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Synovial Sarcoma with Extensive Rhabdoid Differentiation: A Rare Aggressive and Deceptive Histological Subtype

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ABSTRACT

Objective: Synovial sarcoma usually presents with spindle cell morphology with or without epithelial differentiation. Extensive rhabdoid differentiation is a very rare feature with only few cases described in literature.

Case Report: We present two cases of synovial sarcoma with rhabdoid differentiation along with their clinical follow-up. Both cases had tumor in the vicinity of joints and showed lung metastasis during follow-up inspite of R0 resection.

Conclusion: We emphasised that extensive rhabdoid differentiation can be deceptive and challenging for diagnosis in small biopsies and also show an aggressive clinical course with dismal prognosis. Awareness of this rarely described unusual and aggressive histomorphological subtype is prudent due to its distinct diagnostic, prognostic and therapeutic implications.

Keywords: Aggressive, Metastasis, Rhabdoid, SSX18, Synovial Sarcoma

INTRODUCTION

Synovial sarcoma (SS) accounts for 5–10% of soft tissue sarcomas and typically arises in the extremities of young adults, in close association with joints (1-3). Histologically, SS is classically monophasic (spindle cell) or biphasic (spindle and epithelial components). Poorly differentiated SS is less common and may show marked nuclear atypia, high mitotic rate, and necrosis. The poorly differentiated subtype of synovial sarcoma includes rhabdoid differentiation, which is sparsely described in the literature with only a handful of cases (2-5). This uncommon morphology can lead to diagnostic pitfalls, especially on limited biopsy material, because it mimics other epithelioid or rhabdoid neoplasms. We report two cases of SS with extensive rhabdoid features, both of which demonstrated aggressive clinical behavior.

CASE 1

A 49-year-old woman presented with a progressively enlarging swelling of the foot for four months. Magnetic resonance imaging (MRI) suggested a malignant vasoformative tumor. Biopsy review at our tertiary center revealed an epithelioid neoplasm with hemorrhage and focal vasoformative areas (Figure 1A). Many tumor cells showed large polygonal morphology, eccentric nuclei, dense eosinophilic cytoplasm, and hyaline inclusions, consistent with rhabdoid differentiation (Figure 1B). Differential diagnoses included epithelioid sarcoma (ES), epithelioid malignant peripheral nerve sheath tumor (MPNST), rhabdomyosarcoma (RMS), extrarenal malignant rhabdoid tumor (EMRT), and malignant melanoma.

The primary immunohistochemistry (IHC) panel (pancytokeratin, SMA, S100, HMB45, desmin, MyoD1, SOX10) was negative. INI1 expression was significantly reduced but not completely lost (Figure 1C). Extended IHC revealed diffuse nuclear positivity for TLE1 and TRPS1. FISH analysis confirmed SS18 gene rearrangement (Figure 1D). A diagnosis of monophasic SS with extensive rhabdoid differentiation, FNCLCC Grade 3, was made.

The patient underwent below-knee amputation, gross findings as described in Figure 1E. Histopathology showed epithelioid to spindle cell morphology with extensive rhabdoid features, brisk mitosis, and necrosis (Figure 1F). SS18 IHC was diffusely positive (Figure 1G). Multidisciplinary tumor board (MTB) recommended adjuvant chemotherapy, and

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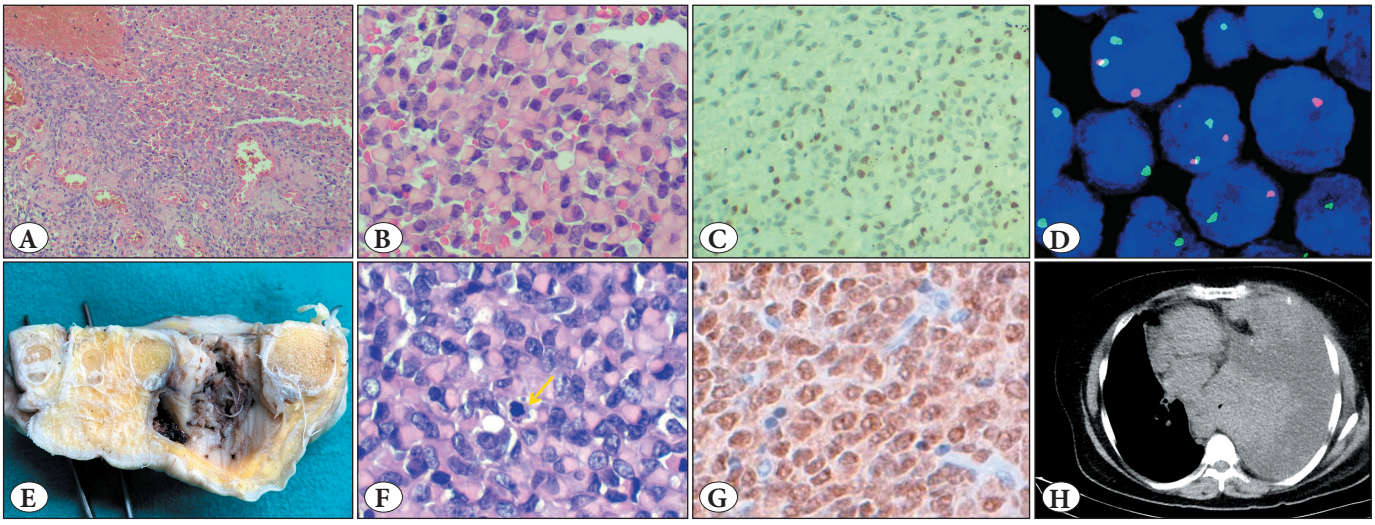


Figure 1: Case 1. A) HE showed an epithelioid tumor with areas of haemorrhage and vasoformative pattern at places. **B)** Significant areas showed large polygonal cells with eccentric nucleus and dense eosinophilic cytoplasm with hyaline inclusion evocative of rhabdoid differentiation. **C)** INI1 immunoexpression was significantly reduced but not completely absent in the tumor cells. **D)** Tumor cells were positive for SS18 gene rearrangement by break-apart fluorescent in situ hybridization. **E)** Gross findings showed a solid cystic infiltrative neoplasm in foot. **F)** HE showed a tumor with epithelioid to spindle cell morphology and extensive rhabdoid differentiation. Mitosis was brisk (arrow). **G)** SS18 exhibited diffuse and strong nuclear positive immunoexpression **H)** Low dose CT chest showed left hemi thorax nodular heterogeneous density along costal, mediastinal and diaphragmatic pleura with gross pleural effusion and collapse of underlying lung and mass effect in form of mediastinal shift of heart towards the right side. Biopsy of the pleural nodule showed metastatic synovial sarcoma with extensive rhabdoid differentiation.

she received six cycles of ifosfamide and adriamycin. At 14 months of follow-up, she developed pleural metastasis with effusion (Figure 1H), biopsy-proven as metastatic SS with rhabdoid differentiation. She deteriorated clinically and was lost to follow-up after opting for local supportive care.

CASE 2

A 35-year-old man was initially treated at another hospital for popliteal fossa swelling, diagnosed as SS. He received three cycles of neoadjuvant gemcitabine–docetaxel chemotherapy, followed by resection, which was reported as high-grade SS. He did not pursue adjuvant therapy. Two months later, he presented with pain, cough, and recurrent popliteal swelling. PET-CT showed residual disease, pulmonary nodules, and suspicious lymphadenopathy (Figure 2A).

At our center, biopsy of a subpleural nodule revealed spindle cells with rhabdoid differentiation (Figure 2B). TLE1, TRPS1, and SS18 IHC were diffusely positive (Figure 2C); INI1 expression was significantly reduced (Figure 2D). MRI showed a recurrent lobulated popliteal mass (Figure 2E). Limb salvage surgery and ilio-inguinal lymph node dissection were performed, revealing monophasic SS, FNCLCC Grade 3, with rhabdoid differentiation (Figure 2F-G), and no nodal involvement. Bilateral thoracoscopic metastatectomy was also performed.

The MTB advised ifosfamide–adriamycin chemotherapy, which the patient completed (six cycles). Subsequent imaging showed no active disease initially, but later follow-up revealed new pulmonary nodules. He was started on pazopanib but progressed with multiple metastases till last follow-up available.

DISCUSSION and CONCLUSION

Both patients presented with SS showing extensive rhabdoid features, confirmed by molecular or fusion-specific IHC studies. The rhabdoid phenotype in SS is extremely rare and underrecognized (2-5). Its deceptive morphology may exclude SS from initial differential diagnosis. In our cases, both patients showed partial INI1 loss—an important clue (6). ES and EMRT usually show complete INI1 loss, while epithelioid MPNST typically shows diffuse S100/SOX10 positivity with INI1 loss. Epithelioid angiosarcoma expresses vascular markers (CD31, ERG, CD34). RMS shows desmin, MyoD1, and myogenin positivity. Melanoma is S100, SOX10, HMB45, and MelanA positive. Recognition of rhabdoid morphology within SS is critical, particularly in tumors near joints, to avoid misclassification.

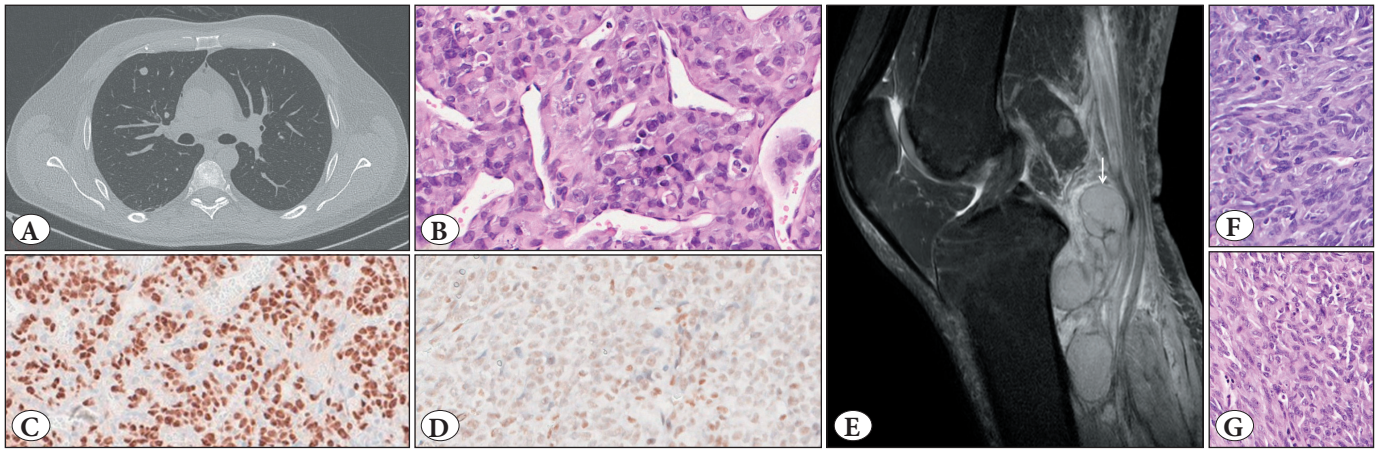


Figure 2: Case 2. A) CT scan chest axial images showing small nodule in anterior lobe of right lung (arrow). **B)** Trucut biopsy from right subpleural nodule revealed a blue spindle cell tumor with areas of rhabdoid differentiation. **C)** The tumor showed positive immunoexpression for SS18, thus confirming metastatic synovial sarcoma. **D)** INI1 immunoexpression was significantly reduced but not completely absent in the tumor cells. **E)** MRI T2-weighted Fat Sat sagittal image showing lobulated hyperintense mass in the popliteal fossa displacing the popliteal vessels (arrow). **F,G)** HPE revealed morphology of monophasic SS, FNCLCC grade 3 with rhabdoid differentiation.

Molecular confirmation is essential. TLE1 is sensitive but not specific, as it may be expressed in MPNST and other sarcomas (1). TRPS1 has emerged as a useful marker, though specificity remains under evaluation (7). SS18-SSX fusion-specific antibody is highly specific and may obviate the need for FISH in many cases (8). In both our patients, confirmation by SS18 positivity and FISH supported the diagnosis.

INI1 immunoexpression has been studied in SS. Kohashi et al. (6) evaluated 95 SS cases and found reduced expression in 69%, but none showed complete loss. Prognosis was not affected by INI1 status. In our cases, INI1 reduction provided a useful diagnostic pointer but was not prognostic. Both cases demonstrated aggressive clinical behavior with early lung metastasis, consistent with previous reports linking rhabdoid morphology to poor outcomes (3,9).

Rhabdoid differentiation in synovial sarcoma is an uncommon but clinically significant histologic pattern. It may mimic several other epithelioid or rhabdoid tumors and complicate diagnosis, especially on small biopsies. Reduced but not absent INI1 expression, combined with strong TLE1/TRPS1 expression and confirmation by fusion-specific studies, is critical in establishing the diagnosis. Awareness of this variant is important for pathologists, as it portends an aggressive course with early metastasis and poor prognosis. Our two cases add to the limited literature and emphasize the need to recognize rhabdoid SS as a distinct, high-grade histological variant with significant therapeutic and prognostic implications.

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Conflict of Interest
The authors declare that they have no conflict of interest.

Ethics Approval
All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the Institutional Review Board (Rajiv Gandhi Cancer Institute & Research Centre); vide the ethical approval letter number RES/SCM/60/2023/76

Informed Consent
Informed consent was obtained from all individual participants included in the study.

Consent for Publication
Consent for publication was obtained for every individual person's data included in the study.

Authorship Contributions
Concept: **SP**, Design: **SP, DB**, Data collection or processing: **SP, DB, HR, RO, AS, VT, UB, SR, AM**, Analysis or Interpretation: **SP, DB, HR, RO, AS, VT, UB, SR, AM,** Literature search: **SP, DB**, Writing: **SP, DB**, Approval: **All Authors.**

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