

Clinical Quiz

Recurrent finger swelling

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Case

A 56 year old female presented to her primary care physician with a painless finger mass. She first noticed the mass about 7 years ago and it had been growing slowly since that time. Her former primary care physician had removed the mass about 5 years prior. She recalled being told at that time that it was a “ganglion cyst.” The mass had since returned and grown back to its former size. It was not frankly painful, though it did feel tight and often got in the way of daily tasks. She denied any numbness or tingling in her finger, and denied any warmth, redness or swelling in her other joints. Her past medical and family histories were non-contributory, including no history of gout, autoimmune disease, or cancer. Physical examination revealed a non-tender, soft, well circumscribed mass on the extensor aspect of the right fifth digit, just proximal to the base of her fingernail (Figure 1A). The mass was approximately 2cm x 2cm and did not transilluminate (Figure 1B). The mass was fluctuant and encapsulated. There was no swelling or effusion in the hand, fingers, or joints. Neurologic exam showed no sensory or motor deficits.

The radiograph showed a non-invasive soft tissue mass on the dorsal aspect of the fifth distal phalanx (Figure 1C). Incisional biopsy was performed. The mass was found to be composed of non-encapsulated fatty tissue, and extended to the extensor tendon sheath. The patient was referred to hand surgery for a definitive excision.

Histological findings

Gross examination of the specimen revealed multiple fragments of lobulated and rubbery tissue which were mostly white

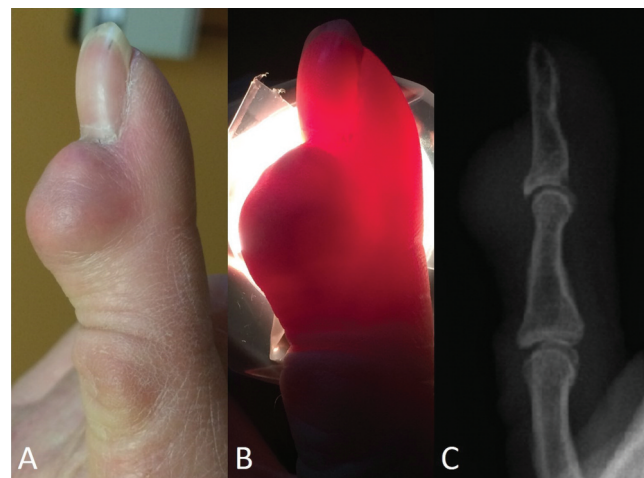


Figure 1. A: Soft tissue growth overlying the dorsal aspect of the right 5th DIP joint. **B:** Non-transilluminating mass. **C:** Radiograph does not reveal any underlying osseous changes.

to grey with focal yellow areas. Histological examination of the specimen stained with hematoxylin-eosin revealed an encapsulated benign neoplasm. The mass was composed of synovial-like mononuclear cells, with a variable number of multinucleate osteoclast-like cells (Figure 2A), and foam cells (Figure 2C). Both the mononuclear cells and the giant cells showed strong reactivity for CD68 (Figure 2B). These findings are consistent with a diagnosis of tenosynovial giant cell tumor, localized type (giant cell tumor of tendon sheath).

Commentary

Tenosynovial giant cell tumor (TGCT) is a rare pathologic entity affecting the synovium and tendon sheath in adults¹⁻³. Tenosynovial giant cell tumors can present as localized or diffuse². The localized type is typically a painless, long-standing, slow-growing mass. Seventy-five percent of these lesions are found in the digits, the most common being the tendon sheath of the fingers. Lesions are usually situated in close proximity

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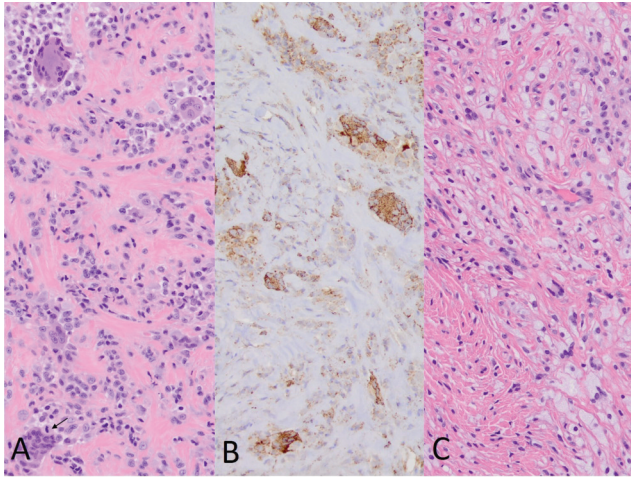


Figure 2. **A:** Osteoclast-like giant cells, small histiocytoid cells, and larger epithelioid cells. Arrow (panel A, low left) demonstrates mitotic figure within the giant cell (hematoxylin and eosin, original magnification x 20). **B:** CD68 positivity is seen in both osteoclast-like giant cells as well as mononuclear cells (original magnification x 20). **C:** Collections of foamy xanthoma cells were seen at the periphery of the lesion (hematoxylin and eosin, original magnification x 20).

to the synovium of the tendon sheath or interphalangeal joint especially on volar surfaces. TGCT of the tendon sheath falls second behind the ganglion cyst as the most common soft tissue tumor in the hand. There is a 2:1 female predominance, with most patients affected between the ages of 30-50².

Surgery is the treatment of choice, with marginal excision as the preferred method for a localized lesion⁴. Localized lesions generally do not behave aggressively and can be treated with re-excision^{1,2,5}. Larger lesions may be found intra-articular with the most common site being the knee. Other sites include the wrist, ankle, and foot¹.

Recurrences may occur approximately 25% (5-44%) of the time. It is unclear what factors cause recurrence, but age, sex, location within the digit and size of the lesion do not affect risk of recurrence⁵. Several factors may be associated with an increased recurrence rate. These include increased cellularity and mitotic activity, a specific gene profile (negative for nm23), adjacent joint degenerative disease, and location on the thumb IP joints, digital DIP joints, flexor tendon, extensor tendon, or joint capsule. All of these factors have been both supported and refuted as carrying an increased risk of recurrence in various studies. The literature does suggest that type II tumors, and tumors which were incompletely excised are more prone to recurrence. It appears that factors which increase the difficulty of complete excision, as well as some intrinsic tumor factors are associated with increased risk of recurrence. However, large scale prospective studies are needed to truly answer this question⁶.

The microscopic pattern of TGCT can be variable based on the proportion of mononuclear cells, multinucleate giant cells,

foamy macrophages (xanthoma cells), hemosiderin-laden macrophages and the amount of stroma present. Osteoclast-like giant cells may be readily apparent, but can be rare in highly cellular lesions. The morphology of the mononuclear cells usually consists of small cells which are either round or spindled. Cytologically, these cells show round to kidney-shaped nuclei with occasional grooves as well as a pale cytoplasm. In addition, more epithelioid-appearing cells with round, vesicular nuclei and glassy cytoplasm are seen. Foamy xanthoma cells are often seen and tend to occur at the edge of the lesion (Figure 2C). Hemosiderin is extremely common. The stroma may show extensive hyalinization (Figure 2A) and give the lesion a lobular architecture. Mitotic activity is not uncommon, and this should not be misinterpreted as evidence of malignancy. Necrosis, however, is rare. In many cases, the mononuclear cells will show positivity for desmin. Though this does not, rare cases may show near diffuse positivity which may mimic rhabdomyosarcoma. Immunohistochemistry is not required for the diagnosis^{1,2}.

TGCTs commonly overexpress colony-stimulating factor 1 (CSF1). In many patients, CSF1 overexpression results from a t(1;2) translocation, which fuses the CSF1 gene to the collagen type VI $\alpha 3$ (COL6A3) promoter. Imatinib mesylate (IM) blocks CSF1 receptor and has been used in treatment for diffuse type TGCT^{3,4}.

Other entities to include in the histologic differential diagnosis include giant cell granuloma (giant cell reparative granuloma) which can involve the bones of the hand. Giant cell granuloma is thought to evolve in response to injury. This entity is typically unencapsulated and shows reactive bone with osteoblastic rimming. Giant cell tumor of bone (osteoclastoma) is uncommon in the hand¹.

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Questions

1. What is the preferred method of treatment of localized TGCT?

- A. Imatinib
- B. Wide excision
- C. Radiation therapy
- D. Marginal excision

Critique

Marginal excision is the preferred treatment for localized TGCT, the other methods can be used for diffuse TGCT.

The correct answer is D.

2. Increased risk of recurrence of localized TGCT has been attributed to which of the following?

- A. Age
- B. Gender
- C. Size of lesion
- D. Dorsal aspect of finger
- E. None of the above

Critique

It is unknown what factors contribute to the reoccurrence of localized TCGT, but there is no evidence that A-D affect risk of recurrence.

The correct answer is E.

3. All of the following are true of tenosynovial giant cell tumor, localized type, except:

- A. Second most common tumor of the hand
- B. Most common in patients 30-50 years of age with a 2:1 female predominance
- C. Mitotic figures are indicative of malignancy
- D. Hemosiderin deposition is common

Critique

Ganglion is the most common soft tissue tumor of the hand. Answer B describes the most common setting for TGCT, localized type, although it can affect any age group. Mitotic figures are commonly seen and can reach up to 20 per 10 high-power fields, although this is not indicative of malignancy. Hemosiderin deposition is almost always identified.

The correct answer is C.

4. Histologically, TGCT, localized type, consists of:

- A. Mononuclear cells and osteoclast-like giant cells
- B. Foam cells and hemosiderin-laden macrophages
- C. CD68 positivity
- D. All of the above

Critique

TGCT is composed of both mononuclear cells as well as variable numbers of osteoclast-like giant cells. Foamy (xanthoma) cells are common especially at the periphery. Hemosiderin-laden macrophages are almost always seen. Both mononuclear cells and giant cells are CD68 positive.

The correct answer is D.