Introduction

Childhood desmoid tumour, also called aggressive fibromatosis, is a tumour that develops in the fibrous tissue that forms tendons and ligaments, usually in the arms, legs or midsection, but also sometimes in the head and neck. Locally, a desmoid tumour is very similar to a malignant (cancerous) tumour called fibrosarcoma in that local recurrence is very high.

However, a desmoid tumour is considered ‘benign’ because it does not metastasise (spread) to other parts of the body.

Regardless of its scientific classification, a desmoid tumour can be invasive to surrounding tissues and difficult to control. It can adhere to, and intertwine with, surrounding structures and organs.

Yogesh Kumar, B., Vidyachara, S. & Vadhiraja, B.M. 2019. “Aggressive fibromatosis is a benign, locally invasive fibroblastic proliferation that can cause compressive effects on adjacent structures. The primary cure of this disease rests in wide excision of the tumor. Unfortunately even when surgical margins are clear of tumor, recurrence rates are high. Postoperative radiotherapy is indicated following surgical excision. We present a 13-year-old girl who had been operated for the intraspinal mass in upper thoracic spine and paraparesis with thoracic limited laminectomy and excision of the tumor mass elsewhere. The histopathological examination was reported to be aggressive fibromatosis. After 2 years, she presented again with 1-year duration of progressive deformity in the upper thoracic spine and weakness of both lower limbs. Focal kyphosis at T4-T5 was measuring 68°. Magnetic resonance imaging (MRI) showed recurrent tumor involvement of posterior elements of T2-T5 and paravertebral soft tissues with signal changes in the cord at T2-T5 vertebral levels with focal kyphosis and internal gibbus. She underwent posterior spinal revision decompression with internal gibbectomy and instrumented fusion. The histopathology showed
features suggestive of aggressive fibromatosis. After wound healing at 2 weeks, she underwent 3-D conformal radiotherapy, based on the preoperative tumor extent on MRI (dose of 45 Gy in 25 fractions over 5 weeks). She had normal neurology at 2-year follow-up and was tumor free on MRI. Hence, aggressive fibromatosis can recur following successful surgical wide excision. Multilevel thoracic laminectomy in growing children can cause progressive spinal deformity and neurological deficits. Operative treatment of recurrent tumor involves en bloc excision with instrumented fusion followed by local radiotherapy. This is the first pediatric recurrent spinal fibromatosis reported with successful treatment as per author’s knowledge.”

Desai, S.R., Dombale, V.D. & Janugade, H.B. 2005. Infantile fibromatosis represents the childhood counter part of musculoaponeurotic fibromatosis & arises as a solitary mass in skeletal muscle, adjacent fascia, aponeurosis or periosteum. The lesion is extremely rare. Microscopically it exists in two forms diffuse (mesenchymal) & desmoid. The less common desmoid form rarely occurs in infancy. Immunophenotype shows vimentin positivity with variable positivity with muscle markers. The differential diagnosis of this type is infantile fibrosarcoma. The tumor may locally recur if inadequately excised. We report a case of infantile fibromatosis of desmoid type occurring in 10 months male child for its extreme rarity.

Incidence of Childhood Desmoid Tumour.
The National Cancer Registry (2012) does not provide any information on the incidence of childhood desmoid tumour.

Childhood desmoid tumour represents one of the rarer types of childhood tumours. They occur in children and young adults and arise from muscle or connective tissue (‘soft tissue’) around muscles or bones, and can appear anywhere in the body. They can also occur at any time throughout childhood.

Desmoid tumours are neither a truly benign nor a truly malignant cancer. It can be life-threatening if located next to vital organs like the spine or trachea (windpipe). Surgical removal of the entire tumour usually achieves a cure, however, if even small amounts of tumour cells remain, the tumour can grow back again. Depending on the location of the tumour, surgical removal may not be possible. In these cases, radiation therapy or chemotherapy may prevent further tumour growth or cause the tumour to disappear.

Causes of Childhood Desmoid Tumour
The cause of desmoid tumours is unknown.

In some patients, desmoid tumours can occur as part of an inherited syndrome called Gardner Syndrome, in which patients also have colon polyps or colon cancer. Desmoid tumours can also occur in pregnant women, which has led to the theory that hormones may influence growth. Most of the time, desmoid tumours occur in previously healthy patients with no other medical problems.
Mutations in the \textit{CTNNB1} gene or the \textit{APC} gene cause desmoid tumours. \textit{CTNNB1} gene mutations account for around 85 percent of sporadic desmoid tumours. \textit{APC} gene mutations cause desmoid tumours associated with familial adenomatous polyposis as well as 10 to 15 percent of sporadic desmoid tumours. Both genes are involved in an important cell signalling pathway that controls the growth and division (proliferation) of cells and the process by which cells mature to carry out specific functions (differentiation).

The \textit{CTNNB1} gene provides instructions for making a protein called beta-catenin. As part of the cell-signalling pathway, beta-catenin interacts with other proteins to control the activity (expression) of particular genes, which helps promote cell proliferation and differentiation. \textit{CTNNB1} gene mutations lead to an abnormally stable beta-catenin protein that is not broken down when it is no longer needed. The protein accumulates in cells, where it continues to function in an uncontrolled way.

The protein produced from the \textit{APC} gene helps regulate levels of beta-catenin in the cell. When beta-catenin is no longer needed, the APC protein attaches (binds) to it, which signals for it to be broken down. Mutations in the \textit{APC} gene that cause desmoid tumours lead to a short APC protein that is unable to interact with beta-catenin. As a result, beta-catenin is not broken down and, instead, accumulates in cells. Excess beta-catenin, whether caused by \textit{CTNNB1} or \textit{APC} gene mutations, promotes uncontrolled growth and division of cells, allowing the formation of desmoid tumours.

\textbf{Signs and Symptoms of Childhood Desmoid Tumour}

The most common symptom of desmoid tumours is pain. Other signs and symptoms, which are often caused by growth of the tumour into surrounding tissue, vary based on the size and location of the tumour. Intra-abdominal desmoid tumours can block the bowel, causing constipation. Extra-abdominal desmoid tumours can restrict the movement of affected joints and cause limping or difficulty moving the arms or legs.

Desmoid tumours occur frequently in people with an inherited form of colon cancer called familial adenomatous polyposis (FAP). These individuals typically develop intra-abdominal desmoid tumours in addition to abnormal growths (called polyps) and cancerous tumours in the colon. Desmoid tumours that are not part of an inherited condition are described as sporadic (Genetics Home Reference).
Diagnosis of Childhood Desmoid Tumour

CT scanning and MRI are used for the diagnosis and follow-up of desmoid tumours. They can help determine the extent of the tumour and its relationship to nearby structures, especially prior to surgical removal. MRI is superior to CT scanning in defining the pattern and the extent of involvement as well as in determining if recurrence has occurred after surgery.

The preferred diagnostic test is biopsy of the tumour. A fine-needle aspiration biopsy specimen may be considered.

Electron microscopy may be performed. On electron microscopic examination, the spindle cells of desmoid tumours appear to be myofibroblasts. This finding is thought to represent an abnormal proliferation of myofibroblasts, which normally disappear gradually during the later stages of wound healing.

Treatment Options for Nonsurgical Patients

Primary surgery with negative surgical margins is the most successful primary treatment modality for desmoid tumours. Positive margins after surgery reflect a high risk for recurrence.

In those patients who refuse surgery or are not surgical candidates the following options may be considered:

- Radiation therapy may be used as a treatment for recurrent disease or as primary therapy to avoid mutilating surgical resection. It may be used postoperatively, preoperatively, or as the sole treatment.
- Pharmacologic therapy with anti-oestrogens and prostaglandin inhibitors may also be used.
- In cases of recurrent extra-abdominal desmoid tumours in which surgery is contraindicated or in cases of recurrence, a chemotherapeutic regimen of doxorubicin, dacarbazine, and carboplatin may be effective. Intra-abdominal desmoid tumours as a part of Gardner syndrome may respond to systemic doxorubicin, and ifosfamide can be useful for patients with complications from the tumour. Polychemotherapy has been used and can be combined with targeted therapy with imatinib.
- Expanded knowledge of familial adenomatosis polyposis–desmoid tumour molecular underpinnings may aid in the development of novel therapeutic strategies.
- Excision of tumour - aggressive, wide surgical resection is the treatment of choice. Complete surgical excision of desmoid tumours is the most effective method of cure. This sometimes necessitates removal of most of an anterior compartment of a leg. Extensive cases may require excision plus adjuvant treatment including chemotherapy and repeat surgery. In selected patients, radical resection with intraoperative margin evaluation by frozen sections followed by immediate mesh reconstruction may be a safe and effective procedure providing definitive cure yet minimizing functional limitations.

For tumours that are asymptomatic or non-progressive, some prefer a wait-and-see approach.

The goals of pharmacotherapy are to induce remission, to prevent complications, and to reduce morbidity. Local recurrences are frequent after surgery, particularly if margins are positive. Radiotherapy alone for gross disease or after a microscopically incomplete resection yields local control rates of approximately 75-80%.
The following agents inhibit cell growth and proliferation. Pharmacologic agents result in objective response rates of approximately 40-50%; the duration of response is variable.

Doxorubicin (Adriamycin, Rubex)
Inhibits topoisomerase II and produces free radicals, which may cause the destruction of DNA. The combination of these 2 events can, in turn, inhibit the growth of neoplastic cells.

Dacarbazine (DTIC-Dome)
Inhibits DNA, RNA, and protein synthesis. Inhibits cell replication throughout all phases of the cell cycle.

Carboplatin (Paraplatin)
Analog of cisplatin. Has same efficacy as cisplatin but with better toxicity profile.

BACKGROUND: Aggressive fibromatosis (AF) is a soft tissue tumor and is rare in childhood, with high potential for local invasiveness and recurrence. General recommendations for the clinical management of pediatric patients with AF remain undetermined.
METHODS: The authors retrospectively analyzed 13 children with AF who were diagnosed from 1987 until 2004 in the Erasmus MC-Sophia Children’s Hospital, and a review of the pediatric literature was conducted.
RESULTS: Two patients received preoperative chemotherapy with combined vincristine, actinomycin-D, and cyclophosphamide (VAC). All 13 patients underwent surgery. Three of six patients who underwent incomplete resection received adjuvant treatment, two patients received radiotherapy, and one patient received chemotherapy (VAC). The median follow-up was 3.9 years (range, 0.6-14.0 years). Three patients developed recurrent AF, including two recurrences after patients underwent incomplete resection without adjuvant treatment. Secondary resection was performed, which was incomplete in one patient who subsequently received chemotherapy (VAC). At the time of the current report, all 13 patients were in complete remission. Ten pediatric AF studies, including the current study, with a total of 187 patients were reviewed. Incomplete resection was the most important determinant for disease recurrence; in the authors' opinion, the role of adjuvant therapy needs to be studied further.
CONCLUSIONS: Primary surgery with negative surgical margins was found to be the most successful primary treatment modality for children with AF. Positive margins after surgery indicated a high risk for disease recurrence. Multicenter, prospective (randomized) trials will be necessary to clarify the role of adjuvant treatment for patients with pediatric AF.

About Clinical Trials
Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:
- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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Sources and References Consulted or Utilised

APC Gene on Chromosome 5
https://www.google.co.za/search?q=apc+tumor+suppressor+gene&source=lnms&tbm=isch&sa=X&ei=vtHkU9afLbG57Abk4GQDQ&ved=0CAIQ_AUoAQ&biw=1517&bih=714&drp=0.9#facrc=_&imgdii=wCXWAnFG_wqZaM%3A%3B2AR3AsaDuXvR_M%3BwCXWAnFG_wqZaM%3A&imgrc=wCXWAnFG_wqZaM%3A%3BcCG-3l-kkPMAqM%3Bhttp%253A%252F%252Fwww.nlm.nih.gov%252FdynamicImages%252Fchromomap%252FAPC.jpeg%3Bhttp%253A%252F%252Fwww.nlm.nih.gov%252Fgene%252Fgene%252FAPC%3B469%3B175


Childhood Desmoid Tumour
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CTNNB1
https://www.google.co.za/search?q=ctnnb1+gene&source=lnms&tbm=isch&sa=X&ei=8w7AaqoDwCA&sqi=2&ved=0CAIQ_AUoAQ&biw=1517&bih=714&drp=0.9#facrc=_&imgdii=_&imgrc=Idum95XwRVBigM%3A%3B4s37Fccs1GeM%3Bhttp%253A%252F%252Fwww.genecards.org%252Fpics%252Ffloc%252FCTNNB1-genepic.png%3Bhttp%253A%252F%252Fwww.genecards.org%252Fctnnb1-bin%252Fcarddisp.pl%3B53Fgene%252DCTNNB1%3B720%3B890

Researched and Authored by: Prof Michael C Herbst
[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Dip Audiology and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]

Approved by: Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

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