Cancer Association of South Africa (CANSA)

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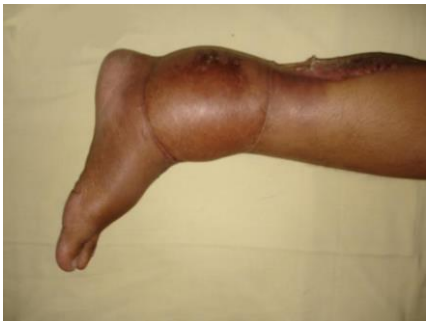
Fact Sheet
on
Synovial Sarcoma of
Childhood and Adolescence

Introduction

Soft-tissue sarcomas that are not rhabdomyosarcomas are classified as non-rhabdyomyosarcoma soft tissue sarcomas (NRSTS). Examples of the many types of NRSTS cancers include fibrosarcoma, leiomyosarcoma, liposarcoma, neurofibrosarcoma, peripheral nerve sheath tumours and synovial sarcoma. These cancerous tumours arise in the soft tissues of the body including tendons, muscles, nerves, fatty tissue and fibrous tissue. NRSTS can essentially occur at any site in the body containing these normal types of tissues, such as in the arms and legs, the head and neck region, the chest, abdomen and pelvis. NRSTS accounts for ~ 5 percent of all paediatric cancers.

[Picture Credit: Synovial Sarcoma]



Certain types of NRSTS are most likely to affect infants (under 1 year of age), while other types are more common in adolescents and young adults. Because soft tissue is expandable, these tumours can sometimes grow rather large before they are felt or cause problems for the patient. Like all cancers, they can invade surrounding tissues and metastasise (spread) to other organs of the body.

Synovial Sarcoma of Childhood and Adolescence

Synovial sarcoma (also referred to as 'SS') is the most common non-rhabdomyosarcamatous childhood soft-tissue sarcoma. The median age of patients at diagnosis is in the third decade of life, with 31% of the cases being in adolescents younger than 20 years of age.

Despite its name, synovial sarcoma is not related to the synovial tissues that are a part of the joints. The disease starts most commonly in the legs or arms, but it can appear in any part of the body. On a pathology report, synovial sarcoma may be classified in different subtypes depending on what it looks like under the microscope or what specific gene mutation is involved. Synovial sarcoma is a high grade tumour. It spreads to distant sites in up to 50% of cases. (Okcu, *et al,* 2003).

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Hickson, M., McHugh, K. & McCarville, B. 2020.

Purpose: To present a pictorial essay of paediatric primary synovial sarcomas from common and less documented anatomical locations. To review the literature for the imaging characteristics and prognostic factors of this rare but important childhood malignancy.

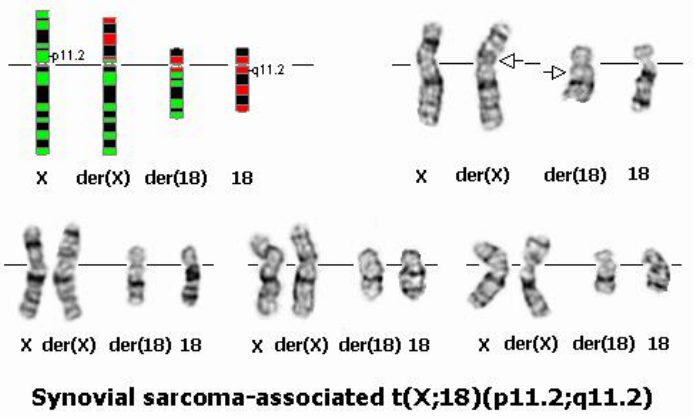
Method: 24 primary synovial sarcoma cases (17 male, 7 female with an age range 4-21 years) were reviewed in a collaborative effort between St Jude Children's Research Hospital and Great Ormond Street Hospital for Children. Images from 19 cases were selected for inclusion, to demonstrate the spectrum of appearances across imaging modalities, in a range of different anatomical locations (upper limb, lower limb, chest/abdomen/pelvis, and head and neck). A literature review depicting the typical radiological features and the prognostic significance of these features, was also conducted.

Results and conclusions: Primary synovial sarcoma can occur in any anatomical location, but typically within the extremities and often in close association with joints. Rarer anatomical locations described in our essay include the gastrohepatic ligament and femoral nerve sheath. We detail the salient imaging characteristics, including the T2 'triple signal' pattern which is believed to be highly specific for this particular sarcoma and in many cases predicts a poor outcome. Other poor prognostic factors include haemorrhage, lack of calcification and tumour size >10 cm. A broad range of radiological appearances are described, and in some cases related to anatomical position and size, however the presence of a soft tissue mass close to a joint in a young patient are suggestive of this diagnosis.

Causes of Synovial Sarcoma of Childhood and Adolescence

There are no well-established risk factors for synovial sarcoma, but the disease is associated with the chromosomal translocation t(X;18) (p11;q11). This means that parts of chromosome 18 and chromosome X have switched places in synovial sarcoma tumour cells. It is not known whether this mutation occurs randomly or follows a specific chain of events.

[Picture Credit: Genetics]



Because of this translocation, synovial sarcoma cells contain a mutant gene. This mutant gene is thought to contribute to the development of the disease. (The Liddy Shriver Sarcoma Initiative).

The exact cause of synovial sarcoma is not entirely understood, however, studies have indicated that genetic alterations may play a role in the formation of soft tissue sarcomas. Researchers have studied a small number of families that contain several members of one generation who have developed soft tissue sarcomas. In addition, limited studies have shown a possible link between soft tissue sarcomas and the development of other types of cancer.

Certain inherited diseases are also associated with an increased risk of developing soft tissue sarcomas. These include people with Li-Fraumeni syndrome (which involves alterations in the p53 gene) or neurofibromatosis (which involves alterations in the NF1 gene). For some soft tissue tumours, there seems to be an association with an Epstein-Barr virus infection.

Epidemiology
Synovial sarcomas typically present in adolescents and young adults (15-40 years of age). There may be a mild (M:F - 1.2:1) male predilection.

Presentation is most often with a slowly enlarging soft tissue mass which may have been noted for a number of years and gives a false impression of a benign (non-cancerous) process.

The most common location for these tumours is within the soft tissues adjacent to large joints, e.g. the knee and popliteal fossa. While these tumours arise near joints, it is rare for them to arise from the joint itself and despite their name, they do not arise from synovial structures, e.g. joints, tendon sheaths and bursae.

Incidence of Synovial Sarcoma of Childhood and Adolescence in South Africa
The National Cancer Registry (2017) does not provide any statistics regarding the incidence of synovial sarcoma of childhood and adolescence.

Signs and Symptoms of Synovial Sarcoma of Childhood and Adolescence
The following are the most common symptoms of synovial sarcoma. However, each child may experience symptoms differently. Symptoms can depend on the size and location of the tumour. Sometimes the symptoms of synovial sarcoma can resemble those of arthritis, bursitis or synovitis.

Symptoms may include:

- Swelling or mass (usually deep-seated)
- Mass that may or may not be accompanied by pain – it may be painful, in particular if nerves are involved
- Limping or difficulty using legs, arms, hands or feet
- The mass may hinder a bodily function. For example, in the head and neck region, it may cause difficulties swallowing and breathing or it may alter the voice.

The symptoms of synovial sarcoma may resemble other conditions. Always consult a children's physician for a diagnosis.

Diagnosis of Synovial Sarcoma of Childhood and Adolescence
The diagnosis usually starts with imaging studies. X-ray, sonogram, CT scan, and MRI scan may be used in the course of evaluating a suspicious mass.

After imaging studies, a next step in diagnosis may include a biopsy to remove a sample of the tumour for further analysis. Among the different types of biopsies, open biopsy (a surgical incision is made to remove the sample) or core needle biopsy (a large needle is used to take the sample) are preferred. The use of a fine needle to remove cells can establish the presence of cancer, but often those cells do not provide enough tissue to best characterise synovial sarcoma.

Once a tumour has been deemed malignant, further imaging studies such as a PET scan of the whole body and/or CT scan of the chest, abdomen or pelvis may be used to look for possible metastases (areas where the cancer has spread to).

Doctors use the material gathered during diagnosis to develop a patient's treatment plan. During this process, they consider many factors that are specific to the patient, including:

- the tumour's size and how invasive it is
- whether or not there is metastasis at the time of diagnosis
- whether or not the lymph nodes are involved.

Treatment of Synovial Sarcoma of Childhood and Adolescence

For tumour size of 5 cm or less, limb-saving surgical resection with generous margin with or without radiation therapy may be recommended. For tumour greater than 5 cm, multi-disciplinary approach using pre-operative (neoadjuvant) chemotherapy, plus pre-operative radiation treatment, followed by surgery is sometimes recommended, although the role of chemotherapy continues to be debated.

Ingley, K.M., Cohen-Gogo, S. & Gupta, A.A. 2020.

"Soft-tissue sarcoma (sts) is rare and represents approximately 7% of cancers in children and in adolescents less than 20 years of age. Rhabdomyosarcoma (rms) is most prevalent in children less than 10 years of age and peaks again during adolescence (16-19 years of age). Multi-agent chemotherapy constitutes the mainstay of treatment for rms. In other non-rhabdomyosarcoma soft-tissue tumours, such as synovial sarcoma, evidence for routine use of chemotherapy is less robust, and alternative treatment options, including targeted agents and immunotherapy, are being explored. In this review, we focus on chemotherapy for pediatric-type rms and discuss the advances and challenges in systemic treatment for select non-rhabdomyosarcoma soft-tissue tumours in children and adolescents. We support an increasingly cooperative approach for treating pediatric and adult sts."

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

Dana-Farber Cancer Institute
http://www.dana-farber.org/Health-Library/Childhood-Synovial-Sarcoma.aspx

Genetics
https://www.google.co.za/search?q=t(X%3B18)+(p11%3Bq11)&source=lnms&tbm=isch&sa=X&ei=U3fkU6vzG6fH7Aac74DoCQ&ved=0CAcQ_AUoAg&biw=1517&bih=714&dpr=0.9#facrc=_&imgdii=_&imgrc=82srsF0LjMIIEM%253A%3Blw4vhjiFFTeUOM%3Bhttp%253A%252F%252Fatlasgeneticsoncology.org%252FTumors%252FImages%252FXtX18p11q11G.jpg%3Bhttp%253A%252F%252Fatlasgeneticsoncology.org%252FTumors%252FSynovSarcID5044.html%3B488%3B292

Hale, R., Sandakly, S., Shipley, J. & Walters, Z. 2019. Epigenetic targets in synovial sarcoma: a mini-review. *Front Oncol*. 2019 Oct 18;9:1078. doi: 10.3389/fonc.2019.01078. eCollection 2019

Hickson, M., McHugh, K. & McCarville, B. 2020. Primary synovial sarcomas in the paediatric and young adult population: a pictorial review. *Eur J Radiol*. 2020 Dec;133:109376.

Ingley, K.M., Cohen-Gogo, S. & Gupta, A.A. 2020. Systemic therapy in pediatric-type soft-tissue sarcoma. *Curr Oncol*. 2020 Feb;27(Suppl 1):6-16. doi: 10.3747/co.27.5481. Epub 2020 Feb 1.

Khoury, J.D., Coffin, C.M., Spunt, S.L., Anderson, J.R., Meyer, W.H. & Parham, D.M. 2010. Grading on non-rhadcomyosarcoma soft tissue sarcoma in children and adolescents: a comparison of parameters used for the FNCLCC and POG systems. *Cancer*, 116 (9):2266-2274.

Lowery, C.D., Blosser, W., Dowless, M., Renschler, M., Perez, LV. Stephens, J., Pytowski, B., Wasserstrom, H., Stancato, L.F. & Falcon, B. 2019. Anti-VEGFR2 Therapy Delays Growth of Preclinical Pediatric Tumor Models and Enhances Anti-Tumor Activity of Chemotherapy. *Oncotarget*. 2019 Sep 17;10(53):5523-5533. doi: 10.18632/oncotarget.27148.

National Cancer Institute
http://www.cancer.gov/about-cancer/treatment/clinical-trials

Okcu, M.F., Munsell, M., Treuner, J., Maltke, A., Pappo, Al., Cain, A., Ferrari, A., Casanova, M.,Ozkan, A. & Raney, B. 2003. Synovial sarcoma of childhood and adolescence: a multicentre, multivariate analysis of outcome. Journal of Clinical Oncology, 21(8):1602-1611.

Radiopaedia.org
http://radiopaedia.org/articles/synovial-sarcoma

Sarcoma Foundation of America
http://www.curesarcoma.org/index.php/patient_resources/subtypes/synovial_sarcoma

Synovial Sarcoma
https://www.google.co.za/search?q=synovial+sarcoma&source=lnms&tbm=isch&sa=X&ei=dXTkU7-NFumM7Aar0YDYDw&sqi=2&ved=0CAYQ_AUoAQ&biw=1517&bih=714&dpr=0.9#facrc=_&imgdii=_&imgrc=OGTVquyQqgaqWM%253A%3BRXFgNvvhXpCBNM%3Bhttp%253A%252F%252Ffaoj.files.wordpress.com%252F2009%252F03%252Ffossfig3c.jpg%3Bhttp%253A%252F%252Ffaoj.org%252F2009%252F03%252F01%252Ffunctional-outcomes-of-reconstruction-for-soft-tissue-sarcomas-of-the-foot-and-ankle%252F%3B640%3B480

The Liddy Shriver Sarcoma Initiative
http://sarcomahelp.org/synovial-sarcoma.html

University of Chicago Medicine
http://www.uchicagokidshospital.org/specialties/cancer/sarcoma/non-rhabdomyosarcoma/