ABSTRACT

Tenosynovial giant cell tumors (TGCTs) arise from the synovium of joint, bursa, and tendon sheath, and are classified into localized and diffuse types. Diffused type often affects the large joint, and has more recurrence, metastasis, and malignant transformation potential compared to the localized type. Malignant diffused TGCT (D-TGCT) usually occurs as a large tumor (>5 cm), in older patients, and its histopathologic features include necrosis, cellular anaplasia, prominent nucleoli, high nuclear cytoplasmic ratio, brisk mitosis, discohesion of tumor cells, paucity of giant cells, and a diffuse growth pattern.

At least five of these criteria are required for the histopathologic diagnosis of malignant TGCT because the benign TGCT also shares many of these morphological features. We describe the cytomorphologic features of a malignant D-TGCT from an unusual case of pulmonary metastasis in an adult patient. Fine needle aspiration cytologic features of malignant D-TGCT have not been described earlier in the English literature.

Key words: D-TGCT; FNAC; joint; malignant tenosynovial giant cell tumor; metastasis

Introduction

Tenosynovial giant cell tumor (TGCT) initially was designated by Jaffe et al. in 1941. Diffuse TGCTs (D-TGCTs) are mostly benign, non-metastasizing, and locally invasive fibrohistiocytic neoplasms; malignancy can occur rarely. It is characterized by benign giant cell lesion with coexisting frankly malignant areas or a malignant transformation in a recurrent benign giant cell lesion. Both benign and malignant TGCT share many similar clinical and morphological features. Malignant D-TGCTs, however, are more destructive and show frequent metastasis and cellular anaplasia, and patients with this tumor have poor prognosis. Less than 50 cases of malignant D-TGCT have been reported mostly as case reports, and the diagnosis is made on the basis of histopathological examination. We describe the cytomorphologic features of a malignant D-TGCT from a lung metastasis.

Case History

A 50-year-old male presented with a history of a slowly progressive, painless swelling in the right knee for 6 months. Radiologic investigation suggested a D-TGCT. The lesion was excised in a private hospital and reported as D-TGCT. Postoperative local radiotherapy was given.

The patient was asymptomatic for approximately 4 years, following which the lesion recurred. Radiologic investigation...
revealed a large 5.5 × 4.7 × 3.4 cm well-defined soft tissue mass in the prepatellar area. It was isointense on T1-weighted and hyperintense on T2-weighted magnetic resonance (MR) images. There was no intra-articular extension and the underlying bones were normal. The radiologic features were suggestive of recurrent D-TGCT. Again local excision was done followed by radiotherapy. Approximately 1 year later, he presented to our chest medicine outpatient department with complaints of cough and chest pain for 6 weeks, two episodes of hemoptysis in 1 month, and swelling in the right knee. Chest X-ray was unremarkable; however, computerized tomography (CT) of the chest revealed two soft tissue masses, one in the right middle lobe and another in the left lower lobe, without any calcification or necrosis. The largest nodule measured 3 cm in maximum dimension [Figure 1].

Previous biopsy material was not available for review. Transbronchial fine needle aspiration (FNA) from the mass showed a discohesive cellular tumor comprising stromal cells admixed with osteoclastic giant cells. The stromal cells exhibited severe cellular atypia with marked anisonucleosis, enlarged hyperchromatic nuclei, irregular nuclei, thick nuclear membrane, coarse clumped chromatin, prominent nucleoli, high N: C ratio, and frequent mitoses [Figure 2a and b]. No matrix was seen. In the context of the recurrent joint tumor, the cytomorphological features were suggestive of metastatic malignant D-TGCT.

Transbronchial needle biopsy from the mass also showed pleomorphic stromal cells admixed with osteoclastic giant cells. Stromal cells revealed hyperchromatic nuclei, conspicuous nucleoli, eosinophilic cytoplasm, and frequent mitoses (18–20/10 HPF) including atypical forms [Figure 2c and d]. Stromal cells and osteoclastic giant cells were immunoreactive to CD68 [Figure 2e]. Ki-67 labelling index was approximately 40% [Figure 2f]. Histopathological features were in favor of metastatic malignant D-TGCT. Chemotherapy was given, however, the patient died of metastatic disease after 6 months.

Discussion

D-TGCT is generally regarded as a benign, non-metastasizing, locally aggressive fibrohistiocytic neoplasm of synovium. It is mostly seen in young adults with a female predominance (M:F = 1:2), but any age can be affected. Localized variant primarily occurs in hands, while the diffuse type has a predilection for knee, hip, ankle, elbow, and shoulder, and rarely, temporomandibular and spinal facet joints often involving periarticular tissue. The common clinical manifestations include pain, tenderness, swelling, restriction of motion, and hemorrhagic joint effusion. Radiographic images usually show an ill-defined periarticular mass with decreased signal intensity in both T1-weighted and T2-weighted MR images. An expansive or infiltrative lesion with presence of frequent lobulation and heterogeneous signals may indicate a malignant TGCT. D-TGCTs are generally large (> 5 cm), multinodular (extra-articular), or may have villous pattern also known as pigmented villonodular synovitis. Alternative white, yellowish, and brownish areas can be seen grossly. Microscopically, D-TGCTs show two types of mononuclear cells and osteoclastic giant cells. The small sized ovoid to spindle-shaped histiocytic cells exhibit longitudinal nuclear grooves, fine chromatin, and pale cytoplasm. While the larger rounded cells show reniform

Figure 1: Sagittal MR images of T1W (a) and T2W fat saturated. (b) sequences show a large well-defined soft tissue mass (arrows) which in isointense on T1W image and hyperintense on T2W image in the prepatellar area. Joint cavity and underlying bones are normal. Chest X-ray, (c) is unremarkable. Axial CT section. (d) of chest shows two soft tissue masses one in the right middle lobe and another in the left lower lobe without any calcification or necrosis (arrows)

Figure 2: Smear shows discohesive stromal cells and osteoclastic giant cells (a: Pap stain x100). Stromal cells are pleomorphic with hyperchromatic large irregular nuclei, thick nuclear membrane, clumped chromatin, prominent nucleoli, high N: C ratio, and frequent mitoses (green arrows) (b: Pap stain x400). Sections show pleomorphic stromal cells with frequent mitoses and admixed osteoclastic giant cells (c: H and E stain x100; d: H and E stain x400). Neoplastic stromal cells and osteoclastic giant cells are immunoreactive to CD68 (e: IHC: CD68 x200). Ki67 LI is approximately 40% (f: IHC: Ki67 x200)
or lobulated vesicular nuclei, thick nuclear membrane and abundant pale to deeply amphophilic cytoplasm. Foam cells, lymphocytes, variable hemosiderophilic deposition, and stromal fibrosis may be seen. These features can also be observed in FNA cytology. The histologic criteria for malignant TGCT include five out of eight characteristics including diffuse pleomorphism, prominent nuclei, high nucleocytoplasmic ratio, mitosis > 10/10 HPFs, necrosis, discohesion of tumor cells, paucity of giant cells, and a diffuse growth pattern. FNA cytology of our case showed diffuse pleomorphism, prominent nuclei, high nucleocytoplasmic ratio, frequent mitoses, and discohesion of tumor cells. The differential diagnoses of malignant D-TGCT are undifferentiated pleomorphic sarcoma, fibrosarcoma, and myxosarcoma. In our case, the initial tumor could be a low grade malignancy with low metastatic potential, or a benign tumor which was slowly progressive, controlled by local excision and radiotherapy for approximately 4 years. Undifferentiated pleomorphic sarcoma, fibrosarcoma, and myxosarcoma show progressive disease with early relapse and metastasis, which were not seen in our case in the initial phase. However, multiple lung metastases after a long interval, recurrent joint swelling, significant cytologic atypia, and a rapidly progressive, uncontrolled disease in this case suggested a malignancy possibly arising in benign D-TGCT. The cytomorphic differential diagnoses in our case were a metastasis from a giant cell tumor (GCT) of bone and metastatic giant cell rich osteosarcoma. Periarticular location of the tumor without any bone involvement in our case excluded the possibility of GCT of bone and osteosarcoma. The mononucleated cells are immunoreactive to CD163, CD68, smooth muscle actin, desmin, and S100 protein, whereas osteoclastic giant cells are positive with CD68.

In our case, CD68 was positive in both stromal cells and giant cells. DNA aneuploidy and chromosomal aberrations, such as trisomy 7 and 5, translocations involving 1p11-13, 2q35-37, or 16q22-24 have been identified in TGCT. COL6A3-CSF1 fusion following a recurrent translocation, t(1;2) (p13;q37) has been characteristically seen, but present in a minority (2–16%) of the intratumoural cells. Fluorescence in situ hybridization (FISH) studies were not done in our case; however, the characteristic radiographic, cytomorphicologic, and histopathological features suggested a D-TGCT.

The patients with malignant D-TGCT are treated by surgical excision or amputation with or without radiotherapy and or chemotherapy. However, most patients develop early local recurrences, regional nodal and distant metastases to the lung, vertebra or disseminated disease, and die of the disease within a few months of diagnosis. Chemotherapy with CSF1R targeted imatinib, adriamycin, and ifosfamide has shown limited success. Our case also showed rapidly progressive disease with lung metastases and died of the disease. Though no single clinical, cytomorphicologic, or radiologic characteristic can separate benign from malignant D-TGCT, atypical cytologic features in a recurrent, infiltrative, or a metastatic lesion should raise the suspicion for malignancy.

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Conflicts of interest
There are no conflicts of interest.

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