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# Juvenile Aggressive Fibromatosis: Review of Literature

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**ABSTRACT**

Extra abdominal desmoid tumours also called as Aggressive fibromatosis (AF) or Juvenile aggressive fibromatosis (JAF) are rare, benign, slow growing, locally destructive tumours of musculoaponeurotic tissue. They are a type of desmoid tumour with a propensity to occur in the head and neck region and can occur at a young age. Early identification and diagnosis is crucial in management of this condition because of its locally aggressive biological behaviour. This article attempts to better understand this rare pathology with a review on its aetiology, clinical course and treatment options.

**Key words:** Juvenile, Musculoaponeurotic, Aggressive, Tissue Fibromatosis:

## INTRODUCTION

### Background

Muller[1] in 1838 coined the term desmoids from greek “desmos” meaning tendon like for this lesion which was first described by Macfarlane in 1832.[2]Desmoids tumours are of two types, an intra abdominal variant and an extra abdominal variant. Extra abdominal desmoids tumours also called aggressive fibromatosis is histologicaly benign but exhibit variable biological behaviour and can be locally aggressive, leading to destructive infiltration of surrounding anatomical structures. They are sometimes classified under low-grade fibrosarcomas in spite of their benign histopathology because of their locally aggressive characteristics. They account for 0.03% of neoplasms in general.[3] Studies show age of incidence peaking between 25-35 years with a slight female predilection.[4, 5]

### Aetiology

The exact aetiology of extrabdominal desmoid tumours isnot fully understood. They are however associated with familial adenomatous polyposis (FAP) syndrome as well as Gardner syndrome[6, 7, 8] in many cases although sporadic idiopathic occurrence is also seen. Mutation in APC gene is seen in cases occurring in association with Gardner syndrome, where-as mutation in the ?-catenincoding CTNNB1 gene has been noted in idiopathic lesions.[9]Elevated levels of ?-Catenin proteins are found in patients having desmoids tumours.[10,11]The role of exogenous and endogenous female sex hormones in the pathogenesis of these tumours have also been postulated as it has been seen to occur during pregnancy and studies have shown its response to selective oestrogen receptor modulators.[12,13] The role of pervious trauma and surgery as a contributing factor in development of this neoplasm also has been mulled.

### Clinical Presentation

As it is a fibroproleferative connective tissue disorder, it has been observed in almost every part of the body. Extra abdominal desmoids tend to occur characteristically in the head and neck region and the breast[14,15] with the extremities being involved in a minority of the patients.[16]Most of the

patients present with a smooth, firm swelling which is usually painless. They are usually slow growing but locally aggressive and tend to invade and destroysurroundingstructures. They occasionally become painful when they involve nearby nerve tissue. Overlying skin is usually normal and not fixed to the selling.

In about 10% of the patients the disease is multi-centric in occurrence[17, 18] but usually confined to the same anatomical region. Although desmoids tumours are considered benign, the extra abdominal lesions especially in the head and neck region tend to be aggressive and invade vital organs and can become fatal. Recurrence rate after treatment is high at 30-50%.[19, 20, 21, 22]

**Radiographic Investigation**

An OPG is normally advised but is of limited use showing occasional calcifications, displaying cortical erosion if present of adjacent bone. A non-contrast enhanced computed tomography is not very useful because of the similar attenuation between normal soft tissue and the desmoid tumour. Contrast enhanced CT can show better imaging because of the increased angiogenecity in the tumour mass.[23]The imaging of choice to assess a desmoid tumour for both the extent as well as the extensions into the surrounding tissues is Magnetic resonance imaging (MRI). Usually in MRI the tumour mass is uniformly iso-intense although it may be hyper or hypo-intense in comparisonwith surrounding tissue and is dependent on the collagen content and cellularity of the lesion.

**Histopathology**

Gross examination usually reveals a mass that is confined to the musculature or facia but is not always the case especially in head and neck lesions. Size can vary depending on duration of the lesion ranging from about 5cm to large tumours. Whencut, the mass usually reveals a white, rough surface and can resemble scar tissue.[24]

Microscopic examination reveals a tumour mass that is not confined inside the capsule and shows tumour extending as septae into the surrounding tissue. The tumour is composed of abundant collagen fibres with spindle shaped, normal appearing fibroblasts distributed throughout. Although the infiltrative pattern of the lesional tissue might resemble a fibrosarcoma the absence of cellular atypia as well the low number of mitotic figures precludes the diagnosis. The spindle cells are usually positive for vimentin and smooth muscle actin but are negative for desmin, cytokeratina and s-100.[25] Small thin walled blood vessels are seen usually along with focal aggregates of lymphocytes.

A multitude of treatment options have been tried out to achieve local control keeping in mind the benign nature of the lesion trying to maintain aesthetics and function for the patient. The relative success or failure of each mode of treatment is debatable because of the lack of proper clinical trials and follow up compounded by the rare nature of the disease.

Surgical resection of the tumour mass with a wide margin is the treatment of choice in lesions that can be operated upon without compromising too much on the function and aesthetics. Achieving a negative margin in many cases is extremely difficult because of the invasive nature of the lesion. The higher rate of recurrence could be attributed to this reason. The time of recurrence can vary from a few months up to 12 years in certain cases.[26]Recurrence free survival rate at 5 yrs post surgery with negative margins was 64% while it was 92% with positive margins in a study by Huang *et al.*[27]

In cases where surgery is not feasible, radiotherapy with doses of 50–60 Gy, has yielded local control rates of 75%.[22]It has been reported that in cases where negative margins were not achievable by surgery, adjuvant radiotherapy has reduced recurrence rates by as much as 50% and this suggests a possibility of a combined treatment approach of surgery with radiotherapy to achieve acceptable results that also limits morbidity and maintains long term function for the patients.[24]

Various systemic therapies with anti estrogen compounds and NSAIDs (sulindac) , have shown limited effectiveness with response ratesof about 50% but long term cure in these cases is

doubtful.[28,29]The use of imatinib mesylate in the treatment of desmoid tumours has produced encouraging preliminary results. Joseph mace *et al*[30]in a clinical trial on 2 patients has shown that Imatinib mesylate, a selective kinase inhibitor is effective in treating these lesions but long term, large scale clinical trials using this agent is needed to prove its therapeutic potential.

Patients with recurrence which cannot be treated either by surgery or with radiotherapy and patients with non-operable rapidly growing lesions and those who are highly symptomatic are considered for systemic chemotherapy. Low dose methotrexate along with vinblastine has been proved to be effective with one study showing 10 year survival rate of 67%.[31]In very aggressive life threatening lesions and those lesions which are refractory to other therapies, high dose liposomal doxorubicin and ifosfamide based regimes is the only alternative.[32, 33, 34, 35]

## DISCUSSION

Although aetiology is unknown, a neoplastic pathogenesis is suspected which is supported by findings in a number of cases of clonalchromosomal changes.[36]Desmoidtumours have been associated with hereditary syndromes(Gardner's syndrome), pregnancy, especially second pregnancy andendogenous/ exogenous female sex hormones in adults.[37,38,39]

Fibrosarcoma, reactive fibroblastic proliferations, myxoma, desmoplastioc fibroama and nodular fasciitis are considered as differential diagnosis.[24]The need for a proper biopsy in the diagnosis of AF is emphasised by the possibility that an inadequate biopsy can lead to a misdiagnosis. Areas of these lesions can be indistinguishable from fibrosarcoma and can lead to a false impression. Although computed tomography with intravenous contrast solution is useful, magnetic resonance imaging (MRI) is the investigation of choice for AF as it is the most effective in visualizing the extent of the lesion and also its relationship with the surrounding structures.

A definitive treatment protocol for AF has been difficult to establish for these lesions because of their rarity as well as paucity of literature regarding treatment with long term follow up compounded by inclusion of lesions of varied anatomical sites thereby making it difficult to draw direct comparisons of the efficacy of various treatment modalities. Because of the high rate of recurrence of these tumours the treatment of choice has been resection with a wide surgical margin.Local recurrence aftersurgery is approximately 30–50%.[16]This is attributed to the locally aggressive nature of the lesion and the difficulty of the surgeons to achieve clear margins.

## CONCLUSION

Juvenile Aggressive fibromatosis although considered to be benign, is an extremely rare tumour which is not very well understood and has a very variable clinical course ranging from spontaneous regression to being lethal by local infiltration. The lack of literature on comprehensive long term clinical studies and research makes it all the more difficult to successfully treat it. Although wide margin resection is the treatment of choice, a high recurrence rate points to itsineffectiveness. Further research is advocated into understanding this rare lesion with emphasis on non-surgical treatment modalities based on location and age with a view to achieving lower recurrence rate while preserving adequate function andaesthetics in cases of juvenile aggressive fibromatosis especially of the head and neck region.

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