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Case Report

A rare case of undifferentiated pleomorphic sarcoma of Gracilis muscle: role of histopathology and immunohistochemistry in diagnosis

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ABSTRACT

Undifferentiated pleomorphic sarcoma (UPS) is a high-grade soft tissue malignancy without identifiable differentiation, often presenting as a rapidly enlarging, painless mass in the extremities or other deep-seated locations in elderly population. A 72-year-old male presented with a progressively enlarging, painless mass in the right thigh of four months duration. Magnetic resonance imaging (MRI) revealed a multilobulated solid-cystic lesion located in the medial aspect of the right thigh, within the gracilis muscle plane. Radiologically, a differential diagnosis of myxofibrosarcoma versus intramuscular myxoma was considered. The patient subsequently underwent wide local excision of the lesion. Gross examination: A well-circumscribed soft tissue specimen measuring 14.5×9×4.5 cm was received. The external surface was bosselated. Cut section revealed a grey-white, fleshy solid tumor with focal areas of hemorrhage. Histopathological examination revealed a pleomorphic spindle cell tumor with interlacing fascicles and high mitotic activity. Areas of tumor necrosis are also identified. On immunohistochemical analysis, tumor cells retained nuclear expression of H3K27me3 in while being negative for lineage-specific markers (including epithelial, myogenic, neural, and melanocytic markers), thereby excluding specific lines of differentiation. UPS is a high-grade malignant mesenchymal neoplasm and remains a diagnosis of exclusion. A comprehensive evaluation incorporating histopathology and immunohistochemistry is essential to rule out other pleomorphic sarcomas and mimics, ensuring accurate diagnosis and appropriate management.

Keyword: Undifferentiated pleomorphic sarcoma, Soft tissue sarcoma, Pleomorphic spindle cell tumor, Thigh, Immunohistochemistry, H3K27me3

INTRODUCTION

Soft tissue sarcomas are mesenchymal tumors arising from connective tissues, including muscle, fat, blood vessels, and deep soft tissues. UPS, previously termed malignant fibrous histiocytoma, is a high-grade sarcoma lacking a definable line of differentiation on histopathology and immunohistochemistry.[1,2] It most commonly occurs in the extremities of older adults.[3] Despite advances in diagnostic pathology, UPS remains diagnosis of exclusion and poses a diagnostic challenge due to its pleomorphic morphology.[4] Recent studies highlight its genetic heterogeneity and complex molecular profile rather than a single defining mutation.[5]

CASE REPORT

A 72-year-old male presented with a progressively enlarging, painless swelling over the medial aspect of the right thigh for 4 months, associated with difficulty in walking. There was no history of trauma, weight loss, appetite loss, prior radiation exposure, genetic disorders, chronic inflammation, or environmental carcinogen exposure.

Radiological finding

MRI revealed a multilobulated solid-cystic lesion located in the medial aspect of the right thigh, within the gracilis muscle plane.

Radiologically, a differential diagnosis of myxofibrosarcoma versus intramuscular myxoma considered. The patient subsequently underwent wide local excision of the lesion.

Gross findings

A well-circumscribed soft tissue specimen measuring 14.5×9×4.5 cm was received. The external surface was bosselated. Cut section revealed a grey-white, fleshy solid tumor with focal areas of hemorrhage.

Microscopy

Sections show a relatively circumscribed high-grade spindle cell neoplasm composed of cells arranged in intersecting fascicles and storiform pattern.

The tumor cells exhibit marked nuclear pleomorphism with hyperchromatic nuclei. Numerous multinucleated giant cells including the osteoclast-like giant cells are present.

Areas of stromal hyalinization, focal myxoid change and tumor necrosis are identified. Mitotic activity brisk, exceeding 20 mitoses per 10 high-power fields, including atypical mitotic figures.

Based on the histomorphological features, the differential diagnosis includes UPS, FNCLCC grade 3, and fibrosarcoma. The case was sent for IHC to an outside laboratory for further definitive diagnosis.

Immunohistochemistry

The diagnosis of UPS is ultimately one of exclusion, requiring a comprehensive immunohistochemical (IHC) panel to rule out other morphologically similar entities, including cytokeratins to exclude sarcomatoid carcinoma, S100 and SOX10 for neuroectodermal tumor, smooth muscle actin and desmin for pleomorphic myogenic sarcomas, H-caldesmon for leiomyosarcoma.

MDM2 and CDK4 staining assist in excluding dedifferentiated liposarcoma. In this case the tumor cells were negative for desmin, H-caldesmon, MyoD1, CD34, and S-100P. MDM2 is patchily positive in the osteoclast-like giant cells, while negative in the tumor cells.

The retained expression of H3K27me3, while the absence of specific lineage differentiation on immunohistochemistry supports the diagnosis of UPS, in conjunction with the histomorphological findings.

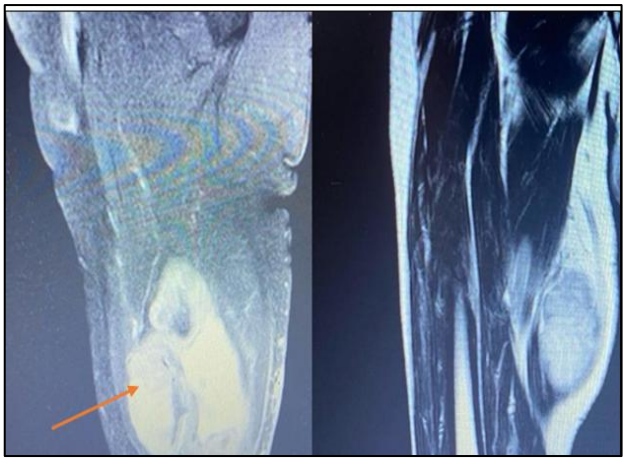

Figure 1: MRI images in coronal and sagittal planes.
*It revealed a well-circumscribed lobulated soft tissue mass in the calf region, appearing heterogeneously hyperintense on T2-weighted sequences with areas of internal necrosis/cystic degeneration. The lesion was seen within the intramuscular compartment causing displacement of adjacent muscles without bony involvement.

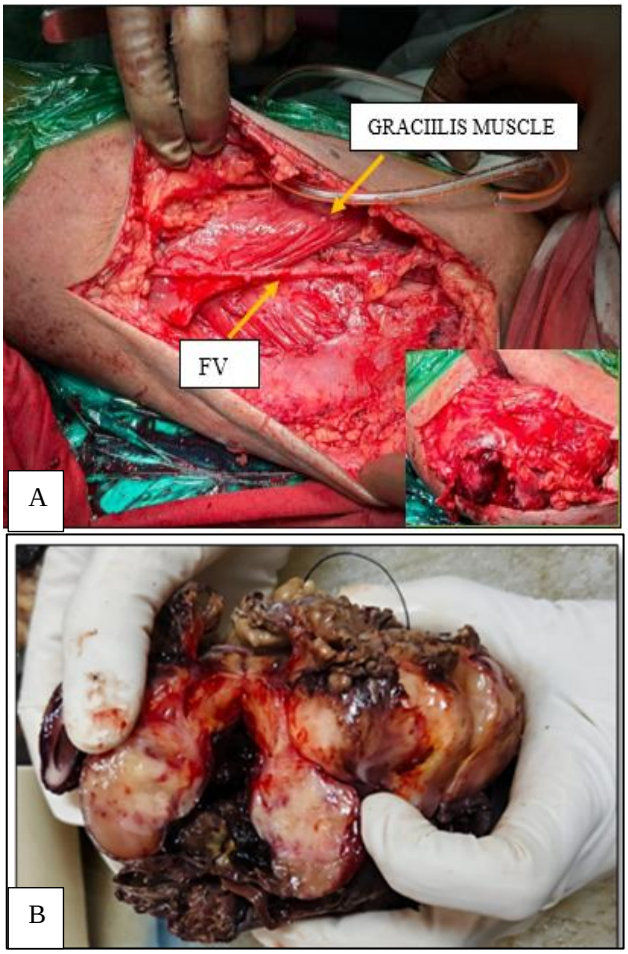

Figure 2 (A and B): A: Plane of dissection. Inset shows tumor mass. B: Gross-A well-circumscribed tumor. The external surface was bosselated. Cut section revealed a grey-white, fleshy solid tumor with focal areas of hemorrhage.

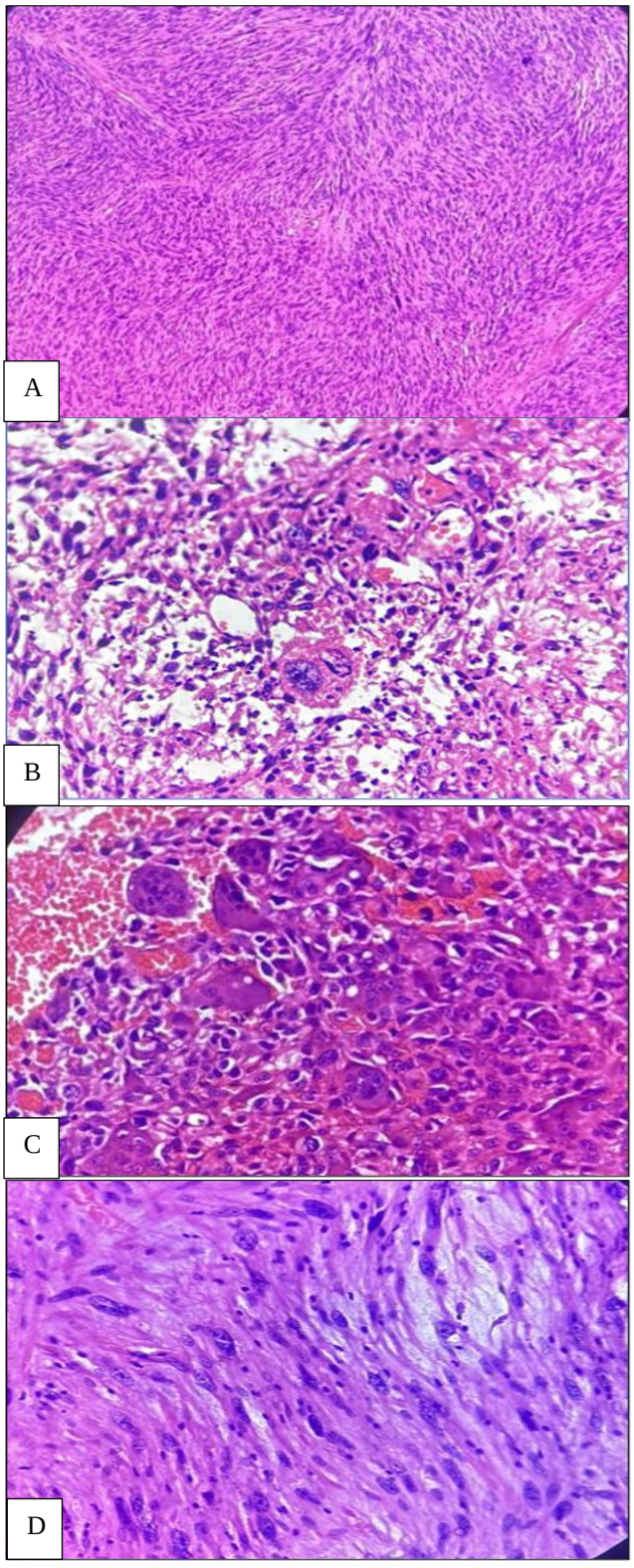

Figure 4 (A-D): A: Tumor cells arranged in a fascicular pattern, characterized by intersecting. B: Marked pleomorphism, with variable cell sizes and hyperchromatic nuclei, consistent with the features of a high-grade sarcoma. C: Numerous multinucleated giant cells, including osteoclast-like giant cells, are present. D: Areas of stromal hyalinization, focal myxoid change are identified.

DISCUSSION

UPS is an aggressive malignancy characterized by high local recurrence and metastatic potential typically presenting as a rapidly enlarging painless mass in the sixth to seventh decades of life.[6]

Histologically, UPS exhibits a highly pleomorphic cellular population arranged in storiform or haphazard patterns with frequent atypical mitoses and areas of tumor necrosis.[7]These features are not specific, so immunohistochemistry is essential to exclude alternative diagnosis.

UPS is staged using tumor, node, and metastasis (TNM) criteria and histologic grade criteria as determined by a tumor's mitotic count, necrosis extension, and differentiation from the French Federation of Cancer Centers Sarcoma Group (FNCLCC). 5-year overall survival (OS) for localized, resectable UPS is 60-70%, with a median survival 10 years.[8]

Recent molecular studies suggest that UPS is characterized by marked genomic instability rather than a specific driver mutation. Common alterations involve tumor suppressor genes such as TP53, RB1, and PTEN; however, no pathognomonic genetic abnormality has been identified.[9]

Management is multidisciplinary. Wide local excision with negative margins (R0 resection) is the corenerstone.[10]

Adjuvant radiotherapy plays a critical role in improving local control, particularly in high-grade tumors, lesions larger than 5 cm and those located in deep soft tissues.

The role of chemotherapy remains selective. Doxorubicin-based regimens, either alone or in combination with ifosfamide, constitute the first-line systemic therapy.[11] Emerging evidence also highlights the role of immunotherapy in selected cases.

In the present case, the diagnosis of UPS was established based on characteristic histomorphological features and along with immunohistochemistry. The patient was managed with surgical excision followed by appropriate adjuvant /therapy in higher center. Revision surgery was subsequently performed for suspected residual tumor; however, on histopathological examination revealed no residual tumor. The patient currently doing well.

CONCLUSION

UPS is an aggressive soft tissue malignancy requiring a multidisciplinary approach for accurate diagnosis and management. Advances in molecular pathology and emerging therapeutic modalities, including immunotherapy, offer promising avenues for improved outcomes. Early diagnosis and complete surgical excision remain critical in reducing recurrence and improving survival.

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