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Original Research Article

# Diagnostic Surprises: Rare Cases of Renal Synovial Sarcoma and Renal Cell Carcinoma with Sarcomatoid Differentiation in a Tertiary Care Centre, Rajasthan

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**Abstract**

**Background:** Renal tumors with spindle cell morphology pose significant diagnostic challenges due to overlapping histopathological features among diverse entities. Primary Renal Synovial Sarcoma (RSS) is an exceptionally rare malignancy, whereas Renal Cell Carcinoma with Sarcomatoid Differentiation (sRCC) represents an aggressive dedifferentiated phenotype of RCC with grave prognosis. Accurate distinction between these entities is critical, as their management and outcomes differ markedly.

**Methods:** We report a case series of two diagnostically challenging renal tumors encountered at a tertiary care centre in Rajasthan. Detailed clinicoradiological correlation, histomorphological examination, and an extensive immunohistochemical (IHC) panel were employed to arrive at the final diagnoses.

**Results:** The first case involved a 24-year-old female with a radiologically benign-appearing renal cyst, which on histopathology revealed a malignant spindle cell neoplasm. Lack of renal epithelial and myogenic markers, along with strong nuclear positivity for TLE, supported a diagnosis of Primary Renal Synovial Sarcoma. The second case was a 65-year-old female with a renal mass showing biphasic morphology comprising clear cell carcinoma and high-grade sarcomatoid areas. IHC positivity for PAX8 and Vimentin confirmed Renal Cell Carcinoma with Sarcomatoid Differentiation. Both cases underscored the limitations of morphology alone and the indispensable role of ancillary testing.

**Conclusion:** Rare renal tumors with spindle cell morphology are important diagnostic "surprises" in renal pathology. Differentiation between primary renal sarcomas and sarcomatoid dedifferentiation in RCC cannot be reliably achieved on routine H&E sections alone. A systematic approach incorporating adequate sampling and judicious use of immunohistochemical markers such as TLE and PAX8 is essential for accurate diagnosis, prognostication, and appropriate therapeutic decision-making.

**Keywords:** Primary synovial sarcoma of kidney, Sarcomatoid RCC, RCC.



## Introduction

Renal cell carcinoma (RCC) is the most prevalent malignancy of the kidney, accounting for approximately 85% of all renal tumors and 3% of adult cancers.[1] For decades, the diagnostic landscape was dominated by the "conventional" clear cell RCC (ccRCC), which comprises roughly 68.8% of these cases, followed by papillary and chromophobe subtypes. [1,2] However, approximately 20% of renal tumors fall into the non-clear cell RCC (nccRCC) category, representing a diverse spectrum of rare entities that pose significant diagnostic and therapeutic challenges. [3,4]

The incidence of renal tumors is notably lower in the Asian region, potentially due to underreporting. [1] Pathologists frequently encounter "surprises" in the form of tumors that deviate from classic clear cell morphology. These rarities often present with overlapping features, such as eosinophilic cytoplasm or spindle cell architecture, creating diagnostic dilemmas that require rigorous ancillary testing. [5,6]

Among the most challenging of these entities are Primary Renal Synovial Sarcoma (RSS) and Renal Cell Carcinoma with Sarcomatoid Differentiation (sRCC). While both can present with similar spindle-cell morphologies, their origins and biological behaviors are distinct. RSS is an exceptionally rare entity, comprising only 1% of all renal tumors. [7] It is traditionally a soft-tissue malignancy affecting the extremities of young adults; its occurrence as a primary visceral tumor in

the kidney is a deviation from its classic clinical presentation, Because RSS lacks specific clinical or radiological features—often appearing merely as large masses or complex cysts—it poses a significant risk of misdiagnosis. [7]

Conversely, sRCC represents a phenomenon of tumor progression rather than a distinct morphogenetic subtype. It arises via epithelial-mesenchymal transition (EMT), where a conventional carcinoma acquires high-grade, sarcoma-like features. [8,9] This dedifferentiation is a critical prognostic indicator; occurring in approximately 4–5% of RCCs, it is associated with a dismal median survival of only 6–13 months, The World Health Organization (2016) guidelines emphasize that the presence of any amount of sarcomatoid dedifferentiation is sufficient to classify a tumor as sRCC, highlighting the necessity for meticulous sampling and reporting.[8,9]

This paper explores two such entities: Primary Renal Synovial Sarcoma (RSS), an exceptionally rare tumor constituting only 1% of renal malignancies, and Renal Cell Carcinoma with Sarcomatoid Differentiation (sRCC), a highly aggressive phenotype resulting from epithelial-mesenchymal transition (EMT). Differentiating these entities is a significant diagnostic challenge; both present with spindle cell morphology yet require vastly different management strategies.

## Material and Methods

**Study Setting and Design:** This study presents a case series of rare renal tumors diagnosed in the Department of Pathology at SMS Medical College and Hospitals in Jaipur, Rajasthan.

**Clinical and Radiological Evaluation:** Patient data regarding age, chief complaints (e.g., flank or abdominal pain, weight loss), past medical history, and family history were obtained from clinical records

Radiological evaluation was performed using Contrast-Enhanced Computed Tomography (CECT) of the abdomen to assess tumor size, location (e.g., lower or upper pole), and characteristics such as contrast enhancement and heterogeneity,

**Pathological Examination:** Surgical specimens, including those from partial nephrectomy, underwent gross examination to assess the tumor's appearance, including color (e.g., grey-white to grey-yellow), consistency, and involvement of the renal cortex and medulla

Tissue samples were processed for routine histopathological examination using Hematoxylin and Eosin (H&E) staining.

**Immunohistochemistry (IHC):** To confirm the diagnosis and rule out differentials, immunohistochemistry was applied to the tissue sections

**For the suspected synovial sarcoma**, the panel included p63, CD10, cytokeratin, CD99, desmin, CD34, and TLE to differentiate the tumor from urothelial malignancy, Wilms tumor, and myogenic or hematopoietic neoplasms

**For the suspected RCC with sarcomatoid differentiation**, markers such as PAX8 and vimentin were utilized to establish renal histogenesis and mesenchymal differentiation

Diagnoses were finalized based on the correlation of histopathological findings with immunohistoche mical profiles

**Case 1:** A 24-year-old female presented with right flank pain persisting for four to five months, with no history of fever or haematuria. The pain was not associated with alerted bowel/bladder habit. There were no aggravating factors. the pain relieved on taking analgesics. The past and family history was not significant. CECT revealed a large cyst (98x86 mm) in the lower pole of the right kidney lacking contrast enhancement, initially suggestive of a benign cortical cyst. [Figure 1] A partial nephrectomy was performed. Microscopic examination showed sheets of large tumor cells with mild-to-moderate eosinophilic cytoplasm, pleomorphism, and hyperchromatic nuclei. [Figure 2] As the morphology was non-specific, IHC was pivotal. The tumor cells were negative for p63, CD10, Cytokeratin, CD99, Desmin, and CD34, effectively ruling out urothelial carcinoma, RCC, Wilms tumor, and myogenic origins. However, the cells showed strong nuclear immunoreactivity for TLE, a specific marker for synovial sarcoma, leading to a final diagnosis of primary renal synovial sarcoma.[Figure 3]

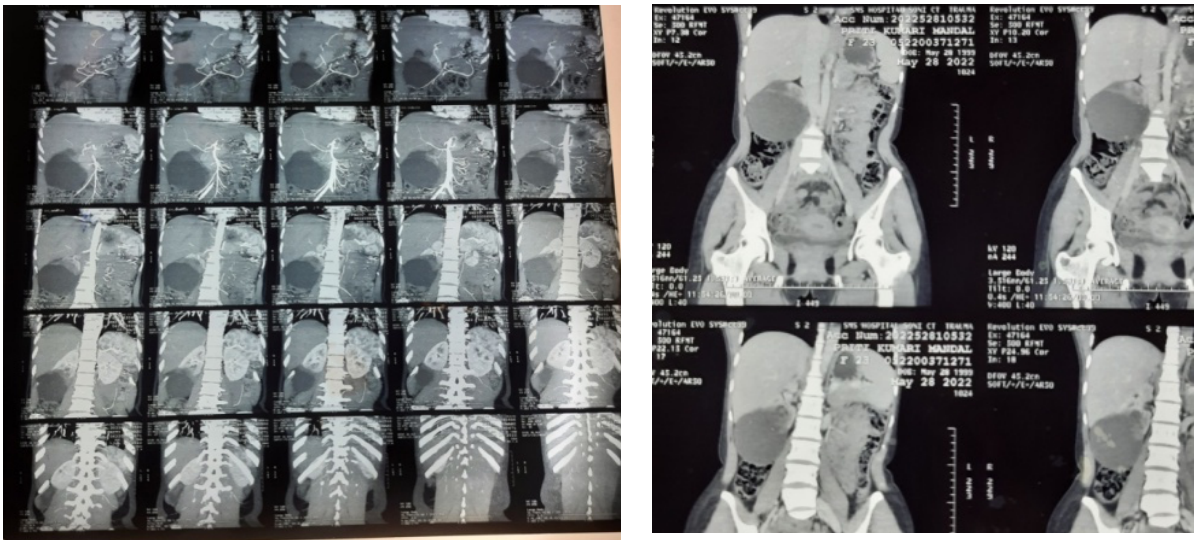
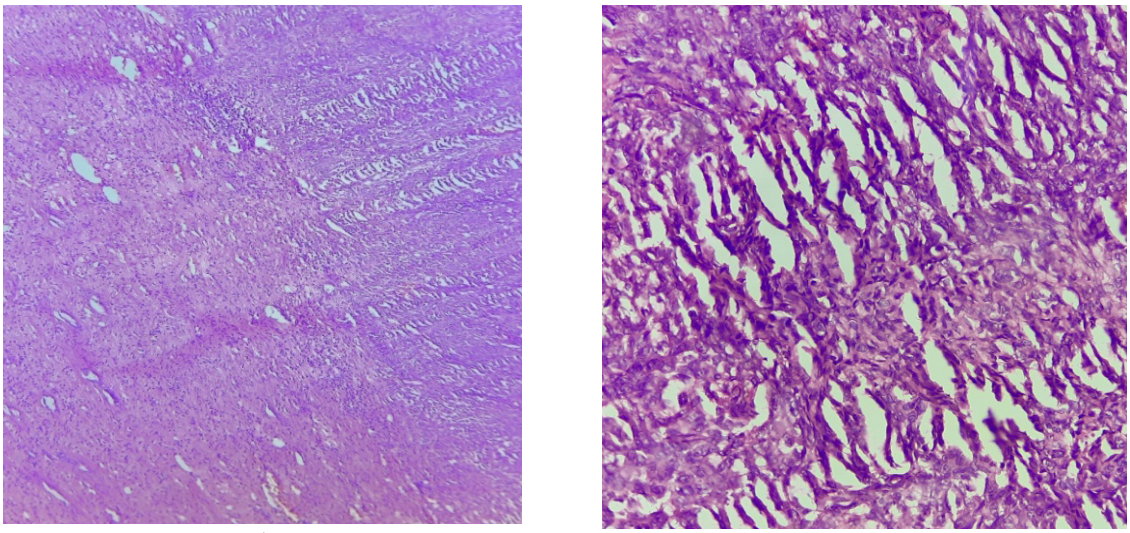
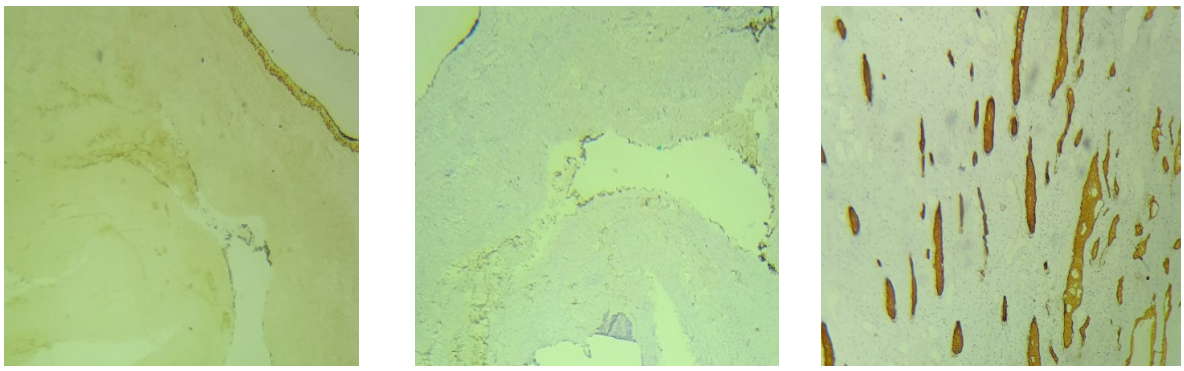


**Figure 1 (A & B): On CT scan – Approx 98x86 mm size cyst in lower pole of right kidney showing no contrast enhancement, suggestive of right renal cortical cyst.**

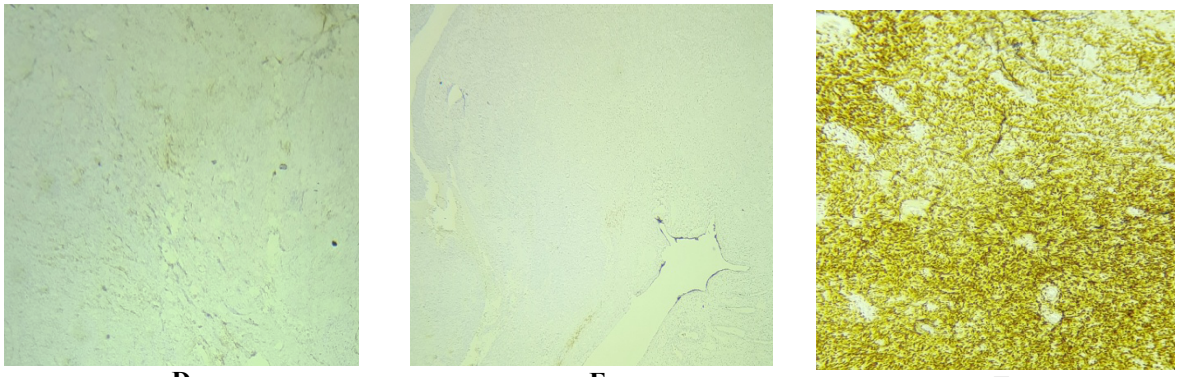


**A** **B**

**Figure 2 (A & B): In low power view tumour cells arranged in sheets (H&E,10X) [A]. On higher magnification, Tumour cells are large having mild to moderate eosinophilic cytoplasm and pleomorphic and hyperchromatic nuclei. (H&E,40X) [B], these tumour cells are not exhibiting any specific morphology.**



**A** **B** **C**



D E F

**Figure 3:**
**A & B: Tumor cells showing negative immunoreactivity for p63 (A) (10x) and CD10 (B) (10x).**
**C: Tumor cells are negative for cytokeratin with positive control (10X)**
**D: Negative immunoreactivity with CD99 (10X)**
**E: Tumor cells are negative for desmin (10X)**
**F: Tumor cells are immunoreactive for TLE (10X)**

**Case 2:** A 65-year-old female presented with right lumbar pain, anorexia, and weight loss over three months. Past history and family history was insignificant. CT imaging revealed a heterogeneous soft tissue mass (68x72x64 mm) at the upper pole of the right kidney with associated lymphadenopathy. Gross examination showed a grey white to yellow growth involving the renal cortex and medulla. [Figure 4] Microscopy revealed a biphasic pattern: areas of classic clear cell carcinoma juxtaposed with high-grade sarcomatoid areas characterized by spindle-shaped nuclei, anisokaryosis, and prominent nucleoli.[Figure 5,6] IHC confirmed the diagnosis; the tumor cells were positive for Vimentin and the renal transcription factor PAX8, confirming the tumor was of renal epithelial origin despite the sarcomatoid appearance.[Figure 7,8]

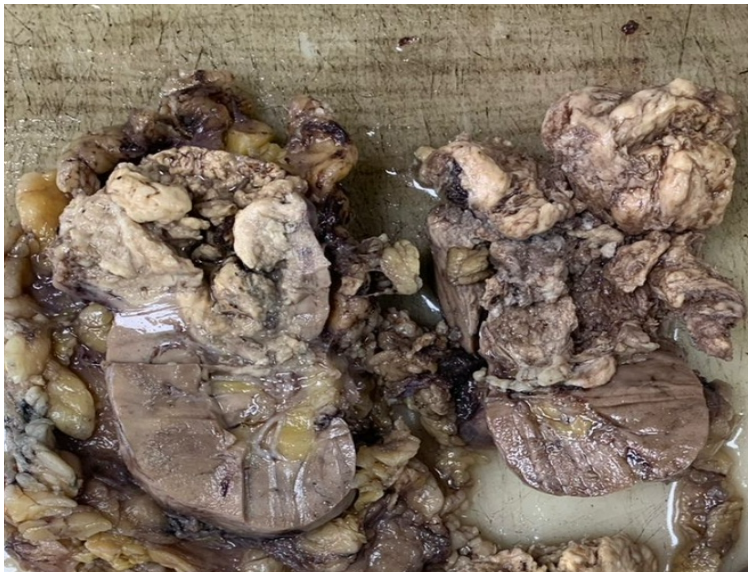


**Figure 4: Gross image shows a grey white to grey, yellow growth at the upper and middle pole of kidney involving cortex and medulla.**

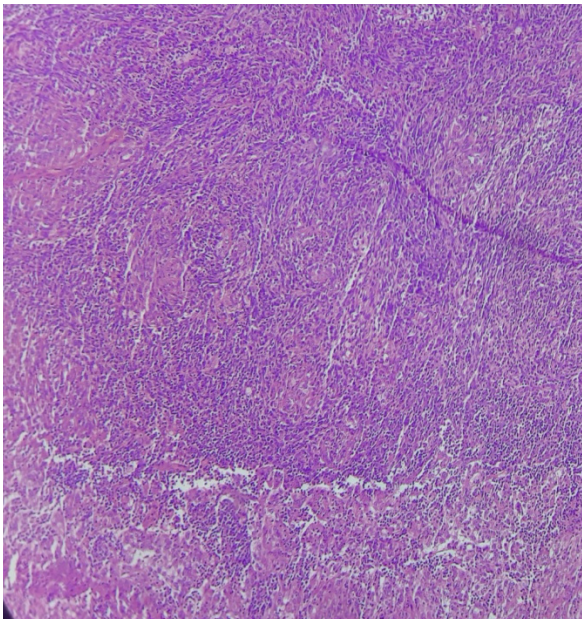


**Figure 5: microscopic image showing clear cell carcinoma (at lower side) with sarcomatoid feature. H&E Stain, 10x**

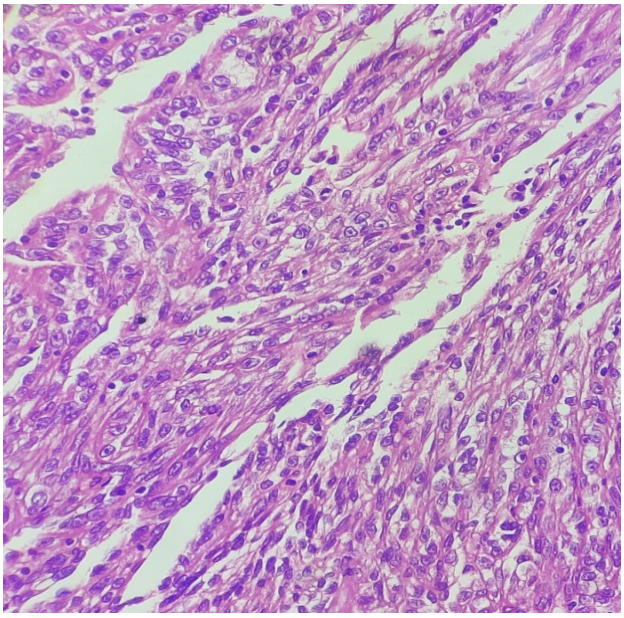


**Figure 6: high power view shows tumor cells with spindle shaped nuclei, anisocaryosis, open chromatin and prominent nucleoli. H & E Stain, 40x.**

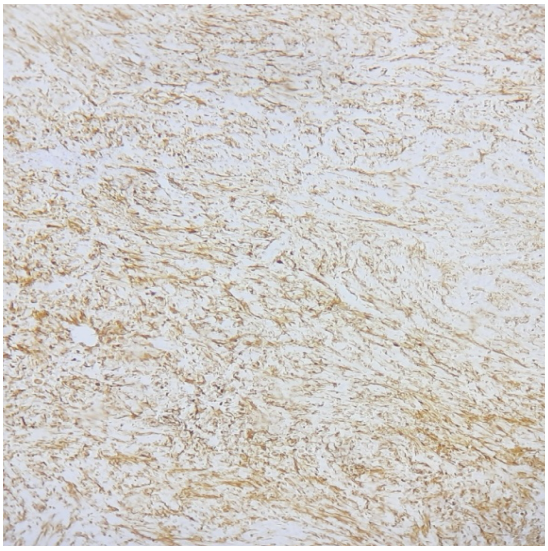


**Figure 7: Tumor Cells Showing Immunoreactivity For Pax 8 (10x)**

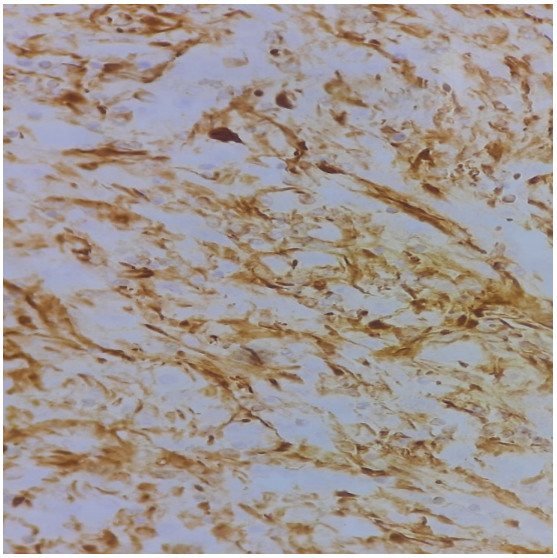


**Figure 8: Tumor Cells Are Positive For Vimentine. (40x)**

## Discussion

Primary Renal Synovial Sarcoma is a diagnostic "surprise" because it typically affects the extremities of young adults; its occurrence in the kidney is rare. It usually presents as a large, circumscribed mass, often associated with cysts, as seen in Case 1. Cysts are lined by mitotically inactive polygonal eosinophilic cells with apically oriented nuclei (hobnailed epithelium). The main challenge is distinguishing the monophasic spindle cell variant from other sarcomas. These tumors harbour characteristic translocation t(X; 18) (p11; q11) described for synovial sarcoma resulting in fusion proteins like SYT-SSX1, SYT-SSX2 and SYT-SSX4. [i] While molecular testing for the t(X;18) translocation is definitive, TLE positivity on IHC is a highly sensitive surrogate for diagnosis.[10] Sarcomatoid variant of RCC is not a distinct subtype but a manifestation of tumor progression via Epithelial-Mesenchymal Transition (EMT). According to the 2016 WHO guidelines, finding any amount of sarcomatoid dedifferentiation qualifies for this diagnosis. This distinction is vital because sRCC carries a significantly worse prognosis than classic RCC, necessitating its inclusion in surgical pathology reports.

Sarcomatoid dedifferentiation is often heterogeneously present within RCCs, making routine imaging and biopsy unreliable for

preoperative detection. Surgical resection for localized disease is the standard of care, with subsequent close monitoring of patients following surgery. [11] The microscopic features of sRCCs often include a mixture of both epithelial and sarcomatoid components. Unlike classic RCCs, the sarcomatoid component does not have recognizable epithelial components and histologically appears similar to sarcomas with pleomorphic and spindle cells with high cellularity and atypia.

In the absence of a low- grade epithelial component IHC markers are useful, as a tumour with spindled morphology having differential diagnosis of sarcomatoid urothelial carcinoma, angiomyolipoma, dedifferentiated liposarcoma, sarcomatoid adrenocortical carcinoma, and mesenchymal neoplasms such as solitary fibrous tumour and synovial sarcoma, and others.

**Approach to Rare Cases in Renal Histopathology:** The primary diagnostic hurdle in these cases is the "spindle cell" morphology. The approach requires a systematic exclusion of mimics:

1. **Morphological Evaluation:** Identifying biphasic patterns (epithelial plus spindle cells) suggests sRCC, whereas a monophasic spindle cell pattern (as in Case 1) mimics various soft tissue sarcomas like fibrosarcoma or malignant peripheral nerve sheath tumors.
2. **Lineage Tracing via IHC:** The application of PAX2 or PAX8 is critical. These transcription factors are required for kidney formation and establish renal epithelial lineage in dedifferentiated tumors like sRCC.
3. **Specific Sarcoma Markers:** When renal markers are negative, markers like TLE becomes essential to identify Synovial Sarcoma, which involves the t(X;18) translocation and SYT-SSX fusion proteins.

## Conclusion

"Rare but real" renal tumors necessitate a high index of suspicion. The distinction between a primary sarcoma (like Synovial Sarcoma) and a dedifferentiated carcinoma (sRCC) is often impossible on H&E staining alone due to overlapping spindle cell features. This study highlights that accurate diagnosis relies heavily on ancillary testing—specifically the use of markers like TLE, CD10, and PAX8. Precise histopathological characterization is the cornerstone for determining prognosis and selecting appropriate adjuvant therapies, such as immunotherapy for sRCC or chemoradiation for sarcoma.

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