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# Intense FDG uptake in an intra-articular localized giant-cell tumor of the tendon sheath (pigmented villonodular synovitis) mimics metastatic melanoma

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We describe a patient with metastatic melanoma, one year following a clinical trial of VEGF Trap anti-angiogenic therapy, in whom a restaging whole-body FDG PET/CT demonstrated a new, intensely FDG-avid, intra-articular soft-tissue mass in the left knee (SUV=25 g/ml). MRI revealed findings compatible with nodular pigmented villonodular synovitis (PVNS), also known as giant-cell tumor of the tendon sheath (GCTTS), which was confirmed by excisional biopsy. Increased FDG uptake within tenosynovial giant-cell tumors can be explained on the basis of their high monocyte/macrophage content. Radiologists must be aware that both melanoma and tenosynovial giant-cell tumors can be intensely FDG-avid, in order to avoid a false-positive interpretation.

## Case report

A 72-year-old Caucasian male underwent wide local excision of an ulcerated, 1.4-mm Breslow thickness, Clark level IV, articular melanoma in 2004. There was no evidence of regression, lymphovascular invasion, perinodal extension, or microsatellitosis at diagnosis. The surgical margins were clear, and the sentinel lymph node biopsy revealed no evidence for additional disease. His initial stage was therefore IIA (T2b, N0, M0). In the fall of 2007, FDG PET/CT showed multiple small pulmonary nodules, with maximum SUV (SUVmax) of 3.8 g/ml. CT-guided needle biopsy of one nodule revealed metastatic melanoma. The patient completed two cycles on a clinical trial of VEGF-

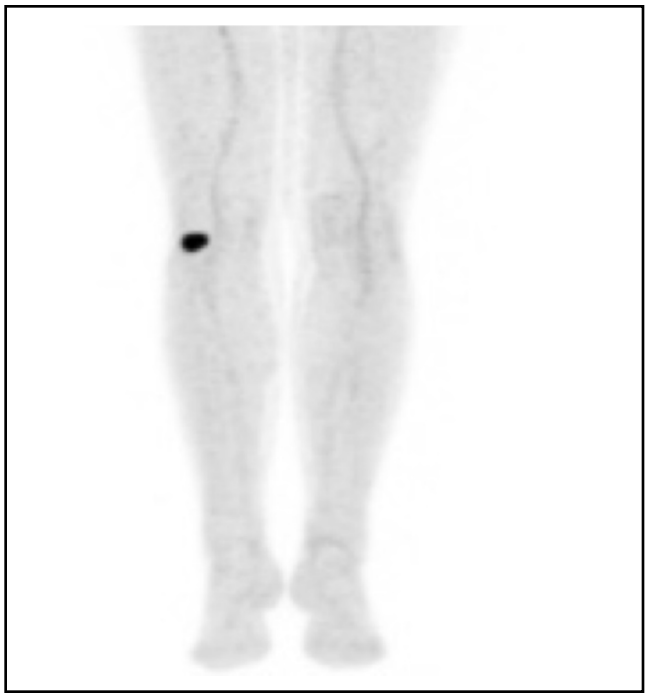

Figure 1A. 72-year-old man with giant-cell tumor of the tendon sheath. FDG PET/CT. Attenuation-corrected, maximum-intensity projection FDG PET shows intense FDG uptake within the lateral compartment of the right knee.

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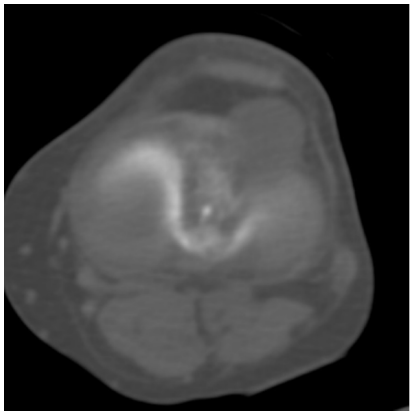

Figure 1B. 72-year-old man with giant-cell tumor of the tendon sheath. FDG PET/CT. Bone-windowed transaxial image from the noncontrast CT component shows a solid, soft-tissue-density, intra-articular mass, centered at the synovium.

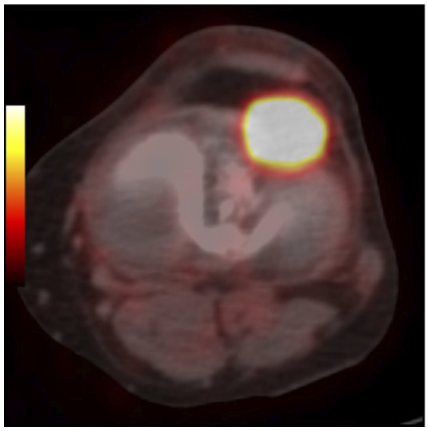

Figure 1C. 72-year-old man with giant-cell tumor of the tendon sheath. FDG PET/CT. Soft-tissue-windowed, transaxial fused PET/CT image shows intense FDG uptake within the mass. Maximum SUV was 25 g/ml.

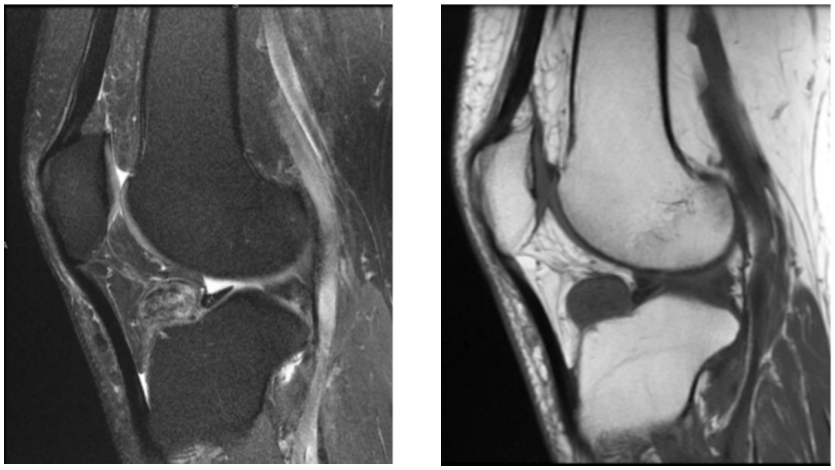

Figure 2. 72-year-old man with giant-cell tumor of the tendon sheath. MR imaging shows findings typical of intra-articular GCTTS (PVNS). Left: Sagittal T1 weighted image shows low signal. Right: Proton density with fat saturation shows intermediate signal.

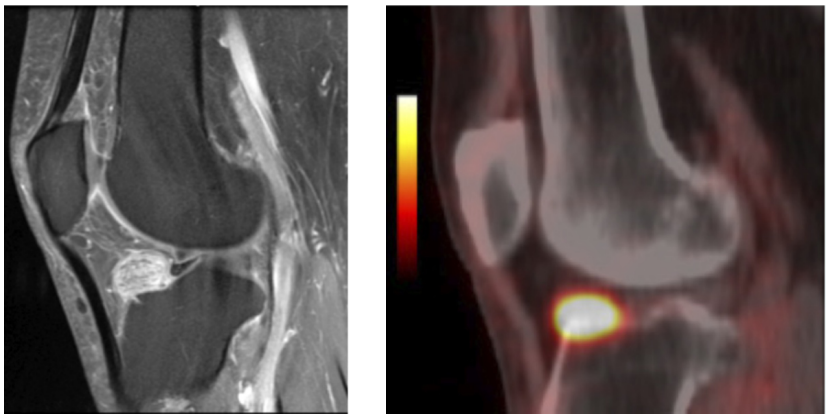

Figure 2. 72-year-old man with giant-cell tumor of the tendon sheath. MR imaging shows findings typical of intra-articular GCTTS (PVNS). Left. Sagittal T1-weighted imaging with fat saturation, post-IV-gadolinium, shows enhancement within the mass. RIght. Corresponding sagittal-fused FDG PET/CT image demonstrates intense FDG uptake, with SUVmax 25 g/ml.

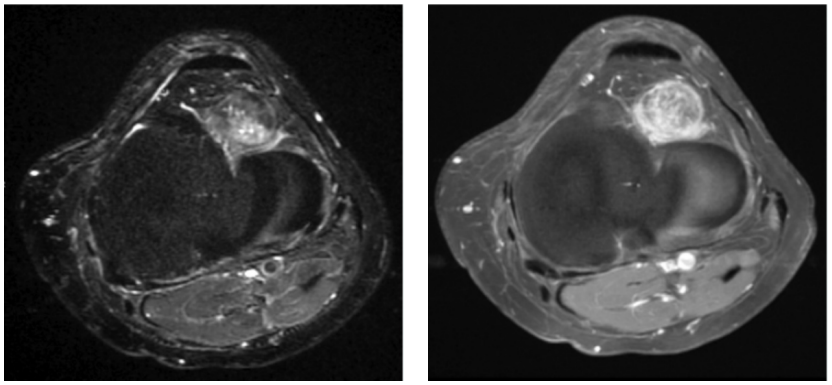

Figure 2. 72-year-old man with giant-cell tumor of the tendon sheath. MRI shows findings typical of intra-articular GCTTS (PVNS). Left. Transaxial MR inversion recovery. Right. T1-weighted fat saturation imaging postgadolinium.

Trap, a novel anti-angiogenesis type therapeutic agent, but had to discontinue therapy in January 2008 because he developed grade IV hypertension as a side effect. His disease remained stable off therapy until April 2009, when a followup noncontrast FDG PET/CT scan revealed an intensely hypermetabolic intra-articular soft-tissue-density lesion in the left knee (SUVmax = 25 g/ml); this was thought to be highly suspicious for metastatic melanoma (Fig. 1), although no prior imaging of the knee was available to establish the chronicity of the finding.

Further investigation with MRI revealed a 2.4 x 1.4 x 2.0-cm lesion within Hoffa's fat pad, demonstrating intermediate T1 signal, heterogeneous low-to-intermediate T2 signal, and heterogeneous contrast enhancement (Fig. 2).

These MRI findings are typical of GCTTS (PVNS), but metastatic melanoma could not be entirely excluded based on MRI. Surgical resection revealed an ovoid, encapsulated mass measuring 2.5 x 2.0 x 1.2 cm, with a smooth pink-tan outer surface and a variegated yellow-tan-brown cut surface. Histopathology revealed histiocyte-like tumor cells, lymphocytes, hemosiderin-laden macrophages, and osteoclast-like giant cells, consistent with localized GTTTS (PVNS). Immunostaining with HMB-45 was negative, thus ruling out metastatic melanoma (Fig. 3).

## Discussion

GCTTS (PVNS) is a benign neoplasm that develops in the synovium of joints, tendon sheaths, and bursae. This tumor has a chromosomal translocation, t(1:2)(p13;q37), which results in overexpression of CSF1, a chemoattractant for macrophages. Histiocytic cells of the monocyte/macrophage cell line constitute the majority of cells in these tumors at biopsy, whereas the polyhedral neoplastic cells account for only 2% to 16% of total cells. The macrophages contain hemosiderin- and lipid-laden vacuoles, and thus can be mistaken for melanoma cells when viewed through the microscope. Immunostaining of GCTTS (PVNS) with HMB-45, a human monoclonal antibody that binds specifically to an antigen expressed by melanocytic tumors, is negative.

Current literature specifically addressing FDG avidity of tenosynovial giant-cell tumors is sparse. Watanabe, et al., in a series of 55 patients with musculoskeletal tumors, describe one GCTTS in the knee of a 28-year-old woman, with the lesion measuring 3 x 4 x 4 cm, and having SUVmax = 4.4 g/ml (1). Wissmeyer, et al. reported a 2.8 x 4.5-cm GCTTS in the hip of a 70-year-old man, with SUVmax = 5.8 g/ml (2). Adler, et al., in a series of 25 patients with mass lesions involving the musculoskeletal system, reported two cases of PVNS, one of which was intraosseous, with average FDG DUR (dose/uptake ratio) of 0.65 and 0.31, but SUVmax for these lesions was not reported (3). Aoki et al., in a series of 114 soft-tissue masses, reported five GCTTS with SUVmax = 5.06 +/- 1.63 g/ml (4). A case of PVNS, with SUV = 11.3, was reported by Kitapci and Coleman (5). We know of no published cases of FDG imaging of tenosynovial giant-cell tumors demonstrating SUVmax in the range of 25 g/ml, or greater than 11.3 g/ml.

The intense FDG avidity of malignant melanoma, on the other hand, is well documented. Although sentinel lymph-node biopsy is the gold standard for detection of micrometastases to regional lymph nodes, FDG PET/CT is widely known to be highly accurate in predicting both residual/recurrent melanoma and distant metastases (6, 7, 8, 9). In general, the likelihood of a lesion to represent malignant melanoma increases with increasing SUVmax.

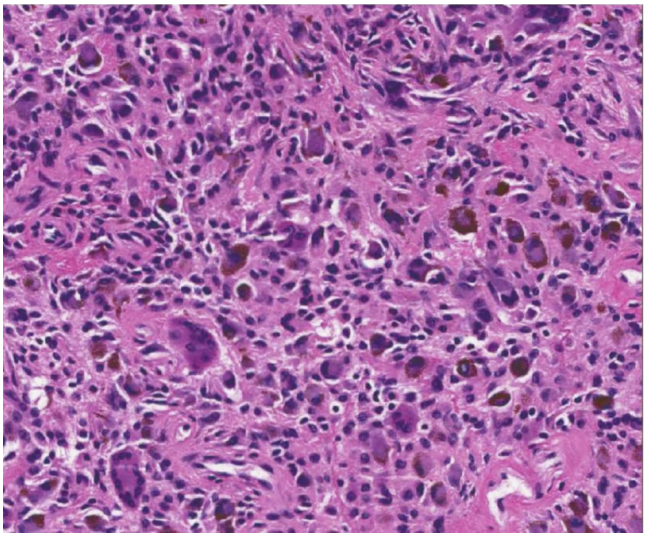

Figure 3. 72-year-old man with giant-cell tumor of the tendon sheath. High-power view (20X) shows histiocyte-like tumor cells, lymphocytes, hemosiderin-laden macrophages and osteoclast-like giant cells consistent with localized GTTTS (PVNS).

Cellular uptake of FDG in human tumor cells has recently been linked to the expression of glucose transporter protein GLUT-1, hexokinase II, and to the upregulation of genes for production of these proteins. Ong et al., found significantly higher amounts of GLUT-1 and hexokinase II in five different human cancer cell lines (as compared to normal cells) using Western blot analysis, and they demonstrated strong correlations between cellular expression of GLUT-1, expression of hexokinase II, in vitro histological FDG uptake assays, and FDG SUVmax (determined by in vivo microPET imaging of intrahepatic tumor models using SCID mice (10]). Hamada et al., in a series of 49 patients with musculoskeletal tumors, showed a positive correlation of FDG SUVmax with the expression of GLUT-1 and hexokinase II (11). Several investigators have previously demonstrated upregulation of GLUT-1 in human monocyte-derived macrophages (12, 13, 14). From studies such as these, we infer that FDG avidity within tenosynovial giant-cell tumors may be explained on the basis of their high monocyte/macrophage content. Of note, granulomatous lesions containing active macrophages are widely rec-

ognized as being causes of false-positive interpretations of FDG PET in oncology. Radiologists and Nuclear Medicine Physicians should be aware that both melanomas and GCTTS (PVNS) can be intensely FDG-avid, and that tenosynovial tumors should be included in the differential diagnosis of intensely FDG-avid neoplasms located within synovial joints, tendon sheaths, or bursae.

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