Cancer Association of South Africa (CANSA)

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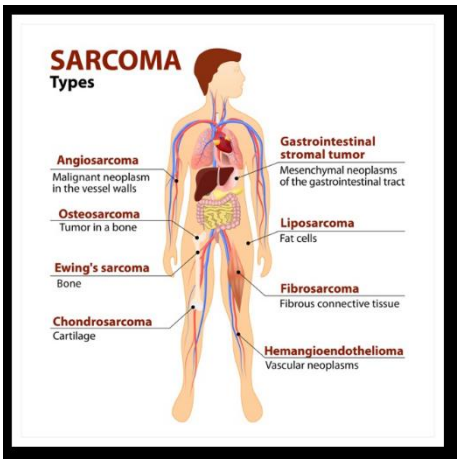
Fact Sheet
on
Synovial Sarcoma

Introduction

Cancerous (malignant) tumours of connective tissues are called "sarcomas". The term sarcoma comes from a Greek word meaning fleshy growth. Sarcoma arises in the connective tissue of the body. Normal connective tissue include, fat, blood vessels, nerves, bones, muscles, deep skin tissues, and cartilage.



[Picture Credit: Sarcoma]

Sarcomas are divided into two main groups, bone sarcomas and soft tissue sarcomas.

They are further sub-classified based on the type of presumed cell of origin found in the tumour. They all share certain microscopic characteristics and have similar symptoms.

Sarcomas can develop in children and adults. For children under 20 approximately 15 percent of cancer diagnosis are sarcomas.

Synovial Sarcoma

Synovial sarcoma is a cancer that can come from different types of soft tissue, such as muscle or ligaments. It is often found in the arm, leg, or foot, and near joints such as the wrist or ankle. It can also form in soft tissues in the lung or abdomen. Synovial sarcoma may also be called malignant synovioma or synovial cell sarcoma. Synovial sarcoma accounts for 5% to 10% of soft-tissue tumours.

One third of patients with synovial sarcoma will be diagnosed under the age of 30. It is somewhat more common in males. It is a high grade tumour which spreads to distant sites in up to 50% of cases.

It is known that in synovial sarcoma, chromosomes (the parts of your cells that contain all of your genes) break apart and get put back together in the wrong way. This can cause cells to not function like they should. In synovial sarcoma, a gene called *SYT* is joined to *SSX* genes. Doctors will look for this change in chromosomes to confirm that it is synovial sarcoma.

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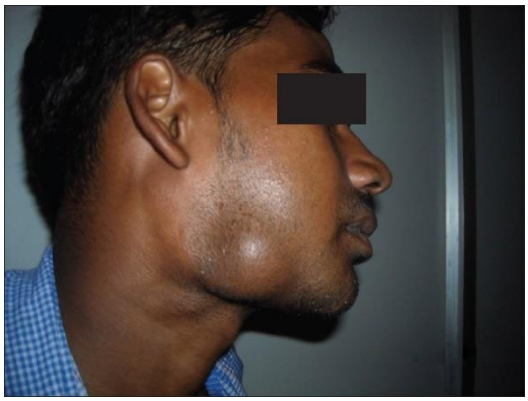
Despite its name, synovial sarcoma is not related to the synovial tissues that are a part of the joints. The disease starts most commonly in the legs or arms, but it can appear in any part of the body. On a pathology report, synovial sarcoma may be classified in different subtypes depending on what it looks like under the microscope or what specific gene mutation is involved.



[Picture Credit: Synovial Sarcoma in Adult]

Hale, R., Sandakly, S., Shipley, J. & Walters, A. 2019.
Synovial Sarcomas (SS) are a type of Soft Tissue Sarcoma (STS) and represent 8-10% of all STS cases. Although SS can arise at any age, it typically affects younger individuals aged 15-35 and is therefore part of both pediatric and adult clinical practices. SS occurs primarily in the limbs, often near joints, but can present anywhere. It is characterized by the recurrent pathognomonic chromosomal translocation t(X;18)(p11.2;q11.2) that most frequently fuses SSX1 or SSX2 genes with SS18. This leads to the expression of the SS18-SSX fusion protein, which causes disturbances in several interacting multiprotein complexes such as the SWItch/Sucrose Non-Fermentable (SWI/SNF) complex, also known as the BAF complex and the Polycomb Repressive Complex 1 and 2 (PRC1 and PRC2). Furthermore, this promotes widespread epigenetic rewiring, leading to aberrant gene expression that drives the pathogenesis of SS. Good prognoses are characterized predominantly by small tumor size and young patient age. Whereas, high tumor grade and an increased genomic complexity of the tumor constitute poor prognostic factors. The current therapeutic strategy relies on chemotherapy and radiotherapy, the latter of which can lead to chronic side effects for pediatric patients.

Cai, H.J., Cao, N., Wang, W., Kong, F.L., Sun, X.X. & Huang, B. 2019.
BACKGROUND: Synovial sarcoma, a rare mesenchymal tumor type with unclear histological origin and direction of differentiation, accounts for 6%-10% of soft tissue tumors. It is mainly located near the joints and tendons of the limbs, and occurs primarily in children or young adults. Primary renal synovial sarcoma (PRSS) is very rare, accounting for approximately 1% of synovial sarcomas. It is a spindle cell tumor type affecting mesenchymal tissue, and has morphological, genetic, and clinical characteristics, and a certain degree of epithelial differentiation. It is highly malignant and has the fourth highest incidence among soft tissue sarcomas. Here, we report a case of PRSS and share some valuable information about the disease.
CASE SUMMARY: A 54-year-old male patient was admitted to the hospital for a space-occupying lesion in the right kidney for 2 d upon ultrasound examination. The patient had no cold or fever; no frequency, urgency or pain of urination; and no other discomfort. The results of a hemogram, blood biochemistry, and tumor markers were in the normal range. The patient was examined by computed tomography (CT), which indicated the presence of a soft tissue density shadow with a diameter of approximately 6.8 cm in the right renal pelvis area, showing uneven enhancement. Ultrasound indicated a cystic solid mass of approximately 6.8 cm × 6.5 cm in the right kidney, with an unclear boundary and irregular shape. Meanwhile, color Doppler flow imaging showed dotted blood flow signals in the periphery and interior. Contrast-enhanced ultrasound (CEUS) showed "slow in and fast out" hyperenhancement of the right renal mass after contrast agent injection. The postoperative pathological diagnosis was (right kidney) synovial sarcoma. Despite postoperative adjuvant chemotherapy, tumor recurrence was detected two years later.
CONCLUSION: PRSS is a rare malignant tumor. To date, no characteristic imaging findings have been observed. The diagnosis is confirmed primarily through postoperative pathological immunohistochemistry and SS18 (SYT) gene detection. In this case, CEUS was used preoperatively. We found that PRSS has the characteristic

of "slow in and fast out" hyperenhancement, and its particular characteristics have diagnostic value. Postoperative adjuvant chemotherapy is not very effective.

Incidence of Synovial Sarcoma

The South African National Cancer Registry does not provide any information regarding any of the Sarcoma types.

Signs and Symptoms of Synovial Sarcoma

In the early stages of the condition, synovial sarcoma may cause no noticeable signs or symptoms. However, as the tumour grows larger, affected people may notice a lump or swelling. In some cases, the tumour can limit range of motion or cause numbness and/or pain if it presses on nearby nerves.

A slow-growing painless mass is common and may give the false impression that it is harmless. When a tumour is painless and deep-seated within the body, it may go unnoticed for a long time.

The following symptoms may arise:

- 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 mass may be painful, in particular if nerves are involved.

Primary site distribution of Synovial Sarcoma:

- Extremities: 68.7%
- Trunk: 15.7%
- Head and neck: 6.3%
- Intra-thoracic: 5.3%
- Intra-abdominal: 1.8%
- Other: 2.2%

Causes and Risk Factors for Synovial Sarcoma

The origin of synovial sarcoma is unclear. Its name notwithstanding, this sarcoma is not associated with synovial joints. The basis for the name synovial cell sarcoma was the similarity between cells of this tumour and primitive synoviocytes.

It has been suggested that there is a neurologic origin for this sarcoma. There is a histologic resemblance between neural cells of malignant peripherical nerve sheath tumour (MPNST) and synovial sarcoma. Synovial sarcoma is associated with a history of a long-standing nodule, sometimes present for years, which increases rapidly in size over a few months; therefore, it is sometimes overlooked. The tumour spreads along fascial planes and can be much more widespread than it appears on initial evaluation.

Some potential risk factors may include:

- having certain inherited conditions such as Li-Fraumeni syndrome or neurofibromatosis type 1
- exposure to radiation
- exposure to chemical carcinogens

Diagnosis of Synovial Sarcoma
Diagnosis may starts with imaging studies:

- X-ray
- Sonogram
- CT scan
- MRI scan

Followed by a Biopsy – removal of a sample of the tumour for further analysis

Cytogenetic analysis may aid the treating physician in detecting the specific chromosomal translocation

Wang, J., Kok, H.K. & Bayat, I. 2019.
"Synovial sarcomas are a rare but aggressive malignancy that primarily affects young patients. Diagnosis is often difficult and delayed due to its insidious onset, heterogenous presentation and mimicry of other pathologies. We present the case of a patient with a history of a slow-growing left arm mass that arose after a traumatic fracture of the humerus. Multimodal imaging was undertaken and reported the mass as being consistent with a vascular malformation of the brachial artery. The patient underwent surgical repair of the artery and intraoperative biopsies confirmed a diagnosis of synovial sarcoma. This case highlights the importance of maintaining suspicion for soft-tissue sarcomas in young patients presenting with a mass, and demonstrates the way in which these tumours may mimic other pathologies both clinically and radiologically. Early referral to a specialist sarcoma centre is key for further investigative workup."

Gao, J., Yuan, Y.S., Liu, T., Lv, H.R. & Xu, H.L. 2019. Synovial sarcoma in the plantar region: a case report and literature review. *World J Clin Cases*. 2019 Sep 6;7(17):2549-2555. doi: 10.12998/wjcc.v7.i17.2549.
BACKGROUND: Synovial sarcoma (SS), a rare malignant soft tissue tumor whose histological origin is still unknown, often occurs in limbs in young people and is easily misdiagnosed.
CASE SUMMARY: We report a 24-year-old man who sought treatment for plantar pain thought to be caused by a foot injury that occurred 4 years prior. Currently, he had been seen at another hospital for a 1-wk history of unexplained pain in the left plantar region and was treated with acupuncture, a kind of therapy of Chinese medicine, which partly relieved the pain. Because of this, the final diagnosis of biphasic SS was made after two subsequent treatments by pathological evaluation after the last operation. SS is rarely seen in the plantar area, and his history of a left plantar injury confused the original diagnosis.
CONCLUSION: This study shows that pathological and imaging examinations may play a vital role in the early diagnosis and treatment of SS.

Liu, Y.F., Jia, C., Zhang, M., Chen, G.S., Zhang, N., Fu, L.B., Wang, L. & He, L.J. 2019.
Objective: To investigate histopathological characteristics, and differential diagnoses of childhood synovial sarcoma.
Methods: HE staining, immunohistochemical staining and fusion gene detection by FISH were performed in 12 cases of synovial sarcoma in childhood at Beijing Children's Hospital from 2016 to 2018.
Results: There were 6 cases of biphasic type, 1 case of monophasic epithelial type, 3 cases of monophasic spindle cell type and 2 cases of poorly differentiated synovial sarcomas. EMA, CKpan, bcl-2, CD99, TLE1 and CD34 immunostain positivities were observed in 10/12, 9/12, 12/12, 10/12, 10/12 and 0/12 cases respectively. Unique INI1 immunohistochemical staining was observed in 9/12 cases. SS18-SSX gene fusion was detected in 8 of 11 cases by FISH.

Conclusions: Synovial sarcoma is rare in children. Histological morphology combined with immunohistochemistry and FISH SS18-SSX fusion gene detection are important for the diagnosis and differential diagnosis of synovial sarcoma in children.

Post, J., Houdek, M., Folpe, A.L., Kakar, S.K. & Wilke, B.K. 2019.
PURPOSE: Previous studies have grouped the treatment of axial and appendicular synovial sarcomas. The purpose of this study was to assess the prognostic variables of upper extremity synovial sarcomas (UESS) and compare the outcomes of those who underwent a nononcologic or inadvertent excision prior to definitive resection to those who underwent an initial oncologic resection.
METHODS: We reviewed the records of 23 UESS treated with definitive surgery at our institution between 1990 and 2014. There were 13 women and 10 men with a median age of 30 years (6-60) and median follow-up of 63 months (15-248). Prognostic variables, recurrence-free survival (RFS), and overall survival (OS) were then assessed.
RESULTS: Fifteen patients (65%) had a prior unplanned excision. Five patients required an amputation to obtain local control of disease. There were 3 observed local recurrences and 2 distant metastases at a median of 45 months from presentation. We found no difference in need for amputation, RFS, or OS between those who had undergone a planned excision and those who had an unplanned excision.
CONCLUSION: While we were unable to find a significant difference in outcomes or amputation rates between those who underwent reexcision of a previously unplanned excision and those who underwent an initial planned resection, the high rate of unplanned excision is troubling and should remind practitioners to consider sarcoma in the differential of all upper extremity masses.

Zhang, Y., Wessman, S., Weide, J. Tani, E. & Haglund, F. 2019.
OBJECTIVE: Synovial sarcomas (SS) are rare soft tissue tumours defined by the SYT-SSX fusion gene. The tumours are composed of mesenchymal cells with varying degrees of epithelial differentiation. Cytomorphological descriptive studies are limited to small series and single cases. In this study we systematically examined the cytological features of SS diagnosed at our institution.
METHODS: SS diagnosed by fine-needle aspiration (FNA) cytology at our institution between 2006 and 2018 were reviewed by a panel of senior cytopathologists. Clinical and cytopathological characteristics were categorised and described.
RESULTS: A total of 38 SS FNAs were identified from 35 patients. The cytomorphology was uniform, presenting as highly cellular smears of clusters and individual cells with mixed round, oval and spindle cells. We frequently observed pericapillary arrangement and occasionally pink background stroma was seen. Glandular formation or epithelial components were identified in the majority of cases which on histology were subtyped as biphasic SS. Pleomorphism and mitoses were rare. Immunocytochemical analysis was frequently positive for vimentin, epithelial membrane antigen, Bcl2 and, in recent cases, TLE1. Pan-cytokeratins and CK7 could occasionally be positive in biphasic cases. The diagnostic SYT-SSX fusion gene was detected in all FNA specimens using polymerase chain reaction or fluorescence in situ hybridisation.
CONCLUSIONS: SS have distinct and uniform cytopathological features. Molecular genetic analysis for SYT-SSX are invaluable for diagnosing SS with FNA and should be implemented in cytopathological laboratories that routinely perform soft tissue diagnostics.

Treatment of 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. Doctors use the

material gathered during diagnosis to develop a patient's treatment plan. During this process, the treating physician may consider various factors that are specific to the patient, including:

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

Surgery is the mainstay of treatment for synovial sarcoma. The goal is to remove the cancer and a margin of healthy tissue around it. This can sometimes mean the removal of an entire muscle or muscle group, or even amputation. To decrease the chances of recurrence, the treating physician may suggest a regimen of radiation therapy or chemotherapy (or a combination of the two) in addition to surgery.

Cheng, Y., Mo, F., Pu, L., Li, Q. & Ma, X. 2019.
Background: Inflammatory indexes have been considered as important prognostic factors in various types of cancers. This study aimed to evaluate prognostic values of neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR) in patients with synovial sarcoma (SS).
Methods: One hundred and three patients diagnosed with SS were collected during 2006-2017 and divided into high or low NLR, PLR, and LMR groups based on receiver operating characteristic curve analysis. Data of clinical variables were collected for univariate and multivariate analyses. The Kaplan-Meier method was used to analyze OS and PFS of SS patients and significance was evaluated by the log-rank test.
Results: The optimal cut-off values of NLR, PLR, and LMR were 2.70, 154.99, and 4.16, respectively. Univariate analyses identified resection surgery, distant metastasis, NLR, PLR, and LMR as the potential predictors of progression-free survival (PFS) and overall survival (OS). In the multivariate analyses, NLR was independent predictors for OS (HR 5.074, 95% CI 1.200-21.463, p = 0.027). Resection surgery, metastasis and LMR was independent predictors for PFS (HR 5.328, p = 0.017; HR 3.114, p = 0.04 and HR 0.202, p = 0.025, respectively).
Conclusion: Resection surgery, distant metastasis, NLR, and LMR were independent prognostic factors of PFS and OS in patients with synovial sarcoma. Surgery as an effective treatment strategy, other than radiotherapy and chemotherapy, can significantly prolong survival of synovial patients. Clinical utility of these inflammatory biomarkers should be validated in a larger sample size study.

Outani, H., Kakunaga, S., Hamada, K., Takenaka, S., Imura, Y., Nagata, S., Tanaka, T., Tamiya, H., Oshima, K., Naka, N., Kudawara, I., Araki, N., Ueda, T. & Yoshikawa, H. 2019.
"Synovial sarcoma (SS) is considered to be a chemosensitive, soft tissue sarcoma. Therefore, neoadjuvant and/or adjuvant chemotherapy (N/AC) is used for the treatment of high-risk SS patients. However, the role of N/AC remains controversial. The present study aimed to review the clinical outcomes of surgically treated localized SS and investigate the effects of N/AC with long-term observation. The clinical outcomes of 54 patients with surgically treated localized SS were retrospectively analyzed. The median patient age was 42 years (range, 8-81 years), and the median follow-up period was 94 months for survivors (range, 7-220 months). A total of 38 patients (70%) received chemotherapy. Of these, 32 (59%) patients received neoadjuvant chemotherapy, 33 (61%) received adjuvant chemotherapy, and 27 (50%) received neoadjuvant and adjuvant chemotherapy. Fourteen patients (26%) received adjuvant radiotherapy. Three patients (6%) had local recurrence and 13 patients (24%) developed distant metastasis. The overall survival (OS) rates at 5 and 10 years were 87 and 84%, respectively. N/AC did not improve survival. In conclusion, we found satisfactory long-term OS among patients with a high utilization rate of N/AC. Further study should be necessary to evaluate which population of SS would benefit from N/AC."

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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Sarcoma
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