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Case Reports

Heterologous osteosarcomatous and rhabdomyosarcomatous elements in dedifferentiated solitary fibrous tumor: further support for the concept of dedifferentiation in solitary fibrous tumor ☆

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ABSTRACT

Dedifferentiation within solitary fibrous tumor is a rare and only recently characterized phenomenon. It differs from malignant solitary fibrous tumor in that there is abrupt transition between classical solitary fibrous tumor and the dedifferentiated component. The latter is a high-grade sarcoma, which can exhibit a number of morphologies, but heterologous differentiation is exceptionally rare. We report a case of dedifferentiated solitary fibrous tumor, with heterologous osteosarcomatous and rhabdomyosarcomatous elements, arising in the deep soft tissue of the thigh of a 59-year-old man. This comprised morphologically and immunohistochemically typical solitary fibrous tumor, juxtaposed to pleomorphic, high-grade malignant neoplasm of 2 distinct lineages. The sharp demarcation between well-differentiated and dedifferentiated components is typical of the dedifferentiation seen in other mesenchymal neoplasms. This expands the range of histopathology of this rare, newly characterized type of malignant progression in solitary fibrous tumor.

1. Introduction

Dedifferentiation is a well-established phenomenon occurring in a subset of mesenchymal neoplasms but is a newly defined concept in solitary fibrous tumor (SFT) [1,2]. Heterologous differentiation in dedifferentiated SFT is, however, exceptionally rare, with only 3 previously defined cases [3]. We describe a further case of dedifferentiated solitary fibrous tumor with distinct heterologous components of osteosarcoma and rhabdomyosarcoma on a background of classical SFT, the first to show clear bidirectional divergence. This adds to the concept of dedifferentiation as a specific phenomenon in SFT, distinct from the well-characterized malignant SFT (in which neoplasms with the essential features of usual SFT exhibit atypical characteristics such as hypercellularity, pleomorphism, and increased mitotic rate) and further expands the histomorphological range of findings of this unusual tumor subtype.

1.1. Case history

A 59-year-old white man presented with a 30-year history of a soft tissue mass on the medial aspect of his right thigh. He related the initial appearance of the mass to an episode of work-related trauma. The mass had stayed static in size until the preceding 8 months, during which it had doubled in size, which the patient had again related to trauma. The patient had no other symptoms and no previous medical or family history of note. Clinical examination showed a large, firm mass deep in the muscle of the medial right thigh and extending to subcutis, which was consistent with an aggressive sarcoma. Magnetic resonance imaging showed a solid vascular 11 × 8 × 8 cm mass arising from the proximal right sartorius muscle, involving the anterior fibers of the adductor longus muscle and the saphenous vein, and consistent with an aggressive neoplasm, likely to represent a high-grade sarcoma. Imaging of the chest showed no metastatic disease. Given the concerning magnetic resonance imaging appearances raising suspicion of a high-grade soft tissue neoplasm, the mass was widely resected with portions of sartorius and adductor longus muscles. Large feeding vessels were noted around the tumor at the time of surgery. In view of the tumor size and high-grade features, the patient proceeded to postoperative radiotherapy. He is free of disease 7 months after diagnosis.

2. Materials and methods

The histopathologic features were noted, and a comprehensive immunohistochemical panel was applied (antibody dilutions and sources in Table). Molecular cytogenetic analysis was performed on formalin-fixed, paraffin-embedded material, to assess for *MDM2* amplification (to support the exclusion of dedifferentiated liposarcoma)

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by fluorescence in situ hybridization (FISH). One-micrometer-thick formalin-fixed, paraffin-embedded sections were dewaxed overnight at 60°C, treated with hot buffer wash at 80°C (2-3 hour) then proteolytic enzyme treatment at 37Cº, and washed in distilled water then an alcohol series before addition of *MDM2* and *CEP12* DNA probes (Abbott Laboratories Ltd, Maidenhead, UK). Hybridization was performed overnight according to manufacturer's protocols.

3. Results

3.1. Histopathologic findings

Grossly, the tumor comprised a 10 × 7 × 6.5 cm largely circumscribed mass present within skeletal muscle and subcutaneous fat. The cut surface was lobulated and mostly firm, with myxoid areas and foci of cystic degeneration. The tumor alternated between pale, spongy homogeneous areas of medium firm consistency (Fig. 1A), many of these sited peripherally, and tan colored, often variegated and heterogeneous areas that varied in consistency from soft to firm (Fig. 1A), with focal hemorrhage and prominent necrosis, the latter accounting for approximately 20% of the tumor area.

Microscopically, the lesion was partly circumscribed and encapsulated but showed areas of infiltration and was composed of 3 distinct components. The first, corresponding to the pale spongy areas noted grossly, consisted of an encapsulated neoplasm of alternating hypocellular and hypercellular distributions of relatively small and uniform cells with plump but bland ovoid vesicular nuclei and fibrillary cytoplasm (Fig. 1B-D) present in patternless arrangements (Fig. 1C-D). The mitotic index was up to 2/10 high-power fields (HPF). Numerous thin-walled hemangiopericytic vessels were interspersed. The stroma was densely hyalinized, and there was focal calcification (Fig. 1E). This component showed strong and diffuse expression of CD34 and bcl-2 but was negative for CD99, desmin, smooth muscle actin (SMA), CD31, S100 protein, and AE1/AE3. The proliferation index by MIB1 varied from low to focally moderate, labeling approximately 5% to 20% of nuclei. This portion of the tumor showed all the typical features of classical solitary fibrous tumor.

The second component, which corresponded to the firm, heterogeneous, and variegated macroscopic foci, was markedly cellular and was abruptly demarcated from the bland areas described above (Figs. 1F and 2A). It comprised sheets and nodules of pleomorphic cells with large ovoid vesicular nuclei with coarse chromatin, large prominent nucleoli, and moderate to abundant amounts of amphophilic or eosinophilic cytoplasm (Fig. 2A-B). Nuclear atypia was marked and widespread, with many bizarre cells (Fig. 2C) as well as multinucleate tumor giant cells (Fig. 2B). The tumor giant cells showed abundant cytoplasm, but no conclusive cross striations or features of rhabdomyoblasts were identified. The mitotic index was 23/10 HPF including numerous atypical forms, and there was focal coagulative necrosis (Fig. 2D). In very rare foci, there were sheets of ovoid cells that appeared to be intermediate between the bland cells of the classical SFT and the markedly anaplastic areas (Fig. 2E). The third component had essentially similar morphological features to the second, also showing abrupt demarcation from the bland first component. In addition, this showed prominent areas of tumoral osteoid (Figs. 2F and 3A), with osteoblastic rimming and calcification. These areas as well as the nonossifying areas included rare osteoclast-type giant cells.

Immunohistochemically, CD34 was absent in all pleomorphic areas (components 2 and 3), and there was abrupt transition between the strong expression seen in the bland cells of the classical SFT and its absence in the pleomorphic elements (Fig. 3B-C). Numerous large tumor nodules in component 2 showed strong and diffuse desmin expression (Fig. 3D). The desmin-positive areas were focally positive in nuclei for myogenin (Fig. 3E). There was occasional nuclear expression of p16. The pleomorphic tumor was negative for CD99, CDK4, SMA, h-caldesmon, CD31, S100 protein, and AE1/AE3. The proliferation index by MIB1 was high, labeling approximately 80% of nuclei (Fig. 3F).

These portions of the tumor, therefore, comprised high-grade sarcoma, with osteosarcomatous and (pleomorphic) rhabdomyosarcomatous differentiation. The findings of high-grade osteosarcoma and rhabdomyosarcoma juxtaposed to conventional solitary fibrous tumor were therefore interpreted as dedifferentiated solitary fibrous tumor with heterologous osteosarcomatous and rhabdomyosarcomatous components. The tumor was completely excised from its circumferential margins.

3.2. Molecular cytogenetic findings

Fluorescence in situ hybridization showed cells that had 3 or 4 pairs of *CEP12* and *MDM2* signals and some with up to 10 instead of the usual 2. These were, therefore, consistent with derivation from an abnormal clone with polyploidy and/or with gains of all or part of chromosome 12. This picture was, however, not typical of amplification of the *MDM2* gene at 12q15 and did not support diagnoses of well-differentiated or dedifferentiated liposarcoma.

Table
Antibodies used for immunohistochemistry

Antibody	Source	Dilution
AE1/AE3	Zymed Laboratories, South San Francisco, CA	1:50
Desmin	Dako, Glostrop, Denmark	1:50
SMA	Dako	1:200
Myogenin	Dako	1:100
MyoD1	Novocastra Laboratories, Newcastle upon Tyne, UK	1:50
h-caldesmon	Dako	1:50
S100 protein	Dako	1:1500
CD34	Novocastra Laboratories	1:30
CD31	Dako	1:20
CD99	Dako	1:100
bcl-2	Dako	1:15
INI1	Becton Dickinson, Plymouth, UK	1:100
CDK4	Invitrogen, Paisley, UK	1:25
p16	MTM Laboratories, Heidelberg, Germany	Ready diluted (kit form)
MIB1	Dako	1:100

4. Discussion

We describe a case of dedifferentiated solitary fibrous tumor, showing morphologically and immunophenotypically conventional SFT juxtaposed to high-grade osteosarcoma and pleomorphic rhabdomyosarcoma. Dedifferentiation occurs in a subset of mesenchymal neoplasms [4-11] and generally indicates the presence of high-grade tumor without evidence of the line of differentiation of the original neoplasm (although heterologous differentiation toward other lines might be present). Dedifferentiation can occur de novo or as a complication of recurrent previously well-differentiated tumor and confers more aggressive behavior. Histologically, there is usually abrupt transition between well-differentiated and dedifferentiated tumor.

Solitary fibrous tumor is a fibroblastic mesenchymal tumor that was initially described in the pleura but has subsequently been described in almost any organ or anatomical site. Thoracic and extrathoracic SFTs have been shown to have similar clinical and pathologic features [12-14]. Although most typical SFTs behave in an indolent manner, the biology of SFT is unpredictable [15-17]. Long-term follow-up is mandatory, as a subset of tumors with bland histology have been shown to behave aggressively. Retrospective studies suggest that surgical excision with clear margins should be the treatment of choice where feasible, as this appears to improve survival [18,19], but up to 20% of cases display local recurrence or metastatic