repeat CT showed a stable post-operative appearance without evidence of recurrence but due to ongoing clinical concerns of recurrence the patient underwent a PET scan and biopsy of the new lesion. The PET scan revealed a focal intense region of FDG avidity in the anterior and right sided maxilla which was suggestive of either recurrence or post-surgical inflammatory changes. Histopathology from the biopsy showed stroma of low cellularity with a focally nodular sclerotic appearance without dysplastic appearance, with differentials including recurrence or scar formation. To further characterise the lesion, he also underwent MRI which demonstrated a rind of soft tissue of low T1/T2 signal intensity wrapping around the right fibular free flap reconstruction contiguous with a high T2 signal mucosal thickening.

He underwent a re-excision of the hard palate lesion, with additional margins taken from the right inferior turbinate, left inferior turbinate and posterior septum via a facial degloving approach. This offered better access than a revision Weber Ferguson approach to the site of recurrence in the cartilaginous septum, and also avoided scarring through the initial healed surgical site. The soft palate was spared. Intra-operatively, the lesion was difficult to ascertain from post-surgical scar. This had been anticipated, and for this reason, the patient was planned for a delayed reconstruction until margins were proven to be clear.

In the interim, a palatal obturator prosthesis was fabricated, and retained by circumzygomatic wires during this process *(Figure 3)*. Histopathology showed an infiltrative submucosal infiltration of paucicellular fibrous tissue with whorling architecture and some myxoid stromal changes. The deep aspect of the lesion infiltrated through skeletal muscle and showed destruction of bone. This suggested recurrence of the desmoplastic fibroma. Margins were positive on the left and right along the posterior half of the specimen. Anteriorly, it was difficult to distinguish between recurrence and post-surgical changes.

He underwent three further re-excisions until clear margins were achieved. An obturator was placed with circumzygomatic wires to allow speech and function during this time. At this point, reconstruction options involved another fibula free flap reconstruction or a zygomatic prosthesis. Given the improved surveillance for further recurrence possible with a retained prosthesis, he had quad zygomatic implants inserted. He continues to be followed up closely and was free of recurrence eight months following the last excision.

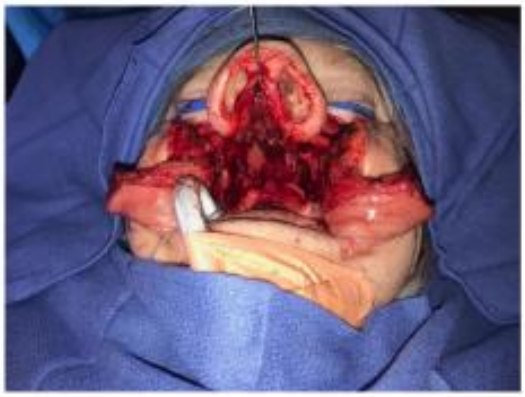

Figure 3 Intra-operative clinical photograph of bilateral Weber Ferguson approach after completion of maxillectomy, showing surgical defect (published with patient consent)

DISCUSSION

Desmoplastic fibroma, as classified by the World Health Organization (WHO), is a locally aggressive but benign neoplasm of bone, accounting for less than 0.1% of all primary bone tumours. It is thought to be the intraosseous counterpart of desmoid-type fibromatosis (aggressive fibromatosis), and most commonly affects the mandible, as well as other long bones of the body including the femur and tibia.[4] Reports of DF in the maxilla, such as that presented in this case, are rare. In a review of cases of desmoplastic fibroma in the jaw in 2006, Said-Al-Naief et al found 86% of cases were reported in the mandible, with the remainder in the maxilla.[3]

The most common presentation of desmoplastic fibroma at all sites, including at the maxilla, is painless swelling[4]. Other signs and symptoms reported include pain and bleeding. In the mandible, there have been reports of trismus, tooth mobility and displacement, facial asymmetry and symptoms mimicking odontogenic infection.[3,5] Previous reports have highlighted a slight female predilection, but there is a largely even gender distribution in cases of desmoplastic fibroma of the maxilla.[3] Most cases have been reported in younger patients, with 84% of cases in the jaw being under 30 years of age.[3] The aetiology of DF remains unknown. There have been some likely genetic factors identified, with several cases being described in patients with tuberous sclerosis.[6]

Imaging findings have been non-specific and varied. Most common findings in the literature describe a lytic, ill-defined lesion, with a previous review in 2005 describing lytic lesions in up to 65% of cases on CT, similar to the rate of 50% identified in DF in the maxilla.[7] However, sclerotic or mixed lesions have also been reported.[7] Cortical continuity is an important radiological sign in differentiating between benign and malignant processes, as DF usually demonstrates cortical thinning and expansion, while malignancy usually produces erosion and perforation of the cortex.[5] However, a sun-ray appearance on CT may mimic osteosarcoma, and while this may form an important differential, there is potential for misdiagnosis based on this feature.[8] Other differential diagnoses based on imaging findings include fibromatosis, rhabdomyosarcoma, neuroblastoma and lymphoma.[9]

MRI has also been used to further characterise lesions suspicious for DF. T2 shortening (or low signal intensity) of an osteolytic intraosseous fibrous lesion on MRI may narrow down the differential diagnoses, as this has otherwise only seen in giant-cell tumours, fibrous dysplasia, lymphoma and leiomyosarcoma of bone.[7,10] This low intensity on T2 images is believed to be due to the relative acellularity of these lesions in DF, similar to that seen in aggressive fibromatosis.[10] Positive Emission Tomography (PET) is not often used as a diagnostic imaging modality, however a case report of desmoplastic fibroma of the scapula revealed moderate focal fluorodeaxyglucose (FDG) uptake.[11]

DF remains a diagnosis of exclusion, given overlaps in imaging and histopathology and without any specific immunohistochemical markers. On histopathology, it has an appearance of spindle fibroblasts in a collagenous matrix, arranged in whorls or long fascicles, with minimal atypia and mitoses. Cellularity may be variable. This appearance is similar to desmoid type fibromatosis (or aggressive fibromatosis).[4] Importantly, there may be overlap in this appearance with low-grade osteosarcoma, which may lack the typical herringbone appearance of high grade osteosarcoma, and may not have overt atypia or mitoses.[12] It has been postulated that karyotyping and cytogenetics may be useful in differentiating between the two, with the CTNNB1 (β-catenin) S45F mutation found in DF and the CDK4 amplification in osteosarcoma, however, there have been very few reports to support this.[12,14] Interestingly, it has also been shown that the CTNNB1 S45F mutation is present in desmoid-type fibromatosis.[14]

The value of immunohistochemistry in diagnosis is unclear. -catenin as previously noted has been identified as a potential marker for DF. The connection between desmoid type fibromatosis and β-catenin has been established. Desmoid type fibromatosis may present sporadically or as part of Gardner Syndrome, a genetic syndrome which includes familial adenomatous polyposis coli (FAP) and multiple osteomas. FAP is characterised by a mutation in the APC gene, which regulates the Wnt pathway which involves the regulation of β-catenin.[15] However, while there have been some reports of positive staining for β-catenin in DF, it seems that the Wnt pathway is not implicated in DF, which distinguishes it from desmoid-type fibromatosis.[8,15,16]

Surgical excision is the appropriate treatment for desmoplastic fibroma. Recurrence rates are reported to be high, with rates of 17% with resection and 55-72% without resection.[4] There have been varying levels of recurrence based on surgical approach. Comparing excision or enucleation to wide local excision, Iwai et al found that no recurrence in patients with managed with wide local excision and rates of up to 20-40% in simple excision, and

up to 70% when treated with curettage alone.[9] Given the variable surgical approaches reported in the literature, there is no consensus on the margins to aim for with resection, and given no current evidence, wide margins (>10mm) would apply to ensure low recurrence rates. Evidently this needs to be weighed up against morbidity of resection on a case-by-case basis.

Data for use of radiotherapy and chemotherapy in desmoplastic fibroma are minimal, and most have been extrapolated from use in desmoid-type fibromatosis. With new literature now separating the two entities on a pathophysiological basis, this may be inappropriate. A comparative review of recurrence rates of surgery alone and surgery with radiotherapy in desmoid-type fibromatosis found better control in the latter group regardless of margins following surgery, however increased rates of complications including pathological fractures and induction of osteosarcoma were identified with the use of radiotherapy.[17]

There is limited data on the use of chemotherapy in DF, including the use of vincristine, doxorubicin and dacarbazine with mixed response to treatment.[5] A recent case study of the use of vincristine, actinomycin D, and cyclophosphamide in a case of mandibular DF showed halted progression without resolution of the tumour.[18] The use of chemotherapy, with its significant morbidity must be carefully considered for benign disease such as DF. The slow growth of DF may also make it relatively chemotherapy resistant.

Desmoplastic fibroma of the maxilla remains a rare but locally aggressive entity, at risk of misdiagnosis. We present here a case with diagnostic and management strategies to address the dilemmas of this challenging condition.

Conflict of interest statement

All authors have no real or perceived conflicts to declare in the publication of this paper.

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