

# Cancer Association of South Africa (CANSA)



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## Fact Sheet on Childhood Fibrosarcoma

### Introduction

A fibrosarcoma is a malignant (cancerous) tumour that originates in the connective fibrous tissue found at the ends of bones of the arm or legs, and then spreads to other surrounding soft tissues.

[Picture Credit: Fibrosarcoma]

Soft tissues include:

- fat
- muscles
- tendons (bands of fibre that connect bones to muscle)
- nerves
- joint tissue
- blood vessels
- other fibrous tissue



The condition most commonly affects either a lower leg or arm.

### Childhood Fibrosarcoma

There are generally two forms of this disease:

Infantile (childhood) or congenital fibrosarcoma - this type of tumour is the most common soft tissue sarcoma found in children under one year of age. It presents as a rapidly growing mass at birth or shortly after. This form of fibrosarcoma is usually slow-growing, and tends to be more benign than fibrosarcoma in older children, which behaves more like the type found in adults.

Adult form fibrosarcoma - the adult form of this disease can occur in older children and in adolescents, roughly between the ages of 10 and 15. It is more aggressive than the infantile form and generally involves more complex treatment.

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There are many different types of soft tissue sarcomas:

- Fat tissue tumours
- Bone and cartilage tumours
- Fibrous (connective) tissue tumours
- Skeletal muscle tumours
- Smooth muscle tumours
- So-called fibrohistiocytic tumours
- Nerve sheath tumours
- Pericytic (Perivascular) tumours
- Tumours of unknown cell origin
- Blood vessel tumours.

### **Incidence of Childhood Fibrosarcoma in South Africa**

The National Cancer Registry (2017) does not provide any statistics on the incidence of Fibrosarcoma in South Africa.

### **Differences and Similarities with Other Bone Sarcomas**

As the name implies, fibrosarcoma results from abnormal fibroblast cell division. Osteosarcoma and chondrosarcoma are distinguished by the extracellular matrix (material) the malignant cells produce. Osteosarcoma is characterised by production of osteoid (the organic matrix of bone) whereas chondrosarcoma neoplasms make abundant cartilage. In contrast, fibrosarcomas produce neither bone nor cartilage. Collagen is the predominant product produced by the malignant cells in fibrosarcoma. The amount of collagen production is inversely proportional to the histological grade (i.e., high grade tumours produce less collagen and vice versa). It is the rapidly dividing and spreading cells in sarcoma (not the matrix produced) that can threaten life and limb.

Distinguishing between different bone tumours can be challenging. The differential diagnosis for any given bone lesion often includes both benign and malignant processes. Lesions that may appear similar to fibrosarcoma on radiographs include malignant solitary fibrous tumour, leiomyosarcoma, myofibromatosis, myeloma, osteosarcoma, lymphoma, metastatic disease, malignant fibrous histiocytoma of bone, and desmoplastic fibroma.

Fibrosarcoma can be confused with osteosarcoma because both can affect young patients, including patients in the second decade of life (ages 10 to 19). Both have a predilection for the distal femur and radiographically can appear as aggressive lesions. The telangiectatic variant of osteosarcoma may be particularly confusing, radiographically, since it forms a rapidly destructive, lytic (destroying) lesion.

When comparing osteosarcoma to fibrosarcoma, the latter has a broader age distribution and is even less common than osteosarcoma. Radiographically, bone lesions of fibrosarcoma are generally osteolytic (bone destroying). Osteosarcoma can be osteolytic, osteoblastic (bone forming), or have a mixed lytic and blastic appearance.

## Categories of Childhood Fibrosarcoma

Fibrosarcoma can be divided into the following categories:

- Primary medullary fibrosarcoma
- Primary surface fibrosarcoma
- Secondary fibrosarcoma
- Multi-centric fibrosarcoma
- Congenital fibrosarcoma

The last two types are exceptionally rare.

## Causes of Childhood Fibrosarcoma

For many years, it has been the hope, expressed in many epidemiological studies, to identify the cause or causes of malignancies that occur in early life. In particular, the limited temporal nature of intrauterine development provides a unique opportunity to identify carcinogenic stimuli. Foetal and/or maternal exposure to exogenous factors, including ionizing irradiation, drugs and viruses, may start the biological mechanisms responsible for tumour formation.

A genetic model of carcinogenesis has also been introduced in an attempt to clarify the pathogenesis and behavioural peculiarities of certain embryonic tumours. According to this hypothesis, embryonal neoplasms arise as a result of two mutational events in the genome. The first mutation is prezygotic in familial cases and postzygotic in non-familial; the second mutation is always postzygotic

**Auger, N., Goudie, C., Low, N., Healy-Profítós, J., Lo, E. & Luu, T.M.** 2019.

**BACKGROUND:** Previous studies provide conflicting evidence of a link between maternal substance use and risk of childhood cancer.

**METHODS:** We analyzed a cohort of 785,438 newborns in Quebec (2006-2016). We identified infants whose mothers had problematic illicit drug, tobacco, or alcohol use before or during pregnancy. The primary outcomes were childhood hematopoietic cancer or solid tumors within 0-5 years of age. Using Cox proportional hazards models, we computed hazard ratios (HR) and 95% confidence intervals (CI) for the association between maternal substance use and childhood cancer, adjusted for potential confounders.

**RESULTS:** A total of 925 cases of cancer occurred during 3.5 million person-years of follow-up. Children exposed to any maternal substance use had marginally elevated cancer incidence rates compared with unexposed children (29.4 vs. 26.1 per 100,000 person-years). Maternal illicit drug use was associated with the risk of acute lymphoblastic leukemia (HR 1.63, 95% CI 0.79-3.36) and fibrosarcoma (HR 2.11, 95% CI 0.86-5.16). Maternal tobacco use was associated with acute myeloid leukemia (HR 2.01, 95% CI 0.72-5.60) and fibrosarcoma (HR 2.13, 95% CI 1.05-4.32), but a weak association with neuroblastoma (HR 1.21, 95% CI 0.61-2.40) and renal tumors (HR 1.14, 95% CI 0.42-3.13) also appeared to be present.

**CONCLUSIONS:** We found a potential association between maternal substance use and certain types of early childhood cancer. Although effects were modest, maternal substance use may contribute to some types of childhood cancer, especially leukemia and fibrosarcoma.

## Diagnosis of Childhood Fibrosarcoma

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A soft tissue sarcoma usually produces no signs and symptoms in its early stages. As the tumour grows, it may cause:

- A noticeable lump or swelling
- Pain, if it presses on nerves or muscles
- A blockage in the stomach or intestines or gastrointestinal bleeding if the tumor is located in the abdomen or digestive tract

Soft tissue sarcomas can occur anywhere in your body, but the most common types of soft tissue sarcomas are gastrointestinal stromal tumours and soft tissue sarcomas that affect the extremities. About 60 percent of soft tissue sarcomas occur in the arms, legs, buttocks, hands or feet. Another 20 percent occur in the chest and abdomen. About 10 percent are found in the head and neck.

The following tests and procedures may also be used:

Physical examination and history - an exam of the body to check general signs of health, including checking for signs of disease, such as lumps or anything else that seems unusual. A history of the patient's health habits and past illnesses and treatments will also be taken.

X-rays - an x-ray is a type of energy beam that can go through the body onto film, making pictures of areas inside the body. A series of x-rays may be done to check the lump or painful area.

MRI (magnetic resonance imaging) - a procedure that uses a magnet, radio waves, and a computer to make a series of detailed pictures of areas inside the body. This procedure is also called nuclear magnetic resonance imaging (NMRI).

If these tests show there may be a soft tissue sarcoma, a biopsy is done. One of the following types of biopsies may be used:

Fine-needle aspiration (FNA) biopsy - the removal of tissue or fluid using a thin needle. A pathologist views the tissue or fluid under a microscope to look for cancer cells.

Core biopsy - the removal of tissue using a wide needle. A pathologist views the tissue under a microscope to look for cancer cells.

Incisional biopsy - the removal of part of a lump or a sample of tissue. A pathologist views the tissue under a microscope to look for cancer cells.

Excisional biopsy - the removal of an entire lump or area of tissue that doesn't look normal. A pathologist views the tissue under a microscope to look for cancer cells. An excisional biopsy may be used to completely remove smaller tumours that are near the surface of the skin.

In order to plan the best treatment, a large sample of tissue may be removed during the biopsy to find out the type of soft tissue sarcoma and do laboratory tests. Tissue samples will be taken from the primary tumour, lymph nodes, and other areas that may have a tumour. A pathologist views the tissue under a microscope to look for cancer cells and to find out the type and grade of the tumour. The grade of a tumour depends on how abnormal the cancer cells look under a microscope and how

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quickly the cells are dividing. High-grade tumours usually grow and spread more quickly than low-grade tumours. Because soft tissue sarcoma can be hard to diagnose, patients should ask to have biopsy samples checked by a pathologist who has experience in diagnosing soft tissue sarcoma.

One or more of the following laboratory tests may be done to study the tissue samples:

Cytogenetic analysis - a laboratory test in which cells in a sample of tissue are viewed under a microscope to look for certain changes in the chromosomes.

Immunohistochemistry study - a laboratory test in which dyes or enzymes are added to a blood or bone marrow sample to test for certain antigens (proteins that stimulate the body's immune response).

Immunocytochemistry study - a laboratory test that uses different substances to stain (colour) cells in a sample of tissue. This is used to tell the difference between the different types of soft tissue sarcoma.

Light and electron microscopy - a laboratory test in which cells in a sample of tissue are viewed under regular and high-powered microscopes to look for certain changes in the cells.

**Boutillier, B., Cardoen, L., Alison, M., Berrebi, D., Rosenblatt, J., Virlovet, A.L., Michon, J., Soudée, S. & Bonnard, A. 2019.**

"Infantile fibrosarcoma (IFS) is a rare nonrhabdomyosarcoma soft tissue tumor and accounts for less than 1% of childhood cancers. Forty per cent are present at birth and only 10% of IFS occurs in the abdomen. Our case of neonatal fibrosarcoma presented as a distal small bowel stenosis complicated with meconium peritonitis. The diagnosis was by histology of the surgical resection. The diagnosis of IFS is challenging as there are no specific features of IFS on imaging. Any unexpected solid lesion should raise the suspicion of complicated bowel tumoral lesion. If a neoplastic lesion is suspected extensive, surgery may be postponed until the final diagnosis is made."

**Edwards, T.M., Duran, M.S. & Meeker, T.M. 2017.**

**BACKGROUND:** Congenital infantile fibrosarcoma (CIF) is rare and represents less than 1% of all childhood cancers. It is a tumor that originates in the connective fibrous tissue found at the ends of long bones and then spreads to other surrounding soft tissues. These lesions are typically large, grow rapidly, and can often be mistaken for teratomas. Diagnosis is confirmed by pathology, where cellular proliferation of fibroblasts occurs. Imaging is an important part of the diagnosis, which includes the use of magnetic resonance imaging and/or computed tomography scan. Although surgical resection is the primary treatment, chemotherapeutic agents may be used as adjuvant therapy.

**PURPOSE:** To describe modalities for accurate diagnosis and treatment of CIF.

**METHODS/SEARCH STRATEGY:** PubMed was searched using terms "congenital infantile fibrosarcoma" and "infantile fibrosarcoma." Eleven relevant, English language articles were identified and utilized in the preparation of this case presentation.

**FINDINGS/RESULTS:** Complications addressed in this case presentation are prenatal diagnostic challenges, pharmacologic interventions in the setting of prematurity, immunosuppression, and acute liver and renal failure. Pharmacologic treatments will include chemotherapy agents, antimicrobial agents, as well as granulocyte colony-stimulating factor for immunosuppression. Nursing challenges included positioning and integumentary disturbances.

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**IMPLICATIONS FOR PRACTICE:** Utilization of diagnostic imaging and pathology to accurately identify and diagnose CIF is essential.

**IMPLICATIONS FOR RESEARCH:** Safety and efficacy of chemotherapeutic agents in premature infants with CIF need to be established.

### **Staging of Childhood Fibrosarcoma**

After childhood soft tissue sarcoma has been diagnosed, tests are done to find out if cancer cells have spread to other parts of the body.

The process used to find out if cancer has spread within the soft tissue or to other parts of the body is called staging. There is no standard staging system for childhood soft tissue sarcoma. Two methods that are commonly used for staging are based on the amount of tumour remaining after surgery to remove the tumour and/or the grade and size of the tumour and whether it has spread to the lymph nodes or other parts of the body. It is important to know the stage in order to plan treatment.

The tumour grade normally guides the treatment regimen:

#### **Grade I Tumour**

Surgery, in many cases limb-sparing surgery (wide excision with reconstruction)

Survival rate: 80% at 10 years

#### **Grade II Tumour**

Surgery plus adjuvant chemotherapy, although no definitive recommendations exist regarding chemotherapy for these intermediate-grade tumours

#### **Grade III Tumour**

Induction chemotherapy, limb-sparing surgical resection, and postoperative chemotherapy.

The overall 5-year survival rate ranges from 35% to 70%.

### **Treatment of Childhood Fibrosarcoma**

Treatment of newly diagnosed infantile fibrosarcoma may include the following:

- Surgery to remove the tumour when possible, followed by observation.
- Surgery followed by chemotherapy.
- Chemotherapy to shrink the tumour, followed by surgery.
- Targeted therapy ([crizotinib](#) and [larotrectinib](#)).
- A clinical trial that checks a sample of the patient's tumour for certain gene changes. The type of targeted therapy that will be given to the patient depends on the type of gene change.
- A clinical trial of targeted therapy ([larotrectinib](#), [entrectinib](#), or [selitrectinib](#)).

The treatment of childhood fibrosarcoma, therefore, may include:

**Surgery** - Surgery for fibrosarcoma involves the biopsy, surgical removal of the tumour, bone/skin grafts, limb salvage procedures, amputation and/or reconstruction, all performed by a surgeon. The type of surgery will depend on the size and location of the tumour, and whether the cancer has spread.

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Limb-sparing surgery - It is sometimes necessary to remove all or part of a limb. In most cases, however, limb-sparing surgery is used to avoid amputation.

- Through limb-sparing surgery, all of the bone and cartilage involved with the tumour, including some degree of muscle surrounding it, is removed, while nearby tendons, nerves and vessels are saved.
- The bone that is removed is replaced with a bone graft or with a metal prosthesis.
- Subsequent surgery may be needed to repair or replace rods, which can become loose or break.
- Patients who have undergone limb-sparing surgery need intensive rehabilitation. It may take as long as a year for a child to regain full use of a limb following limb-sparing surgery.
- Rarely, patients who undergo limb-sparing surgery may eventually have to have the limb amputated because of a severe complication or tumour.

Amputation - If the child's team determines that the tumour cannot be removed because it involves important nerves and blood vessels, amputation is the only surgical option.

[Picture Credit: Prosthesis]

During the operation, doctors ensure that muscles and skin form a cuff around the amputated bone. As the swelling decreases, (10 to 14 days), the child will be fitted for a plastic, temporary socket and prosthesis, which is used for two to four months until the stump is healed sufficiently to accept a permanent artificial limb.



The advantages of an amputation are that it is a simple operation with minimal chances of surgical complication and it definitively removes the local tumour. The functional outcome is good with the modern prostheses available today and with 'immediate-fit' prostheses applied in the operating room.

Although the child will probably have a limp with above-the-knee amputations, the procedure is functional and stable.

She/he will be able to walk, climb stairs, swim (with the prosthesis on or off) and participate in many sports such as skiing, basketball, baseball and tennis, although running will be limited.

Chemotherapy - Chemotherapy is a drug treatment that works by interfering with the cancer cell's ability to grow or reproduce.

While chemotherapy can be quite effective in treating certain cancers, the agents do not differentiate normal healthy cells from cancer cells.

Because of this, there can be many adverse side effects during treatment. Being able to anticipate these side effects can help the care team, parents, and child prepare, and, in some cases, prevent these symptoms from occurring, if possible.

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Chemotherapy is systemic treatment, meaning it is introduced to the bloodstream and travels throughout the body to kill cancer cells.

Chemotherapy can be given:

- as a pill to swallow
- as an injection into the muscle or fat tissue
- intravenously (directly to the bloodstream)
- intrathecally (directly into the spinal column)

**Bender, J., Anderson, B., Bloom, D.A., Rabah, R., McDougall, R., Vats, P. & Mody, R. 2019.**

“Infantile fibrosarcoma (IFS) is a rare soft-tissue sarcoma, which classically presents as an aggressive and rapidly enlarging tumor over the distal extremities of children in their first year of life. The presence of *ETV6* and *NTRK3* gene rearrangement is characteristic of IFS, which can be detected on routine fluorescence in situ hybridization (FISH) testing. Patients with IFS typically respond well to surgical resection and chemotherapy and have an overall survival of ~90%. In this report, we outline the use of integrative clinical sequencing (ICS) including RNA-seq in a patient with refractory, metastatic IFS to reveal an unusual fusion (*LMNA-NTRK1*), not detected by routine FISH testing, which was treated with oral crizotinib and resulted in a complete and durable long-term response. This study highlights the utility of ICS in identifying cryptic gene fusions, especially in refractory malignancies, and demonstrates how such information can be used to select targeted therapies in patients with actionable molecular alterations.”

**Janz, T.A., Nagasubaramanian, R. & Wei, J.L. 2019.**

**OBJECTIVE:** To examine pediatric head and neck fibrosarcoma cases and review the demographics, management, and survival for these patients.

**METHODS:** Pediatric patients in the Surveillance, Epidemiology, and End Results (SEER) database were included from 1973 to 2014 based on a diagnosis of a head and neck fibrosarcoma using ICD-O-3 head and neck primary sites and histology codes. Patients were included from birth-18 years of age. Additionally, a pediatric case of a head and neck infantile fibrosarcoma treated at the Nemours Children's hospital in Orlando, Florida is presented.

**RESULTS:** One hundred-thirteen pediatric head and neck fibrosarcomas were identified within the SEER database over the study period. The mean age at diagnosis was 9.8 years (SD: 6.2, range: 0.0-18.0). The mean age at diagnosis for infantile fibrosarcomas was 1.7 years (SD: 3.2, range: 0.0-12.0). Fifty-one (45.1%) patients were female. A majority (N = 67, 59.3%) of patients had dermatofibrosarcoma followed by 18 (15.9%) who had infantile fibrosarcomas. Nearly all patients (N = 107, 94.7%) received surgical intervention. 27.8% of patients with an infantile fibrosarcoma received chemotherapy as a part of their care compared to 1.5% of patients with a dermatofibrosarcoma (p = .004). The 5-year disease-specific survival was 97%.

**CONCLUSIONS:** Pediatric patients with head and neck fibrosarcomas are most likely to present in Caucasian males or females during late childhood or early adolescence. Infantile fibrosarcomas present in pediatric patients at a much earlier age. Surgical management is common for pediatric head and neck fibrosarcomas. Additionally, chemotherapy may be used for infantile fibrosarcomas of the head and neck. Survival rates for pediatric patients with a head and neck fibrosarcoma are excellent.

Rehabilitation - Rehabilitation includes physical and occupational therapy along with psychosocial support.

Supportive care - Supportive care includes any type of treatment to prevent and treat infections, side effects of treatments, and complications, and to keep the child comfortable during treatment.

Continual follow-up care - A schedule of follow-up care will be determined by the child's physician and other members of the care team to monitor ongoing response to treatment and possible late effects of treatment.

### **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/](http://www.sanctr.gov.za/)

### **Medical Disclaimer**

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### Dana Faber Cancer Institute

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**TheFetus.Net**

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