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CASE REPORT

Multicentric diffuse-type giant cell tumor of the hand

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Abstract Diffuse-type giant cell tumor (D-TGCT) is relatively rare. We report a case of multicentric D-TGCT located in the finger and wrist. A 79-year-old man presented with a more than two-year history of tumors. Marginal resection was performed. Histological study of the specimens disclosed D-TGCT. Recurrence occurred two years and five months postoperatively and was again excised. Clinical presentation, radiological features and histopathological findings are discussed with reference to the literature.

Keywords Diffuse-type giant cell tumor · Hand · Pigmented villonodular synovitis

Introduction

The concept of the diffuse-type giant cell tumor (D-TGCT) was introduced in 1941 by Jaffe et al. [1]. As D-TGCT often tends to be large, differentiation from other malignant soft tissue tumors can be difficult [2]. Young adults under 40 years old are predominantly affected, and the tumor develops in the knee, foot and thigh [3]. We describe herein a rare case of multicentric D-TGCT of the hand.

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Case report

A 79-year-old man presented with a more than two-year history of tumor in the right little finger, palm and wrist. No history of disease or trauma was elicited. Tumor sizes were 2.0 × 4.0 cm on the little finger, 4.0 × 4.0 cm on the palm, and 3.0 × 4.0 cm on the wrist. All skin surfaces over these tumors were smooth with no signs of inflammation, but borders were unclear. Radiological studies showed an osteolytic lesion of the middle phalanx of the little finger eroded by the soft tissue mass (Fig. 1). Magnetic resonance imaging (MRI) showed low-intensity lesions on T1-weighted imaging and high-intensity lesions on T2-weighted imaging (Fig. 2). Tumors in the finger and palm displayed continuity, but the tumor in the wrist was separate. All tumors displayed gadolinium enhancement. Angiography revealed hypervascularity and ^{99m}Tc scintigraphy showed increased uptake in all lesions, but ^{67}Ga scintigraphy showed slightly increased uptake only in the wrist lesion. Tumors in the finger and hand were clearly separate from tumor in the wrist. Chest radiography and computed tomography (CT) showed no evidence of lung metastasis. Laboratory findings were normal: white blood cell (WBC) count, 4,710 mm^{-3}; C-reactive protein (CRP), 0.2 mg/dl; and alkaline phosphatase (ALP), 279 IU/l. Malignant tumor was suspected from imaging and clinical observations. Biopsy specimens revealed small cells and large rhabdomyoblast-like cells with an inflammatory background. Sheets of foamy cells were observed.

Immunohistochemically, small mononuclear cells and foamy cells were positive for CD45 and CD68, and large mononuclear cells were positive for desmin. Desmin staining highlighted a population of large mononuclear cells with dendritic features. These cells were negative for S-100 protein, smooth muscle actin, MyoD, myogenin,

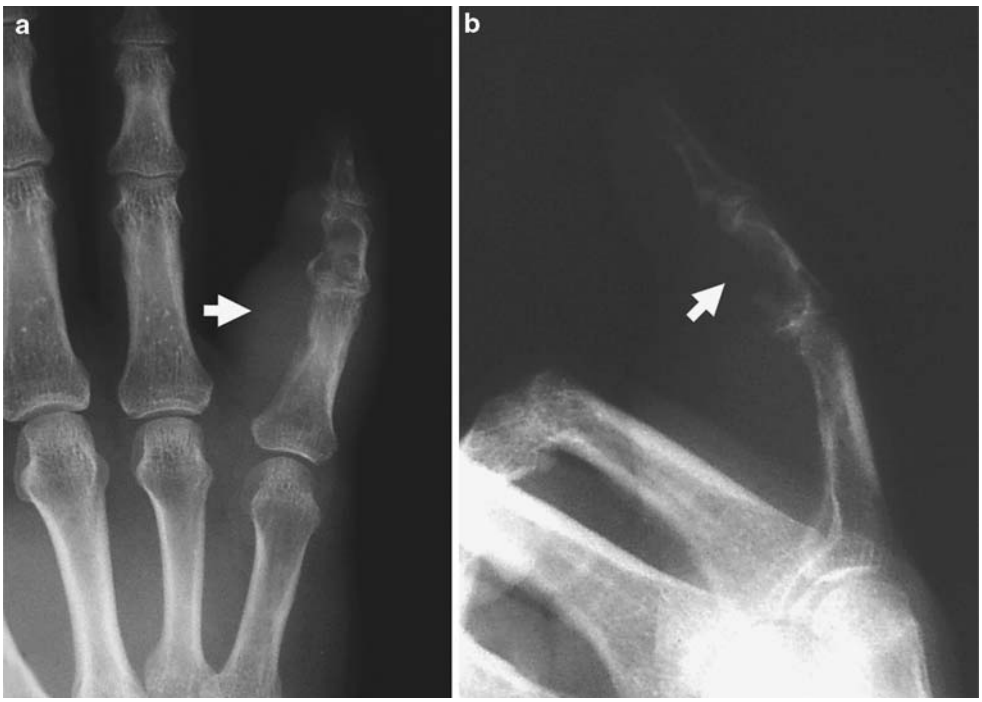

Fig. 1 **a** Radiography shows swelling of soft tissue (*arrow*). **b** An osteolytic lesion in the middle phalanx of the little finger is shown (*arrow*)

epithelial membrane antigen, cytokeratin, CD3 and CD20. These findings confirmed D-TGCT.

Tumor excision was performed in September 2004. Amputation of the little finger was required due to extensive destruction of the middle phalangeal bone and adjacent joint. Both finger and palm tumors were firmly connected and arose diffusely from the tendon sheaths. However, the wrist tumor was isolated and adherent to the tendon sheath. Resected tumors were multinodular and yellowish in color. Complete excision was performed to prevent local recurrence.

Histopathological study of the specimens revealed D-TGCT. Both finger and palm tumors were surrounded by the thin capsule, but the portion was infiltrative of the surrounding tissue (Fig. 3a). They grew as diffuse sheets interrupted by cleft-like or synovial-like spaces (Fig. 3b). Sheets of foamy cells were frequently observed on the periphery of the lesions (Fig. 3c). Small and large mononuclear cells were noted (Fig. 3d), and giant cells were not common. The stroma showed variable degrees of fibrosis and appeared hyalinized. No atypical cells or mitoses were seen. Immunohistochemical findings from the operation were the same as those from biopsy.

Tumor recurred in the middle finger two years and five months postoperatively. Recurrent tumor excision was performed in March 2007. No masses have recurred as of the time of writing, three months after second excision.

Discussion

D-TGCT was first described in 1941 by Jaffe et al. [1] as a lesion from an anatomical unit comprising synovium of the tendon sheath, bursa and joint. They described four extra-articular cases called extraarticular pigmented villonodular synovitis (PVS) [2], with two arising from the popliteal bursa, one from the anserine bursa, and one from the ankle bursa. Since this original description, the reactive or neoplasmic nature of tenosynovial giant cell tumors has remained controversial. D-TGCT has recently been classified among "so-called fibrohistiocytic tumors" [3]. In our case, immunohistochemical examination revealed that tumor cells were positive for CD45 and CD68, suggesting fibrohistiocytic differentiation.

Tenosynovial GCT are usually subtyped according to growth pattern as either localized or diffuse. Localized-type tenosynovial giant cell tumor (L-TGCT) is a giant cell tumor of tendon sheath or nodular tenosynovitis. These subtypes display different clinical characteristics and biological behaviors [4]. In L-TGCT, the age of patients varies widely, but most lesions affect young adults under 40 years old. D-TGCT tends to affect younger patients than L-TGCT. L-TGCT usually occurs in small joints, such as the fingers and toes, while D-TGCT usually occurs in large joints such as the knee, foot, and thigh. D-TGCT occurs in the wrist (18%), knee (16%), thigh (12%), and fingers (10%) [5]. In our case, tumor occurred in a small joint,

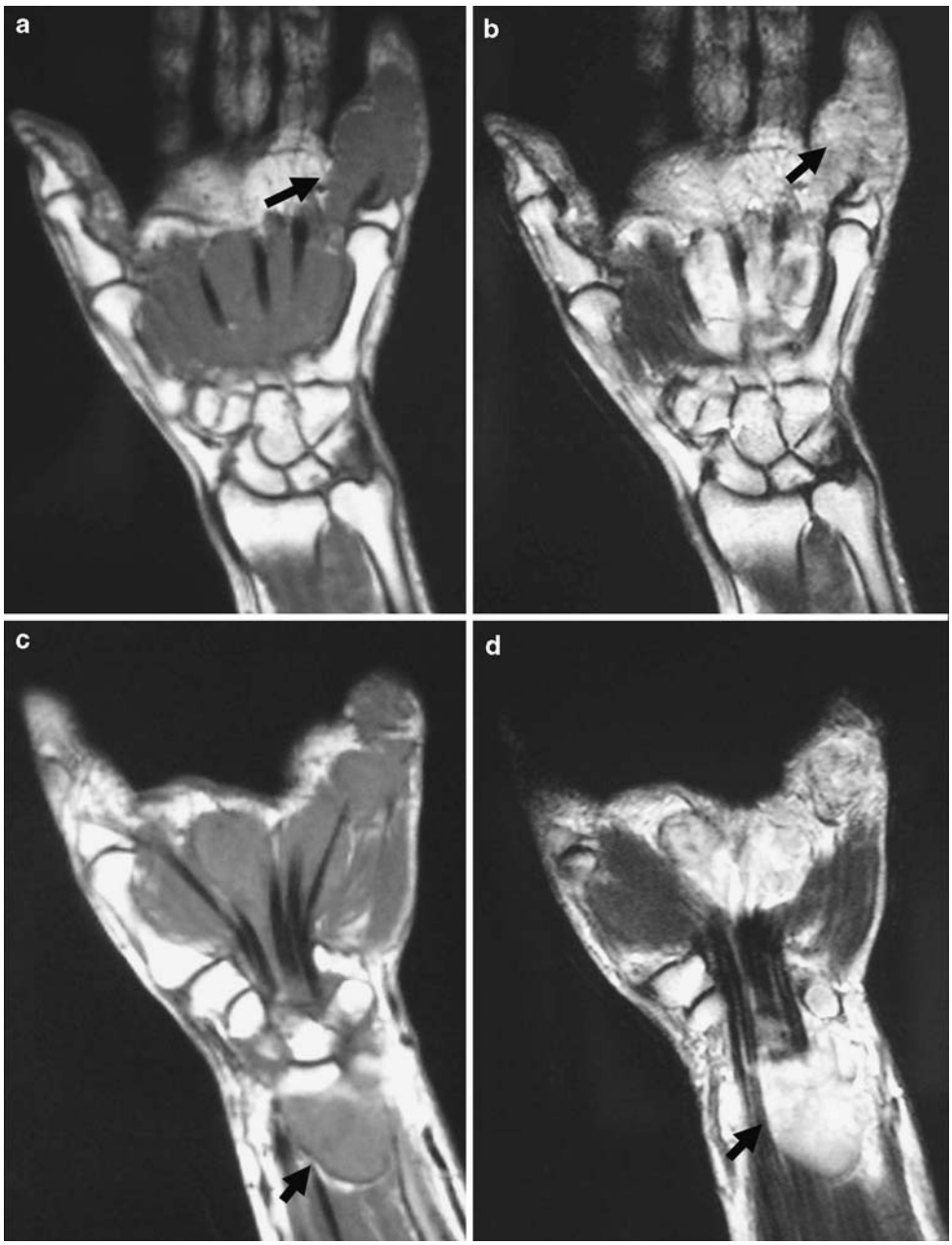

Fig. 2 Frontal magnetic resonance imaging shows a diffuse lesion. **a**, **b** T1- and T2-weighted imaging show continuous lesions in the palm and finger (*arrows*). **c**, **d** T1- and T2-weighted imaging show an isolated lesion in the wrist (*arrows*)

representing an uncommon site for D-TGCT. As the finger is one of the most common sites for L-TGCT, distinguishing D-TGCT from L-TGCT is difficult. At present, the most useful diagnostic tools for distinguishing between D-TGCT and L-TGCT are pathological examination and intraoperative findings. Histopathologically, L-TGCT is usually surrounded by a fibrous capsule, commonly shows focally prominent hyalinization of the stroma and reduced cellularity, and usually contains many more giant cells than D-TGCT [5]. Immunohistochemically, desmin stain highlights a population of large mononuclear cells with dendritic features in 35–40% of D-TGCT cases [3]. Cytogenetic analysis was not performed in the present case, but chromosomal analysis is useful for D-TGCT diagnosis. Rearrangements of the 1q11–13 region have been detected in L-TGCT and D-TGCT. Trisomies of chromosomes 5 and 7 are more frequent in D-TGCT than in L-TGCT [6]. These findings may facilitate diagnosis of D-TGCT, but more histochemical and cytogenetic studies should be performed to clarify the specificity of D-TGCT.

Treatments differ between D-TGCT and L-TGCT, as D-TGCT tends to be locally aggressive with multiple

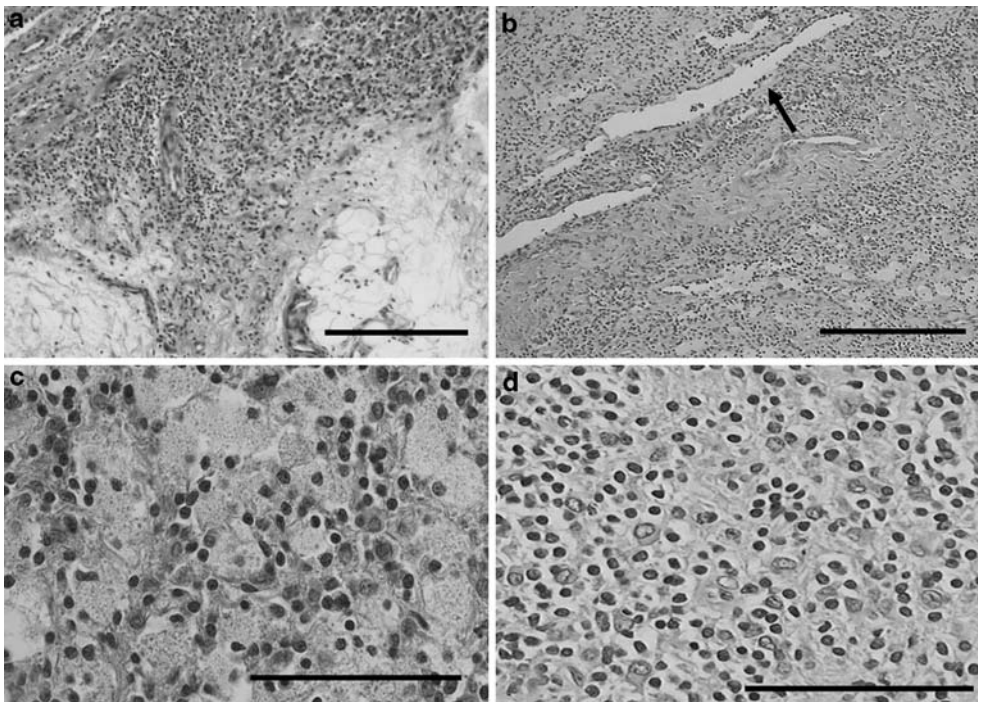

Fig. 3 Histological appearance of surgical specimens. **a** Irregular infiltration into the surrounding tissue is shown (hematoxylin and eosin; *scale bar*, 200 μm). **b** Cleft-like or synovial-like spaces are shown (*arrow*) (hematoxylin and eosin; *scale bar*, 200 μm). **c** Sheets of foamy cells are observed on the periphery of lesions (hematoxylin and eosin; *scale bar*, 100 μm). **d** Proliferation of small and large mononuclear cells is apparent. No atypical cells or mitoses are evident (hematoxylin and eosin; *scale bar*, 100 μm)

recurrences [2]. The recurrence rate is 10–20% for L-TGCT [7], compared to 40–50% for D-TGCT [2]. L-TGCT recurrence is usually cured by re-excision, but additional wide excision is necessary for D-TGCT recurrence. In this case, the tumor recurred two years and five months post-operatively. Schwartz et al. [8] reported a cumulative probability of recurrence of 15% at five years and 35% at 25 years for D-TGCT. A long follow-up is thus necessary.

Strongly increased uptake is usually seen on ^{67}Ga scintigraphy, but ^{99m}Tc scintigraphy does not show increased uptake for soft tissue tumors. Kobayashi et al. [9] reported that ^{99m}Tc accumulation is stronger than ^{67}Ga accumulation in L-TGCT and D-TGCT, and accumulation is higher in D-TGCT than in L-TGCT. These findings suggest that ^{99m}Tc scintigraphy is useful in distinguishing D-TGCT from other soft tissue tumors such as L-TGCT and malignant tumors. When lesions are multicentric as in the present case, ^{99m}Tc scintigraphy may be useful for identifying lesions. In addition, when identification of tumor recurrence is difficult due to the presence of post-operative scarring on MRI and CT, ^{99m}Tc scintigraphy is useful for identifying early stage recurrence. Increased uptake on ^{99m}Tc scintigraphy is seen for aggressive fibromatous tumor, but the mechanisms underlying ^{99m}Tc accumulation are yet to be studied.

Multicentric D-TGCT has been reported in two of 50 cases [5]. Locations were the forearm and wrist in both cases, and one case recurred within 2.5 years postoperatively. In the present case, multicentric D-TGCT occurred from finger to palm and in the wrist according to macroscopic and radiographic findings. These findings suggest that D-TGCT in the wrist is a multicentric possibility.

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