Cancer Association of South Africa (CANSA)

Research • Educate • Support

Fact Sheet on Symptomatic Tenosynovial Giant Cell Tumour (TGCT)

[Picture Credit: TGCT]

Introduction

The majority of benign soft tissue masses are nonneoplastic and of little clinical consequence. However, some locally aggressive fibromatoses (desmoid tumours), infiltrating lipomas, neurofibromas, and vertebral hemangiomas may cause significant morbidity and, in some cases, mortality.

Tenosynovial giant cell tumour (TGCT) is a group of rare tumors that form in the joints. TGCT is not typically cancerous, but it can grow and damage surrounding structures. These tumours grow in three areas of the joint: synovium: the thin layer of tissue that lines the inner joint surfaces.

TGCTs are divided into types based on where they are and how quickly they grow.
Localized giant cell tumours grow slowly. They start in smaller joints like the hand. These tumours are called giant cell tumours of the tendon sheath (GCTTS).

Diffuse giant cell tumours grow quickly and affect large joints like the knee, hip, ankle, shoulder, or elbow. These tumours are called pigmented villonodular synovitis (PVNS).

Both localized and diffuse TGCTs are found inside the joint (intra-articular). Diffuse giant cell tumours can also be found outside the joint (extra-articular). In rare cases, they can spread to sites like the lymph nodes or lungs.

Symptomatic Tenosynovial Giant Cell Tumour (TGCT)

Tenosynovial Giant Cell Tumours (TSGCTs) are a group of rare, benign tumours that involve the synovium, bursae and tendon sheath. Synovium is the thin layer of tissue or membrane that covers the inner surface of the joint spaces and the bursae and tendon sheaths. The bursae are small fluid-filled sacs that cushion bones, tendons, and muscles around the joints. A tendon sheath is a layer membrane that covers a tendon. Tendons are fibrous tissue that connect muscle to bone.

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 Audiometry and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]
Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

This condition is often confused to be a type of cancer by individuals affected by this condition.

These tumours cause the affected synovium, bursae, or tendon sheaths to thicken and overgrow. They are benign, which means they are not cancerous and do not spread to other areas of the body (metastasize). However, they can grow and cause damage to the surrounding tissue and structures of the body. Symptoms can include pain, swelling, and limitation of movement of the joint. Large or small joints can be affected depending upon the tumour subtype. Surgery is the main treatment option, but the tumour tends to recur, particularly in pigmented villonodular synovitis, which is the diffuse-type of giant cell tumour. If untreated or if the tumour continually recurs, these tumours can result in damage and degeneration of the affected joint and surrounding tissues or structures. Sometimes, they can cause significant disability.

Monestine, S. & Lazaridis, D. 2020. Pexidartinib (TURALIO™): The First FDA-Indicated Systemic Treatment for Tenosynovial Giant Cell Tumor. *Drugs R D.* 2020 Sep;20(3):189-195.
"Tenosynovial giant cell tumor is a rare proliferative tumor that arises from the synovium, bursae, or tendon sheaths due to an overproduction of colony-stimulating factor 1. Historically, treatment options for patients with local or diffuse tenosynovial giant cell tumor have been limited to surgical interventions. However, for some patients, surgical resection could worsen functional limitations and/or morbidity. In August 2019, the FDA approved pexidartinib (TURALIO™, Daiichi Sankyo), the first systemic treatment option for adult patients with symptomatic tenosynovial giant cell tumor associated with severe morbidity or functional limitations that were not amenable to improvement with surgery. Pexidartinib is an oral tyrosine kinase inhibitor with selective inhibition of colony-stimulating factor 1 receptor and is the first systemic therapy to show significant improvement in overall response rates when compared with placebo. Clinicians using pexidartinib should monitor for liver-related adverse events, which may require treatment interruption, dose reduction, or treatment discontinuation. Pexidartinib provides a novel non-surgical treatment option for patients with tenosynovial giant cell tumor that may significantly improve patients' overall response, range of motion, physical function, tumor volume, and stiffness."

Incidence of Symptomatic Tenosynovial Giant Cell Tumour (TGCT)
Because Symptomatic Tenosynovial Giant Cell Tumour is not typical malignant (cancerous), the National Cancer Registry does not provide any information regarding this condition.

Causes of Symptomatic Tenosynovial Giant Cell Tumour (TGCT)
Researchers have determined that a minority of the cells that make up a tenosynovial giant cell tumour (TSGCT) carry a specific chromosomal translocation. Chromosomes, which are present in the nucleus of human cells, carry the genetic information for each individual. Human body cells normally have 46 chromosomes. Pairs of human chromosomes are numbered from 1 through 22 and the sex chromosomes are designated X and Y. Males have one X and one Y chromosome and females have two X chromosomes. Each chromosome has a short arm designated "p" and a long arm designated "q". Chromosomes are further sub-divided into many bands that are numbered. For example, "chromosome 11p13" refers to band 13 on the short arm of chromosome 11. The numbered bands specify the location of the thousands of genes that are present on each chromosome.

TGCTs are caused by a change to a chromosome, called a translocation. Pieces of a chromosome break off and change places. It isn't clear what causes these translocations.

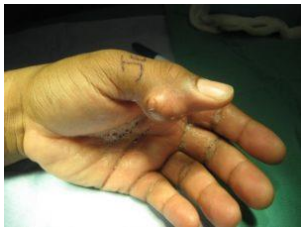
Chromosomes contain the genetic code for producing proteins. The translocation leads to the excess production of a protein called colony-stimulating factor 1 (CSF1).

This protein attracts cells that have CSF1 receptors on their surface, including white blood cells called macrophages. These cells clump together until they eventually form a tumour.

TGCTs often start in people who are in their 30s and 40s. The diffuse type is more common in men. These tumours are extremely rare: only 11 out of every 1 million people in the United States are diagnosed each year.

Synonyms of Tenosynovial Giant Cell Tumour (TGCT)

- giant cell tumour of the tendon sheath (GCTTS)
- nodular tenosynovitis
- diffuse-type giant cell
- pigmented vilonodular synovitis (PVNS)



[Picture Credit: TGCT]

Signs and Symptoms of Symptomatic Tenosynovial Giant Cell Tumour (TGCT)

The signs and symptoms of tenosynovial giant cell tumors (TGCTs) can vary depending upon the exact location involved and the subtype present.

Diffuse TGCT - (also known as diffuse-type giant cell tumor; formerly, PVNS).

Diffuse TGCT usually affects the large joints; the tumor is widespread (diffuse) and affects the entire joint. In most instances, only one joint is involved (monoarticular disease). The knee is most often affected, followed by the hip. The ankle, elbow or shoulder can also be affected. In rare instances, the two joints that connect the jaw bones to the skull (temporomandibular joints) or the joints that connect vertebrae together (spinal facet joints) can be affected.

The initial symptoms are usually pain and swelling of the affected joint. Stiffness of the joint can also occur. Usually, these symptoms have a gradual onset. There may be a feeling of warmth or tenderness on the skin of the affected joint. A painless swelling of the joint is sometimes the first sign. Sometimes, swelling can be significant. Affected individuals may have a sensation of the affected joint 'locking' or 'catching.' There may be a popping sound on occasion and the joint may be unstable.

Diffuse TGCT can progress to cause arthritic damage and degeneration to the joint and damage to the surrounding cartilage and bone. If untreated, diffuse TGCT can potentially cause chronic, debilitating disease and significant functional impairment of the affected joint. Surgery is the main form of treatment, but the disease often recurs.

Localized TGCT - (Intraarticular GCTTS, formerly localized PVNS; extraarticular GCTTS; formerly nodular tenosynovitis).

Localized TGCT usually presents as a small growth or mass of abnormal tissue (nodules) or as a small growth that is connect to the affected area with a stalk of abnormal tissue (pedunculated mass). These tumours are

usually limited to a specific area of the joint (localized) and they typically affect smaller joints such as those of the hands and feet. The initial sign is often a painless swelling. The tumour grows slowly over time. Sometimes they cause pain. Eventually, affected individuals may have a sensation of the affected joint 'locking' or 'catching.' The affected joint may become unstable. Unlike the diffuse form, these tumours are unlikely to cause destructive changes to the joint or surrounding areas and are less likely to recur after treatment.

Diagnosis of Symptomatic Tenosynovial Giant Cell Tumour (TGCT)

Because these common TGCT symptoms are much like those of a number of joint conditions, including arthritis, it is typically diagnosed through:

- computerized tomography (CT)
- magnetic resonance imaging (MRI) scans and
- a tissue biopsy.

Treatment of Symptomatic Tenosynovial Giant Cell Tumour (TGCT)

Currently, surgery remains the treatment of choice for patients with Symptomatic Tenosynovial Giant Cell Tumour. Localized TGCT is managed by marginal excision. Recurrences occur in 8-20% of patients and are easily managed by re-excision.

Diffuse TGCT tends to recur more often (33-50%) and has a much more aggressive clinical course. Patients are often symptomatic and require multiple surgical procedures during their lifetime. For patients with unresectable disease or multiple recurrences, systemic therapy using CSF1R inhibitors may help delay or avoid surgical procedures and improve functional outcomes.

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

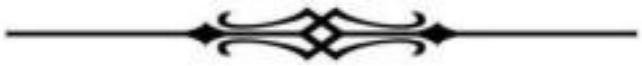
The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact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

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

Medical Disclaimer

This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet.

Whilst the Cancer Association of South Africa (CANSA) has taken every precaution in compiling this Fact Sheet, neither it, nor any contributor(s) to this Fact Sheet can be held responsible for any action (or the lack thereof) taken by any person or organisation wherever they shall be based, as a result, direct or otherwise, of information contained in, or accessed through, this Fact Sheet.



Sources and References Consulted and/or Utilised

Tenosynovial Giant Cell Tumour
https://rarediseases.org/rare-diseases/tenosynovial-giant-cell-tumor/
https://www.oncnet.com/news/fda-approves-pexidartinib-symptomatic-tenosynovial-giant-cell-tumors
https://www.mdedge.com/hematology-oncology/article/205851/sarcoma-gist/fda-approves-turalio-symptomatic-tenosynovial-giant
https://www.uptodate.com/contents/treatment-for-tenosynovial-giant-cell-tumor-and-other-benign-neoplasms-affecting-soft-tissue-and-bone
https://rarediseases.org/rare-diseases/tenosynovial-giant-cell-tumor/

Monestine, S. & Lazaridis, D. 2020. Pexidartinib (TURALIO™): The First FDA-Indicated Systemic Treatment for Tenosynovial Giant Cell Tumor. *Drugs R D.* 2020 Sep;20(3):189-195.

Symptomatic Tenosynovial Giant Cell Tumour (TGCT)
https://medwinpublishers.com/JOBD/JOBD16000172.pdf
https://www.healthline.com/health/tgct/types-symptoms#:~:text=Tenosynovial%20giant%20cell%20tumor%20(TGCT)%20is%20a%20group%20of%20rare,lines%20the%20inner%20joint%20surfaces
https://www.everydayhealth.com/rare-diseases/questions-to-ask-your-doctor-after-a-tenosynovial-giant-cell-tumor-diagnosis/

TGCT
https://www.hand2shoulderclinic.in/giant-cell-tumors-gct-tendon-sheath/