

Case Report

Fibrosarcoma arising from gouty tophi: report of a unique case and review of literature

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Abstract: Fibrosarcoma is a malignant mesenchymal tumor. To the author's best knowledge, no previous case of fibrosarcoma arising from gouty tophi has been reported. Here we reported the first case of fibrosarcoma arising from gouty tophi. A case of 58-year-old man was presented with a mass with ulcer and infection in the second joint of left middle finger for 2 months, with long standing gouty tophi. The tumor was biopsied and the biopsy showed complete excision of the tumor. With the pathological and immunohistochemical features considered, the diagnosis of fibrosarcoma associated with gouty tophi was made. The clinical findings, pathological characteristics and treatment were described.

Keywords: Fibrosarcoma, sarcoma, gouty tophi, gout

Introduction

Gout is a common form of inflammatory arthritis caused by a disorder of purine metabolism and leads to chronic hyperuricemia and deposition of monosodium urate crystals from many tissues like foot and ankle. Gout affects 1%~2% of the population with an increasing trend in the industrialized nations and men have higher prevalence than women [1]. The natural history of gout has four stages-asymptomatic hyperuricaemia, acute gouty arthritis, intercritical gout and chronic tophaceous gout. Gouty tophi can be identified in subcutaneous tissue of skin and happen anywhere in the body and sometimes can result in unusual features.

Fibrosarcoma (FS) is a malignant mesenchymal tumor composed of fibroblasts with variable collagen production. It most occurs in the deep soft tissues of the extremities, trunk, head and neck and accounts for about 5% of all soft sarcomas [2]. No previous case of fibrosarcoma has been reported to arise from gouty tophi. Here, we present a case of 58-year-old man with fibrosarcoma that arises from gouty tophi.

Case report

The patient was a 58-year-old man with a past medical history of gout with acid bilges feeling

joint pain since 2007, which was presented to hospital with a mass with long-standing gouty tophi at the second joint of the left middle finger for 2 months on July 19th, 2011. Physical examination showed a 4 cm×4 cm deep red bulge mass in the left middle finger dorsal where a 3 cm×3 cm ulcer, with mild swelling adjacent skin, was at the second joint accompanied by pain and a small amount of bloody fluid exudation. The patient had ring finger gout excision in the right hand in 2004 and had no history of tuberculosis nor rheumatoid arthritis. Serum levels showed that erythrocyte sedimentation rate (ESR) 64 mm/h and blood uric acid (BUA) 438 μmol/L were beyond normal limits, while other tests including urine routines, renal function examination and tumor markers were all within normal limits. Radiography revealed osteolytic lesion and unclear trabecular bone in the middle proximal phalanx finger of the left hand, stenosis close to the middle finger joint space and swelling of the adjacent soft tissues (**Figure 1**). The tumor was biopsied for histologic examination and the biopsy showed complete excision of the tumor.

Pathological findings

Grossly, the tumor was 3 cm×3 cm×3 cm on average with unclear border and a fish-flesh cut

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Figure 1. Radiography revealed osteolytic lesion and unclear trabecular bone in the middle proximal phalanx finger of the left hand (\blacktriangleleft), stenosis close to the middle finger joint space and swelling of the adjacent soft tissues. The shadow in the 2th left metacarpophalangeal joint (\blacktriangleleft) turned out to be gout tophi after excision.

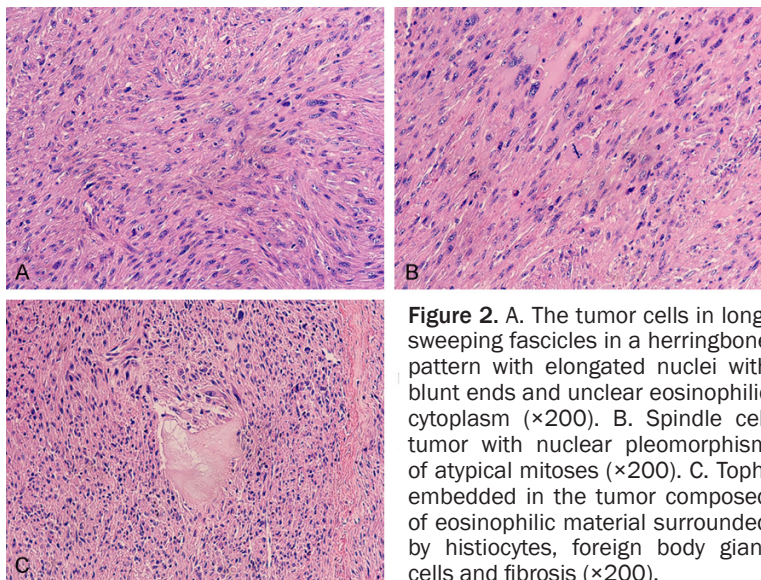


Figure 2. A. The tumor cells in long, sweeping fascicles in a herringbone pattern with elongated nuclei with blunt ends and unclear eosinophilic cytoplasm ($\times 200$). B. Spindle cell tumor with nuclear pleomorphism of atypical mitoses ($\times 200$). C. Tophi embedded in the tumor composed of eosinophilic material surrounded by histiocytes, foreign body giant cells and fibrosis ($\times 200$).

surface and consisted of lime-like substances. HE sections of the excised segment revealed hypercellular and sweeping fascicles and storiform arrangement of spindle-shaped cells. The tumor cells contained elongated nuclei with blunt ends and had unclear eosinophilic cytoplasm (**Figure 2A**). The borders of cells were ragged. The spindle cells had tapered and darkly staining nuclei with visible nuclei and showed some pleomorphism. Mitotic figures were found with a frequency of 10 per 10HPF (**Figure 2B**).

Multiple tophi composed of eosinophilic material surrounded by histiocytes; foreign body giant cells and fibrosis were embedded in the tumor (**Figure 2C**).

To further characterize the nature of the spindle cells, an immunohistochemical study was performed. Immunohistochemistry revealed the tumor cells were positive for Vimentin (**Figure 3A**), CD163 (**Figure 3B**) and negative for CD34, SMA, SYT, S-100, Desmin, MyoD1, EMA, HMB-45, CKpan, with Ki-67 labeling 20% (**Figure 3C**).

For fluorescence in situ hybridization (FISH) analysis, cytospin preparations were denatured and hybridized with the LSI SYT break-apart probe set (Vysis, Downer's Grove, IL) to SSX-SYT fusion gene according to the manufacturer's specifications. Images were acquired using MacProbe Software (Applied Imaging, San Jose, CA) on a Zeiss Axiophot microscope. Tumor proportion of the tested tissues was 90%. At least 60 tumor cells were counted. No splitting of the red or green signals or isolated red signals were detected in tumor cells (**Figure 4**).

Discussion

Gout was a condition that an overload of urate crystals resulted in tophus formation in the tissues of the body and characteristic recurring attacks of acute joint inflammation. Tophus was a common manifestation of gout with urate crystals deposits in the auricle, joints and soft tissues. Monosodium urate crystals were pro-inflammatory stimuli that could initiate, amplify, and sustain an intense inflammatory response [1]. Inflammation caused by urate crystals and eosinophilic urate deposits surrounded by his-

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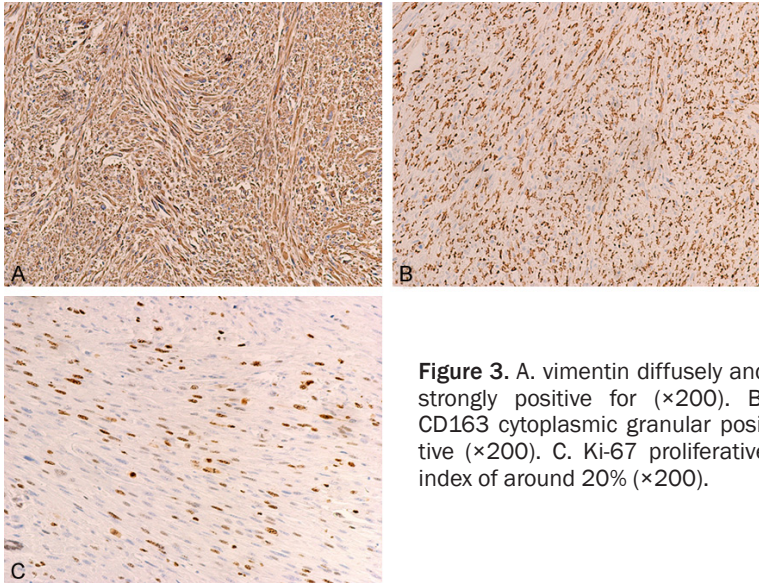


Figure 3. A. vimentin diffusely and strongly positive for ($\times 200$). B. CD163 cytoplasmic granular positive ($\times 200$). C. Ki-67 proliferative index of around 20% ($\times 200$).

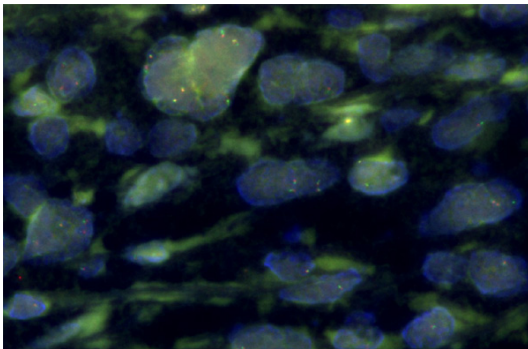


Figure 4. Break apart SSX-SYT fluorescence in situ hybridization (FISH) assay found no plitting of the red or green signals and isolated red signals.

tiocytes, foreign body giant cells, fibroses lied the main pathological features of gout.

Chronic gout could show characteristic features, mainly the consequences of tophus infiltration into bone and Bone erosions were key features on radiography. Fine needle aspiration cytology (FNAC), ultrasonography, CT, and MRI were emerging techniques that could be used for diagnosis and assessment of gout [3-5]. However, Gout had been also known as a great mimicker and could masquerade as diverse medical conditions such as PVNS, infectious arthritis, rheumatoid arthritis and malignancies, such as synovial sarcoma, synovial chondrosarcoma, and presented as an atypical mass in unexpected places like liver, spine and so on [6, 7]. Amber [8] reported an unusual case of intra-articular gouty tophi of the knee joint

presenting as a locked knee and radiologically mimicking a synovial sarcoma and concluded that gout could mimic any condition, even a locked knee or sarcoma.

However, gout trophy might undergo malignant transformation. We reported the case of 58-year-old man associated with fibrosarcoma arising from gouty tophi. To our knowledge, the coexistence of gouty tophi and fibrosarcoma had not been reported. The presented case should be regarded as primary fibrosarcoma since there was no other primary focus being

found after a series of surveys. Furthermore, one had to bear in mind the possible differentials such as malignant fibrous histiocytoma (MFH), leiomyosarcoma, monophasic fibrous synovial sarcoma, malignant peripheral nerve sheath tumor (MPNST), sarcomatoid carcinoma, rhabdomyosarcoma as well as melanoma and other metastatic tumors. The tumor cells were arranged in long, sweeping fascicles in a herringbone pattern. The spindle cells had tapered, unclear red cytoplasm and darkly staining nuclei with visible nuclei and showed some pleomorphism with a mitotic rate of 10/10 HPF. Inside the tumor, multiple tophi composed of eosinophilic material surrounded by histiocytes, foreign body giant cells and fibroses were embedded. Immunohistochemistry revealed the tumor cells were positive for Vimentin, CD163, which indicated fibroblasts or fibrohistiocytes origin, while negative for CD34, SMA, SYT, S-100, Desmin, MyoD1, EMA, HMB45, CKpan. Fluorescence in situ hybridization analysis was negative for SSX-SYT gene rearrangement. Therefore, the diagnosis of fibrosarcoma associated with gouty tophi was made.

However, a variety of other sarcomas, such as angiosarcomas and MFH have been reported to arise in association with gouty tophi. We reviewed related literature and listed the following table (Table 1). As we could see in the chart, related cases mainly occurred in the old man in the extremities. The first 4 cases showed a fast growth of tumor in the gout tophi in a short

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Table1. Literature review of the malignant transformation of gouty trophi

	Sex	Age	History	Site	Tumor	Follow up	
1	male	76	30 years	2 nd , 3 rd dorsal of the LMJ	MFH	Recurrence at 5 months	Pérez-Mies [16]
2	male	76	20 years	2 nd of the LMJ	MFH	No occurrence after 6 months	Carnero [17]
3	male	83	40 years	elbow	MFH	LN metastasis at 10 months later and died within 2 years	Szlabi [18]
4	male	86	Long time gout	elbow	CA	No occurrence after 6 months	Folpe [10]
5	male	47	Long time hyperuricemia without gout	index finger	GCT	No occurrence after 16 months	Schuind [9]

LMJ: left metacarpophalangeal joint; CA: Cutaneous angiosarcoma; MFH: Malignant fibrous histiocytoma; GCT: Giant cell tumor.

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time after a long history of gout just similar with our case. Schuind et al [9] supposed that long time hyperuricemia and urate crystal deposits could be the important transformation factors. Folpe et al [10] hypothesized that this tumor was induced by a mechanism similar to that of foreign body-associated sarcoma and postulated that the tophus and its surrounding dense fibrous capsule might have served as an irritant and that angiosarcoma might have arisen via some pathway analogous to that of foreign body. Similar tumors such as hemangiosarcomas, malignant fibrous histiosarcoma has been observed in association with retained foreign materials [11-13], and Okada et al [14] found that host cells reaction to a foreign body in a mouse induced malignant progression of fibrosarcoma and believed that inflammatory processes might involve the conversion of tumor cells into more malignant cells. Woodward et al [15] reviewed related literature and realized that chronic inflammation might play the possible roles. Therefore, we speculated that the hyperplasia of fibroblasts or fibrohistiocytes might be the important induction factors of fibrosarcoma as the strong chronic inflammation caused by gout deposits.

In the older literature, fibrosarcoma behaviors had been related to grade, tumor size and depth and the probability of local recurrence related to completeness of excision. These lesions were aggressive, with multiple local recurrences, lymph node and parenchymal metastases, and overall survival of < 70% at 2 years and < 55% at 5 years [19]. Our case received no further treatment after excision, with no recurrence on June 12th, 2014.

Conclusion

In summary, primary fibrosarcoma of the gouty tophi is extremely rare, though the etiology of fibrosarcoma arising from gout remains obscure. As gout can mimic any condition, the clinician should be alerted when treated with long history and rapid growth and changes of gout.

Disclosure of conflict of interest

None.

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