Tenosynovial Giant Cell Tumor (formerly Pigmented Villonodular Synovitis)

Tenosynovial giant cell tumors (TGCT) arise from the synovium, tendon sheath, and bursae of a joint. The tumors may be intra-articular, extra-articular, or both. Since tenosynovial giant cell tumors do not metastasize, they are not classified as malignant. However, tenosynovial giant cell tumors can be infiltrative, proliferative, and locally aggressive, for example causing erosion of adjacent bones, damaging ligaments, and leading to degenerative joint disease.

Within the spectrum of tenosynovial giant cell tumors, there are two subtypes: localized and diffuse. The localized form (L-TGCT) is nodular and usually involves a single tumor, commonly seen at the distal joints of the extremities. The diffuse type (D-TGCT) involves multiple tumors with extensive synovial infiltration often extending into extra-articular structures. It is usually found at the knee, hip, ankle, and shoulder joints. While the two subtypes differ in some features, they exist on a spectrum and share the same pathogenesis, molecular drivers, and treating specialists.

Outside of active surveillance, the standard treatment for tenosynovial giant cell tumor is complete surgical resection. Unfortunately, tenosynovial giant cell tumors have high recurrence rates post-resection, with the major risk factors for recurrence being incomplete resection and prior recurrence. Given that the pathogenesis of tenosynovial giant cell tumors involves aberrations in the *colony stimulating factor 1* (*CSF1*) gene, systemic CSF1 inhibitors are also used for symptomatic tumors that are either unlikely to benefit from surgery or where surgery could even worsen function.

Physician specialties caring for individuals with tenosynovial giant cell tumors include medical oncology, orthopedic oncology, orthopedic surgery, and general orthopedics. Sarcoma specialists are frequently involved.

The annual incidence of TGCT is estimated to be 43 new cases per million, or about 14,700 new cases per year in the US. However, incidence alone substantially underrepresents the number of people affected by TGCT. Because TGCT is rarely life-threatening, many individuals live with the disease for decades. As a result, while receiving a diagnosis of TGCT is relatively uncommon, living with TGCT is not. The prevalence of TGCT, representing the total number of people with TGCT in the US, is estimated at 56 per 100,000, or about 191,500 people. Further, the true burden of TGCT is likely greater a result of misdiagnosis and delayed diagnosis, and due to inaccurate reporting associated with clinical reclassification and revised nomenclature in more recent years.

Historically, the disorder was classified as a musculoskeletal inflammatory condition and referred to as pigmented villonodular synovitis (PVNS). However, advances in molecular pathology have fundamentally changed the understanding of its pathophysiology and established that TGCT is a neoplasm rather than a primary inflammatory musculoskeletal disorder. This reclassification followed the discovery of recurrent *CSF1* gene rearrangements, most commonly a fusion of the *CSF1* and *COL6A3* genes, a clonal cytogenetic abnormality characteristic of neoplastic processes, such as

sarcoma. The resulting overexpression of colony-stimulating factor 1 (CSF1) recruits non-neoplastic inflammatory cells and drives tumor growth.

The historical term "pigmented villonodular synovitis" is also misleading because the defining features implied by the name are neither universal nor central to the disease process. Hemosiderin-laden macrophages, which produce characteristic pigmentation, are not always present, and the finger-like villonodular architecture does not develop in every case. Although synovitis and other inflammatory changes commonly occur, they are secondary to the underlying neoplastic process rather than the primary disease and do not respond to anti-inflammatory medications or corticosteroids.

As clinical classification evolved to reflect the true nature of the disorder, inconsistencies in nomenclature led to variability and confusion in documentation and clinical literature. The term “pigmented villonodular synovitis” was recognized as a mischaracterization of the disorder. To resolve this, WHO standardized the nomenclature to “tenosynovial giant cell tumor” in 2013 and reaffirmed the revised nomenclature in 2020. “Tenosynovial giant cell tumor (TGCT)” and “pigmented villonodular synovitis (PVNS)” are the same clinical disorder. However, tenosynovial giant cell tumor is now the standard clinical terminology, with giant cell tumor of tendon sheath also acceptable. The term pigmented villonodular synovitis is specifically identified as “not recommended.”

ICD-10-CM continues to use the nomenclature of villonodular synovitis (pigmented).
As indicated by the WHO standard, this disorder is neoplastic rather than inflammatory. The outdated nomenclature and misclassification have led to the same condition being assigned to multiple different codes across different chapters of ICD-10-CM. As identified in an internal data analysis performed for the patient advocacy group, codes assigned for tenosynovial giant cell tumors include those for pigmented villonodular synovitis as well as those for benign neoplasms, neoplasms of uncertain behavior, synovitis and tenosynovitis, and other disorders of synovium and tendon.

Giant cell tumors are indexed to Neoplasm, uncertain behavior, by site. Notably, ICD-10-CM classifies non-malignant but locally aggressive neoplasms of synovial tissue and tendons to D48.1, Neoplasm of uncertain behavior of connective and other soft tissue. This is indicated by the instructional note in the Table of Neoplasms and exemplified by subcategory D48.11, Desmoid tumor. It is not felt necessary to create separate codes for the two subtypes of tenosynovial giant cell tumor. Beyond their common pathogenesis and management by the same treating specialists, surgical resection remains the mainstay treatment regardless of subtype. In addition, findings from a multidisciplinary survey presented in 2022 found that less than half of providers (47%) indicated a high or very high confidence level in distinguishing between L-TGCT and D-TGCT.

Rectifying the current classification while updating and standardizing the nomenclature will reflect the advances in the clinical understanding of the disorder. This will help ensure that coding will be consistent and appropriately categorized, contributing to cleaner and more accurate data for tracking and research.

This proposal has been proposed by TGCT Support, a program of the patient advocacy organization Life Raft Group. It is supported by the Musculoskeletal Tumor Society, a medical society of orthopedic oncology surgeons and the Connective Tissue Oncology Society, a multi-disciplinary international group of physicians and scientists with a primary interest in the tumors of connective tissues including medical oncologists, orthopedic oncologists, and sarcoma specialists.

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TABULAR MODIFICATIONS

D48 Neoplasm of uncertain behavior of other and unspecified sites

D48.0 Neoplasm of uncertain behavior of bone and articular cartilage

Excludes1: neoplasm of uncertain behavior of synovia (D48.1-)

D48.1	Neoplasm of uncertain behavior of connective and other soft tissue	
	D48.11	Desmoid tumor
New subcategory	D48.12	Tenosynovial giant cell tumor
Add		Giant cell tumor of tendon sheath
Add		Tenosynovial giant cell tumor, diffuse (D-TGCT)
Add		Tenosynovial giant cell tumor, localized (L-TGCT)
Add		TGCT
Add		Villonodular synovitis (pigmented)
New code	D48.120	Tenosynovial giant cell tumor, unspecified site
New sub-subcategory	D48.121	Tenosynovial giant cell tumor, shoulder
New code		D48.1211 Tenosynovial giant cell tumor, right shoulder
New code		D48.1212 Tenosynovial giant cell tumor, left shoulder
New code		D48.1219 Tenosynovial giant cell tumor, unspecified shoulder
New sub-subcategory	D48.122	Tenosynovial giant cell tumor, elbow
New code		D48.1221 Tenosynovial giant cell tumor, right elbow
New code		D48.1222 Tenosynovial giant cell tumor, left elbow
New code		D48.1229 Tenosynovial giant cell tumor, unspecified elbow
New sub-subcategory	D48.123	Tenosynovial giant cell tumor, wrist
New code		D48.1231 Tenosynovial giant cell tumor, right wrist
New code		D48.1232 Tenosynovial giant cell tumor, left wrist
New code		D48.1239 Tenosynovial giant cell tumor, unspecified wrist
New sub-subcategory	D48.124	Tenosynovial giant cell tumor, hand
New code		D48.1241 Tenosynovial giant cell tumor, right hand
New code		D48.1242 Tenosynovial giant cell tumor, left hand
New code		D48.1249 Tenosynovial giant cell tumor, unspecified hand

New sub-subcategory	D48.125	Tenosynovial giant cell tumor, hip
New code	D48.1251	Tenosynovial giant cell tumor, right hip
New code	D48.1252	Tenosynovial giant cell tumor, left hip
New code	D48.1259	Tenosynovial giant cell tumor, unspecified hip
New sub-subcategory	D48.126	Tenosynovial giant cell tumor, knee
New code	D48.1261	Tenosynovial giant cell tumor, right knee
New code	D48.1262	Tenosynovial giant cell tumor, left knee
New code	D48.1269	Tenosynovial giant cell tumor, unspecified knee
New sub-subcategory	D48.127	Tenosynovial giant cell tumor, ankle and foot
New code	D48.1271	Tenosynovial giant cell tumor, right ankle and foot
New code	D48.1272	Tenosynovial giant cell tumor, left ankle and foot
New code	D48.1279	Tenosynovial giant cell tumor, unspecified ankle and foot
New code	D48.128	Tenosynovial giant cell tumor, other specified site
Add		Tenosynovial giant cell tumor, vertebrae
New code	D48.129	Tenosynovial giant cell tumor, multiple sites

M12 Other and unspecified arthropathy

M12.2 Villonodular synovitis (pigmented)

Add **Note: Effective October 1, 2027, due to globally recognized clinical updates in classification and nomenclature, conditions previously classified to subcategory M12.2-, Villonodular synovitis (pigmented), have been reclassified to D48.12-, Tenosynovial giant cell tumor. Codes in M12.2- are maintained for historical data purposes.**