Primary Renal Sarcomas WithBCOR-CCNB3Gene Fusion

A Report of 2 Cases Showing Histologic Overlap With Clear Cell Sarcoma of Kidney, Suggesting Further Link Between BCOR-related Sarcomas of the Kidney and Soft Tissues

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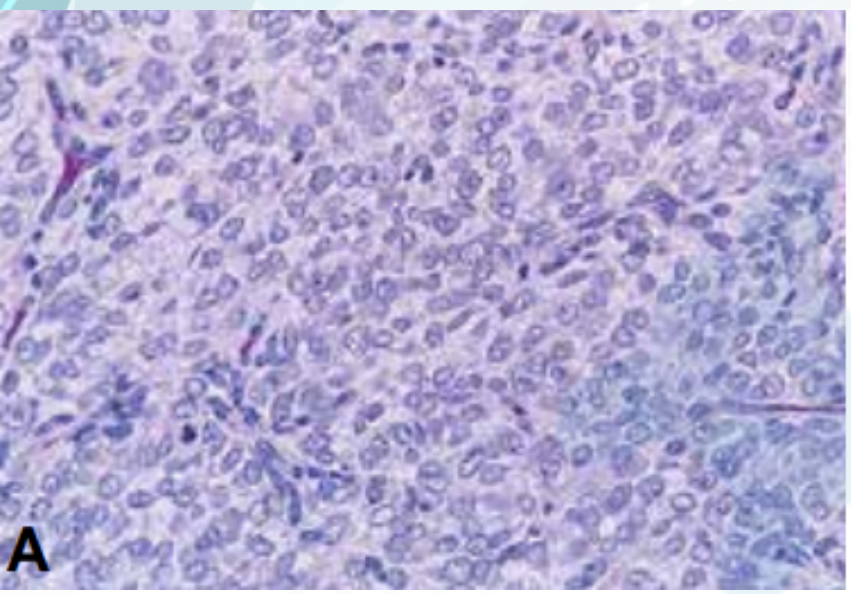
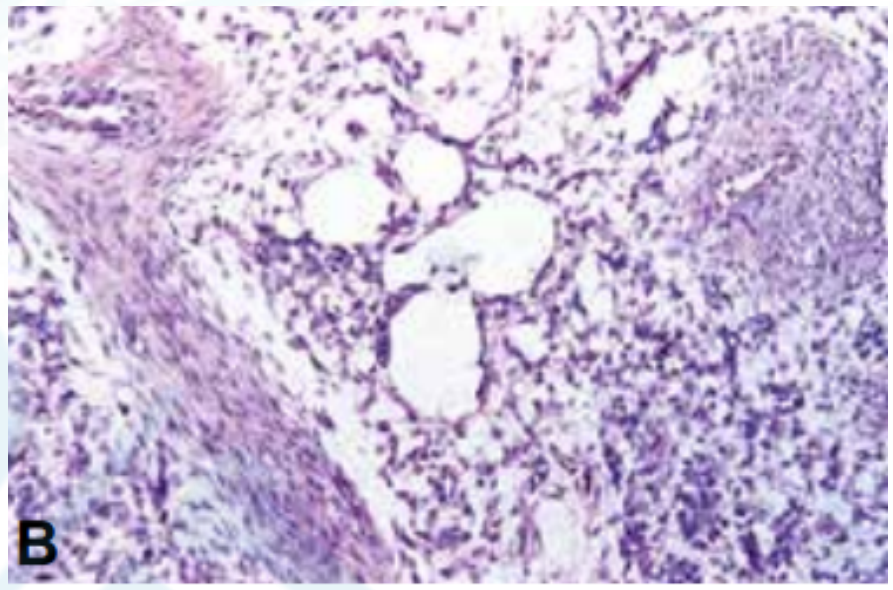
2018-01-17

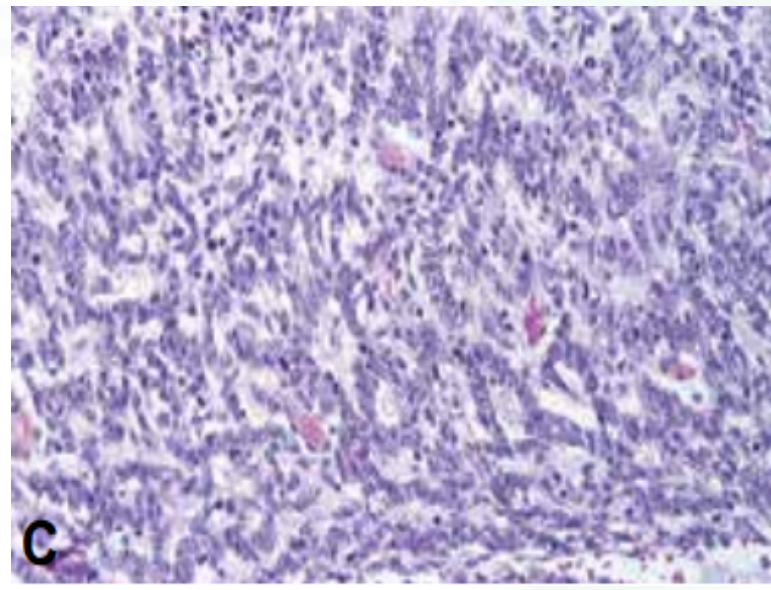
CCSK-肾透明细胞肉瘤

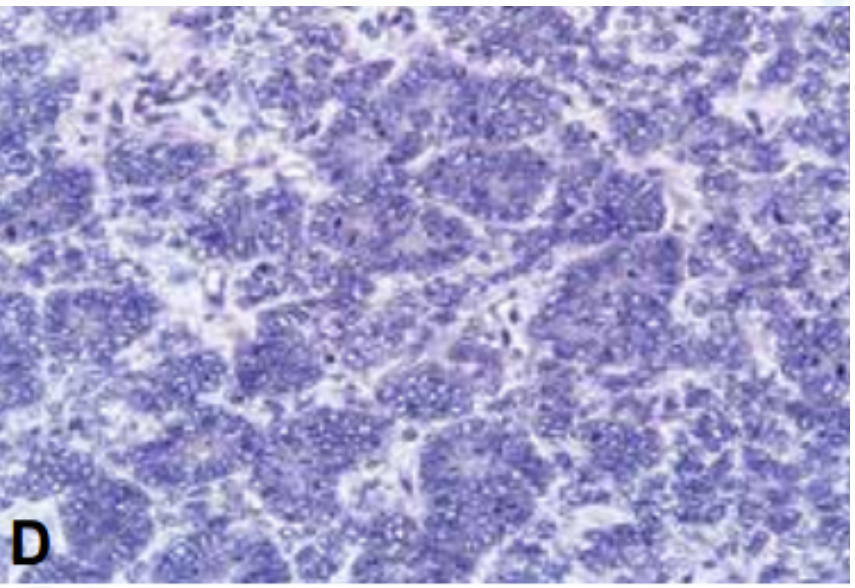
- 大约占儿童恶性肾肿瘤的3%。
- 男女比例 2:1 平均年龄3岁。
- 经典模式：瘤组织被分枝状纤维血管间质分隔成细胞巢或细胞索，瘤细胞呈上皮样或短梭形，被细胞外粘液样基质分隔，类似于透明细胞胞质，核圆形、卵圆形，染色质细腻，核仁不明显。
- 形态多样：黏液型，梭形细胞型，栅栏状型，上皮样型，硬化型，富于细胞型，囊肿型，血管周细胞瘤或血管扩张型。
- 免疫组化：cyclin D1 ，SATB2(+),

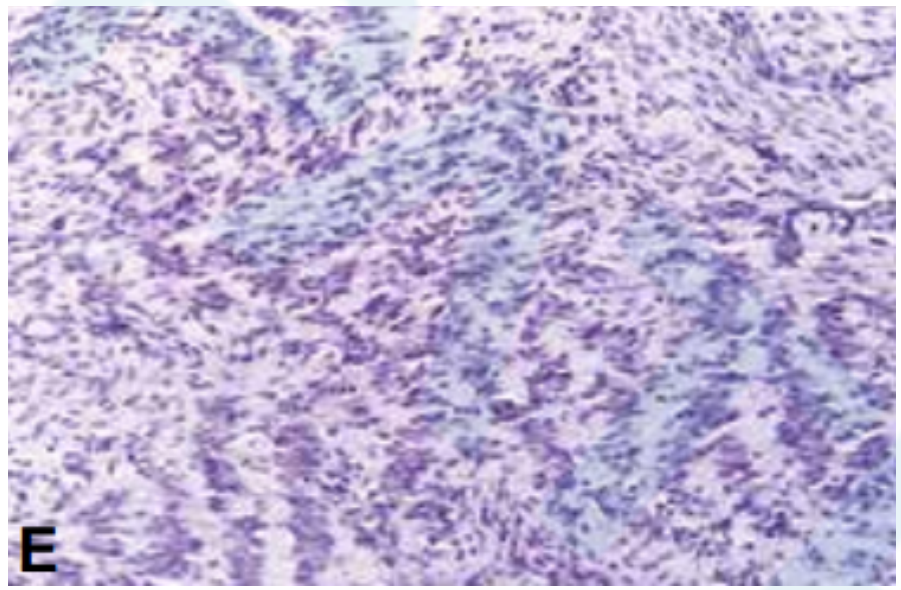
  CD34, S100, desmin, CD99, and cytokeratin (-).











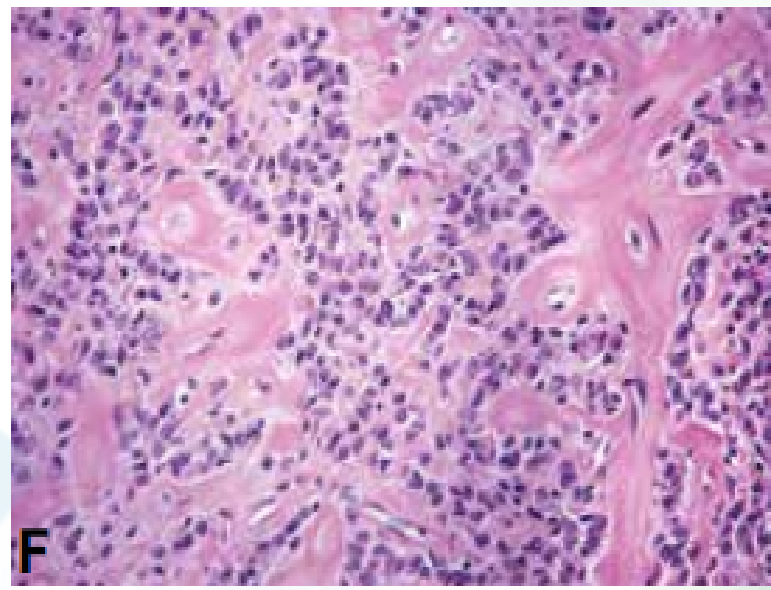


Fig. 1.60 Clear cell sarcoma of the kidney. **A** Classic pattern, demonstrating branching capillary vasculature and open chromatin of the epithelioid cord cells. **B** Myxoid pools and cellular septa. **C** Epithelioid trabecular pattern. **D** Acinar pattern resembling nephroblastoma. **E** Palisading pattern resembling schwannoma. **F** Sclerosing pattern resembling osteoid.

CCSK基因遗传学

- CCSK长期以来一直被认为是一种肾特异性肿瘤，很少在肾外报道。
- >90% of CCSK BCOR -harbor internal tandem duplications (ITD)。
- 一小部分YWHAE-NUTM2B/E 基因融合。
- CCSK中这2种基因的改变是相互排斥的，约<10%其他类型的CCSK缺乏其中一种基因的改变。

背景

- In the past 5 years, upregulation of BCOR by similar mechanisms as found in CCSK has been identified as an underlying genetic alteration in several soft tissue sarcomas of young patients。
- First, BCOR ITD and the YWHAE-NUTM2B/Egene fusion have been identified in undifferentiated round cell sarcoma (URCS) and primitive myxoid mesenchymal tumor of infancy (PMMTI)。 PMMTI, <1 year, overlap significantly morphologically with CCSK。
- Second, a BCOR-CCNB3 gene fusion resulting from an X chromosomal paracentric inversion has been identified in previously unclassified soft tissue and bone sarcomas。

- While the majority of these BCOR-CCNB3 sarcomas were identified among EWSR1-negative Ewing sarcomas and thought to be primarily small round neoplasms, more recently cases with spindled morphology have been described.
- Importantly, high levels BCOR mRNA expression resulting in BCOR protein overexpression as detected by IHC.
- Distinctive BCOR-driven transcriptional profile have been identified in URCS/PMMTI, BCOR-CCNB3 fusion-positive sarcomas, and CCSK, suggesting that all of these neoplasms are highly genetically related.

- However, the existence of BCOR-CCNB3 sarcomas originating in the kidney as well as a relationship between bone/soft tissue sarcomas with the BCOR-CCNB3 fusion and CCSK has not previously been described.

目的

- Describe **2 primary renal sarcomas** (BCOR-CCNB 3 gene fusions)
- Review Control groups : **CCSK**

BCOR-associated Soft Tissue Sarcomas (*BCOR-CCNB3–positive bone/soft tissue sarcoma, BCOR-ITD positive URCS/PMMTI*)

Primary renal synovial sarcoma (*upregulation of BCOR identified in approximately 50% of soft tissue synovial sarcomas*)

方法

Case

- All of the cases in the review cohort in ourfiles were screened by IHC by BCOR, and positively labeling cases were analyzed for the presence of BCOR and CCNB3 fusion/inversion by FISH.

  2 renal sarcomas with BCOR-CCNB3 gene fusion, with overlapping features of CCSK and renal synovial sarcoma

Control Group

- **Review of BCOR-associated Soft Tissue Sarcomas**
- we reviewed a cohort of 20 URCS/PMMTI (all showing BCOR-ITD) and 3 other cases demonstrating the YWHAE-NUTM2B/E fusion from the files of one author (C.R.A.), All but one of these neoplasms had accompanying BCOR IHC.
- 24 cases of genetically confirmed BCOR-CCNB3 bone and soft tissue sarcomas from the files of one author (C.R.A.). 12 of these cases had accompanying BCOR IHC.

- **Primary Renal Synovial Sarcoma**
- We identified 7 genetically confirmed primary renal synovial sarcomas from ourfiles, all of which demonstrated SS18 rearrangements by FISH, 5 males and 2 females, 35 to 66 years。
- **CCSK Control Group**
- We identified 9 CCSK from the files of one author (P.A.). 6 males and 3 females, 6 to 42 months , 9 demonstrated BCOR(+), 5 cases studied genetically, 4 BCOR-ITD, 1 YWHAE-NUTM2B gene fusion.

IHC

BCOR, SATB2, TLE1, Bcl2, CD56, CD99, CD10, desmin, S100, CytokeratinAE1/3 and, cyclin D1 for BCOR-CCNB3 renal sarcoma and the control groups.

结果

- **Case Reports**

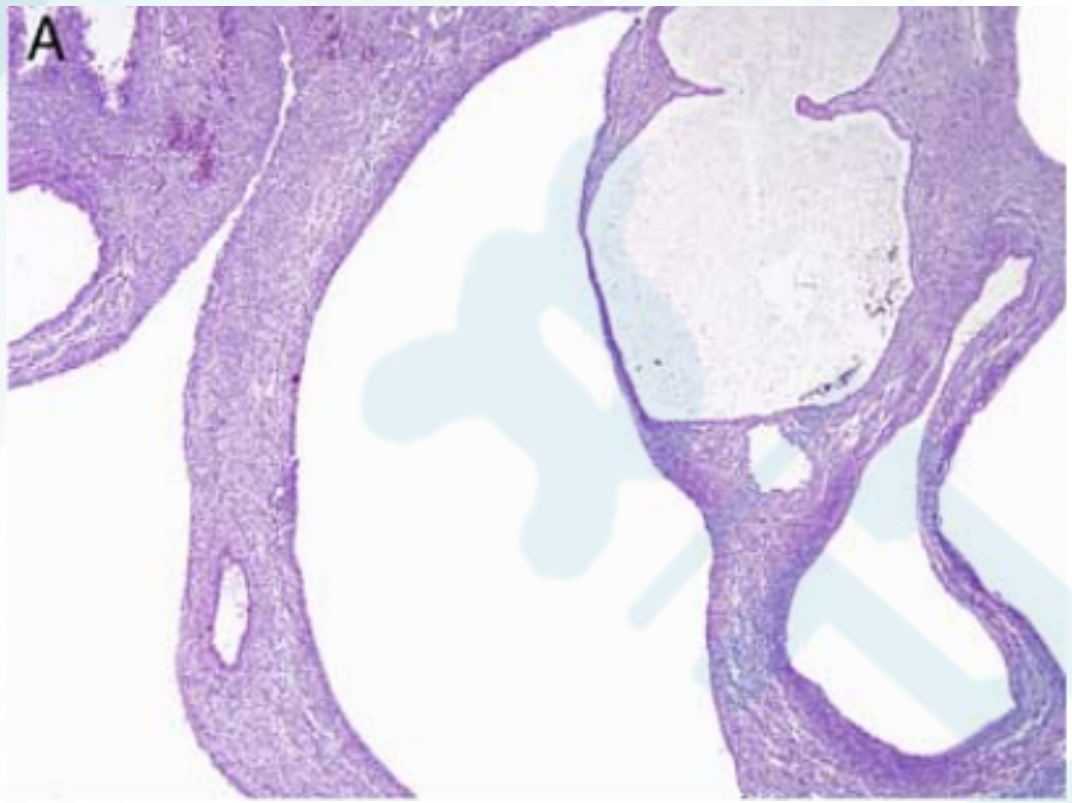
Case 1 was an 11-year-old male who presented with a 27cm cystic renal neoplasm which was treated by radical nephrectomy. The nephrectomy specimen weighed 1845 g and no further follow-up is available.

Case 2 was a 12-year-old male who presented with a 13 cm solid and cystic renal neoplasm which was treated by radical nephrectomy. 15 months later, the patient developed an abdominal mass which represented a recurrence of the prior neoplasm.

In both cases, the primary renal neoplasm was extensively cystic , dilated native renal tubules , lined by non-neoplastic, The cyst walls were variably cellular.

Case 1

- In many areas of case 1, the cyst walls were composed of nondescript, nonpleomorphic, bland spindle cells which condensed beneath the cyst epithelium, creating a “cambium-like”appearance.
- In other areas, these cells became more plump and epithelioid , and alternated with prominent perivascular spindle cells in a pattern reminiscent of the biphasic cord cell-septal pattern of CCSK.
- The more epithelioid cell nuclei were bland, and hadfine, open chromatin similar to that of CCSK.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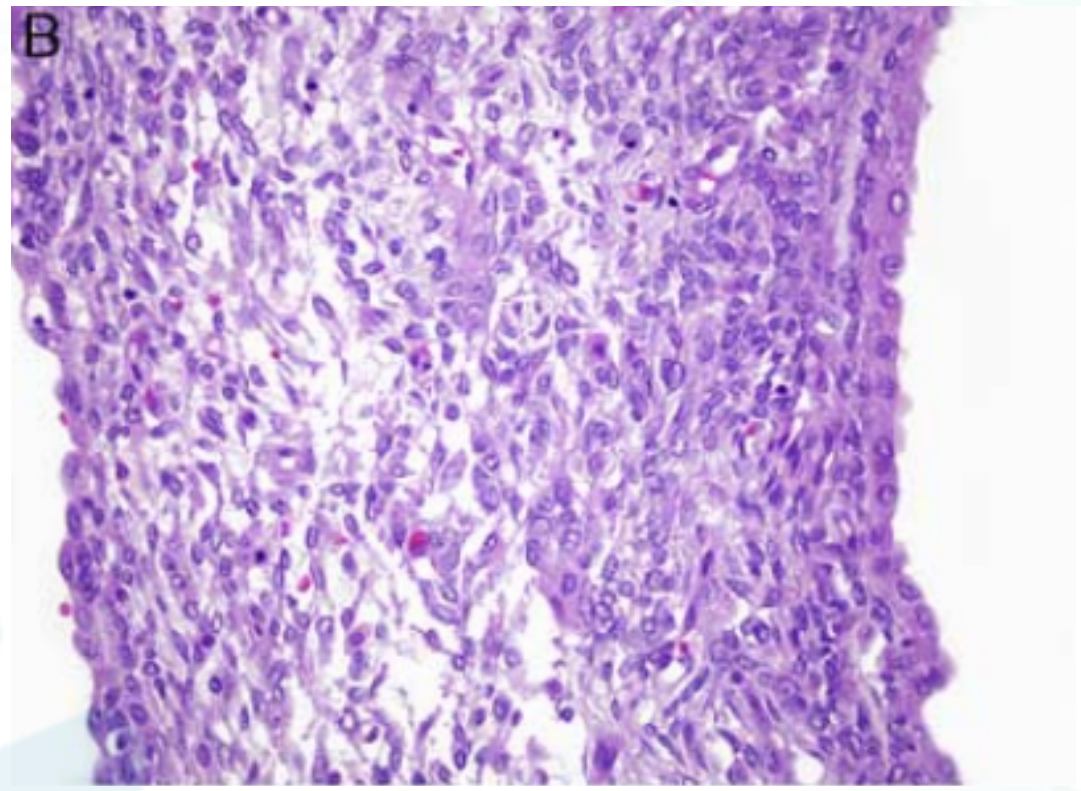
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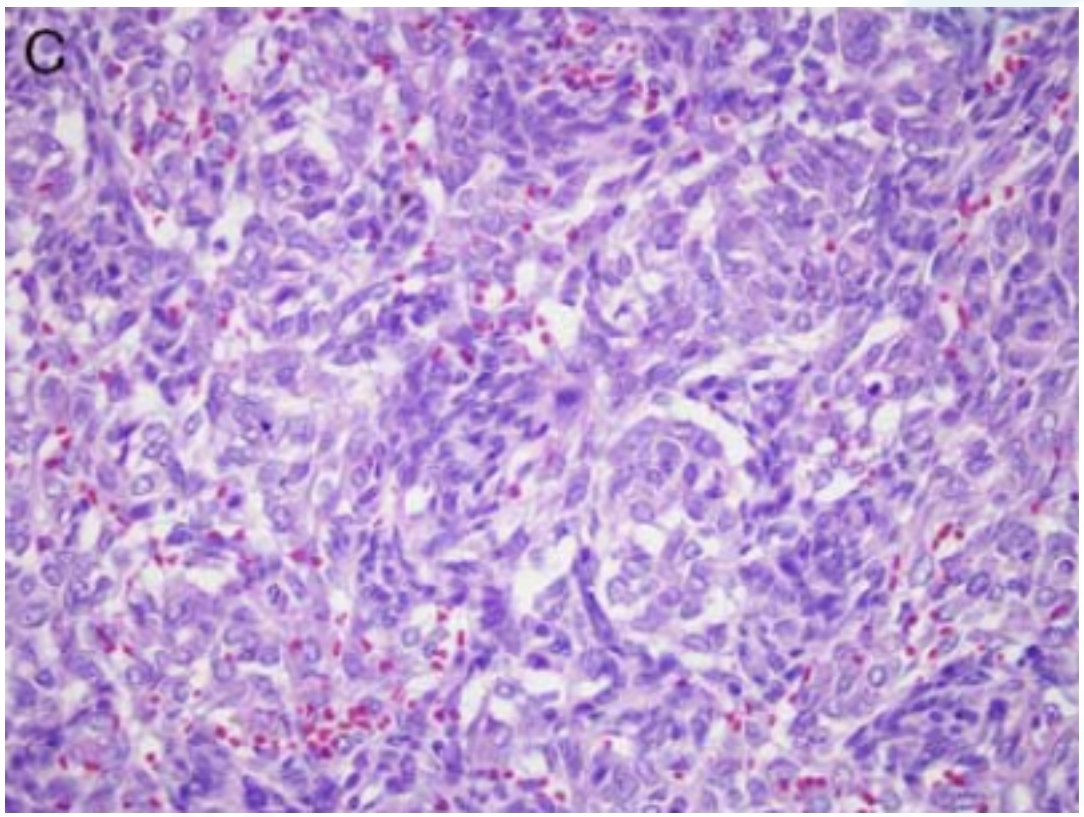
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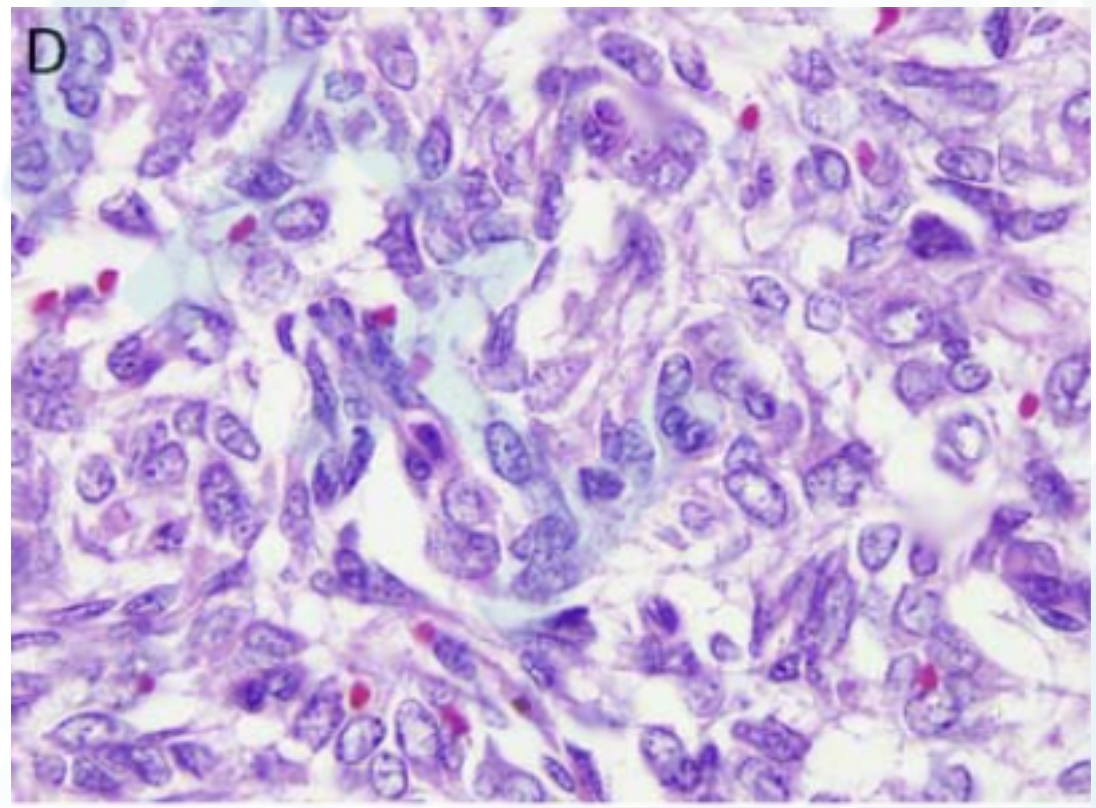
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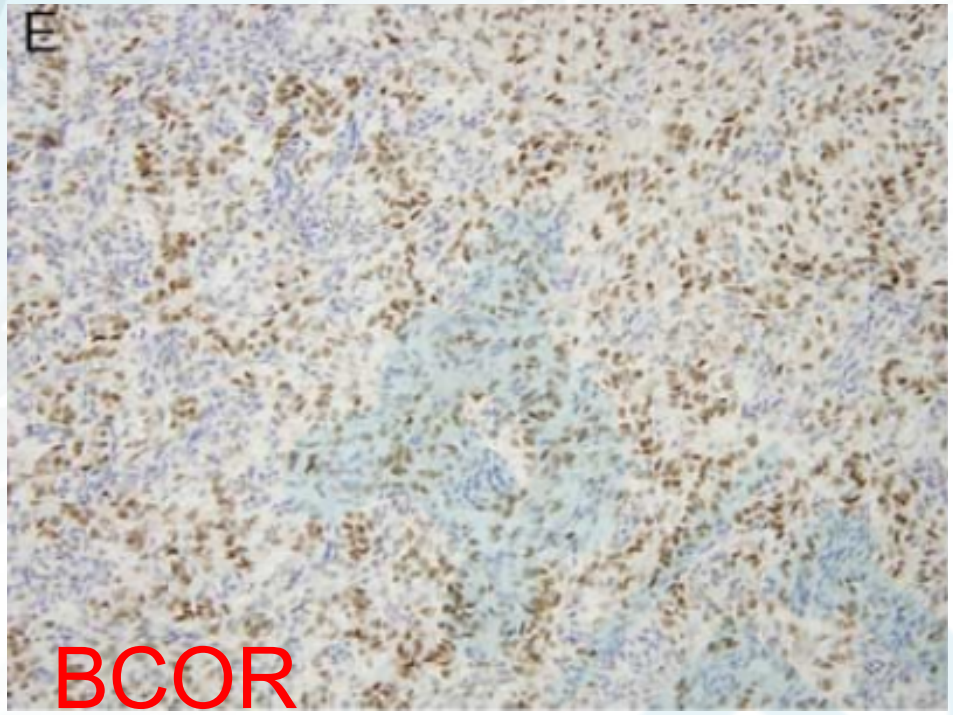
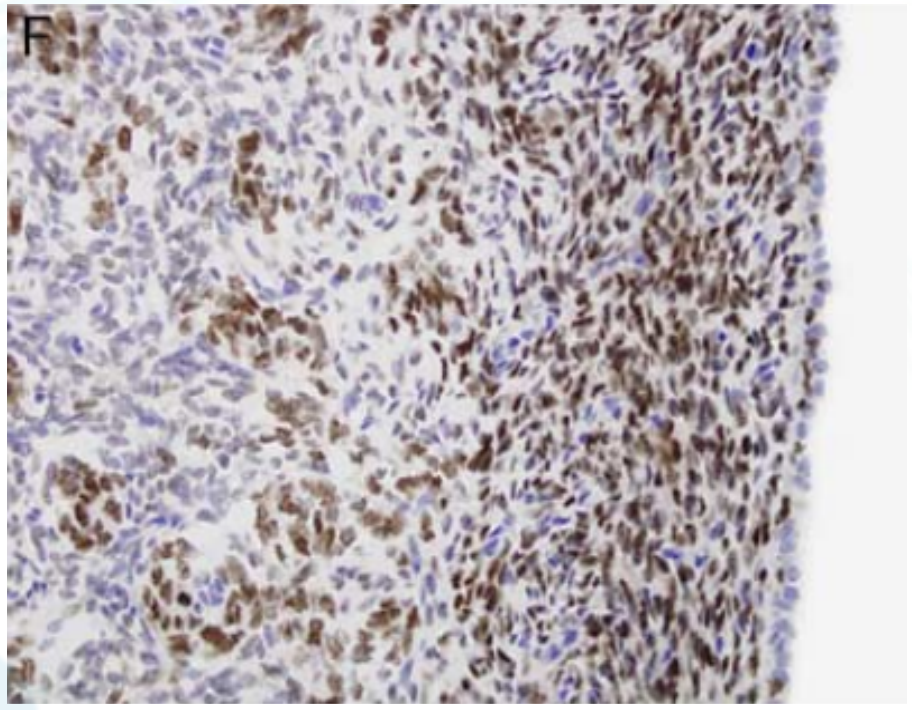
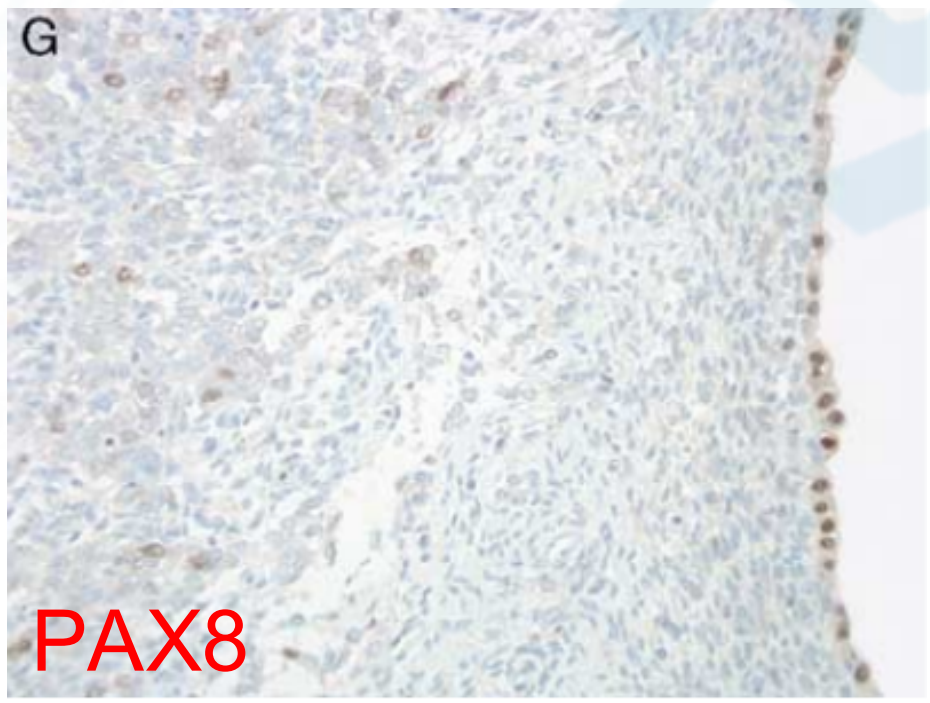






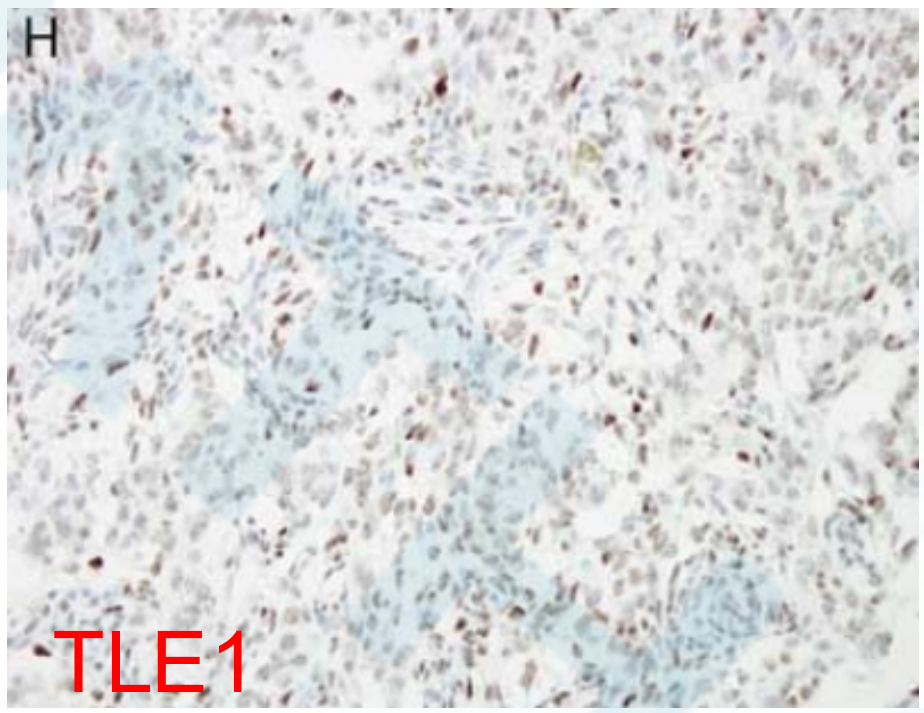
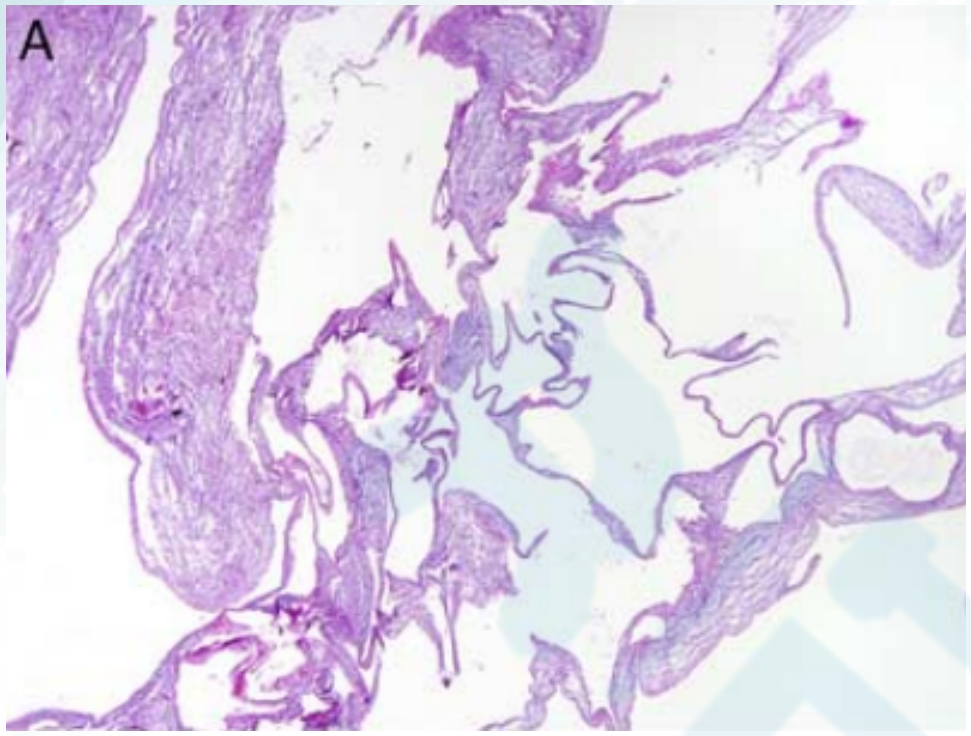


FIGURE 1. Case 1: this 27 cm renal neoplasm was extensively cystic (A). The cysts were lined by bland cuboidal epithelial cells with eosinophilic cytoplasm consistent with native renal tubules, while the stroma was moderately cellular, nonpleomorphic, and demonstrated subepithelial condensations resembling a cambium layer (B). In more cellular areas, one could appreciate a biphasic cord cell-septal cell appearance similar to that seen in CCSK (C). A regular branching capillary vasculature was more evident in these areas. The cord cells demonstrated finely dispersed, open chromatin, particularly relative to the more hyperchromatic septal cells (D). Immunohistochemistry for BCOR highlighted the cord cells (E), and highlighted the cambium layer but not the entrapped cyst lining (F). Focally, the cord cells demonstrated weak labeling for PAX8 relative to the intense staining of the cyst lining (G). The cord cells were immunoreactive for SATB2 (not shown) and TLE1 (H).

Case 2

- In case 2, the cystic primary renal neoplasm was extremely bland.
- The cyst walls were hypocellular and composed predominantly of uniform spindle cells with minimal cytoplasm, creating a resemblance to cystic nephroma or mixed epithelial stromal tumor.
- Focally, the cyst walls were slightly more cellular, and one could appreciate a biphasic cord cell/septal cell pattern that sugested CCSK.
- The abdominal recurrence of this neoplasm, in contrast, demonstrated solid fascicles of cellular, nonpleomorphic spindle cells with frequent mitoticfigures.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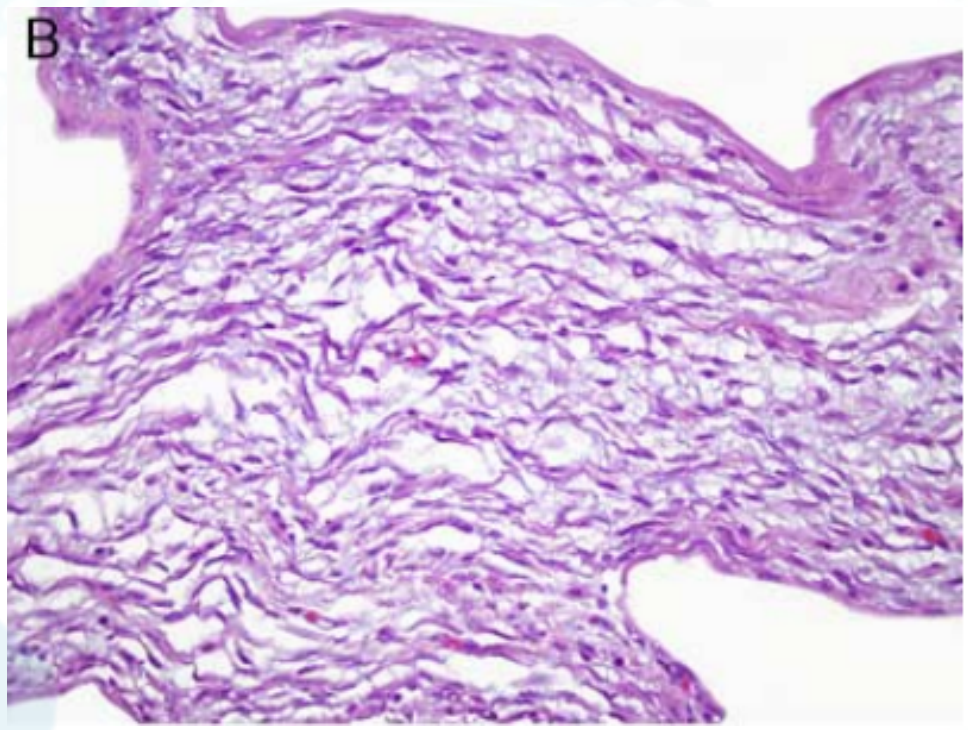
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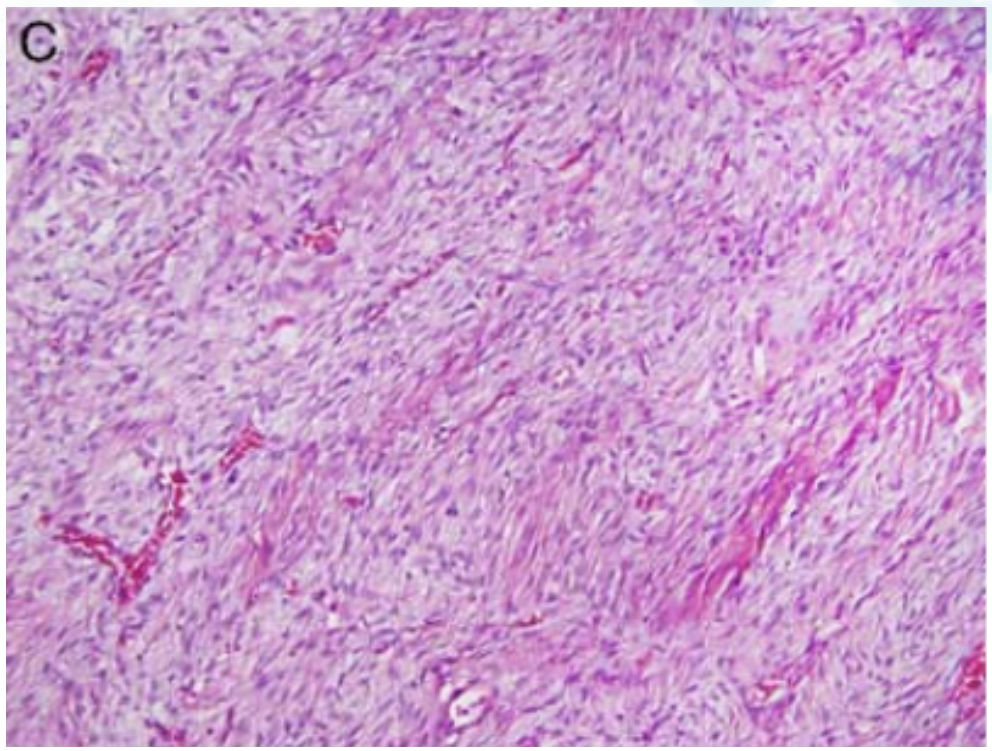
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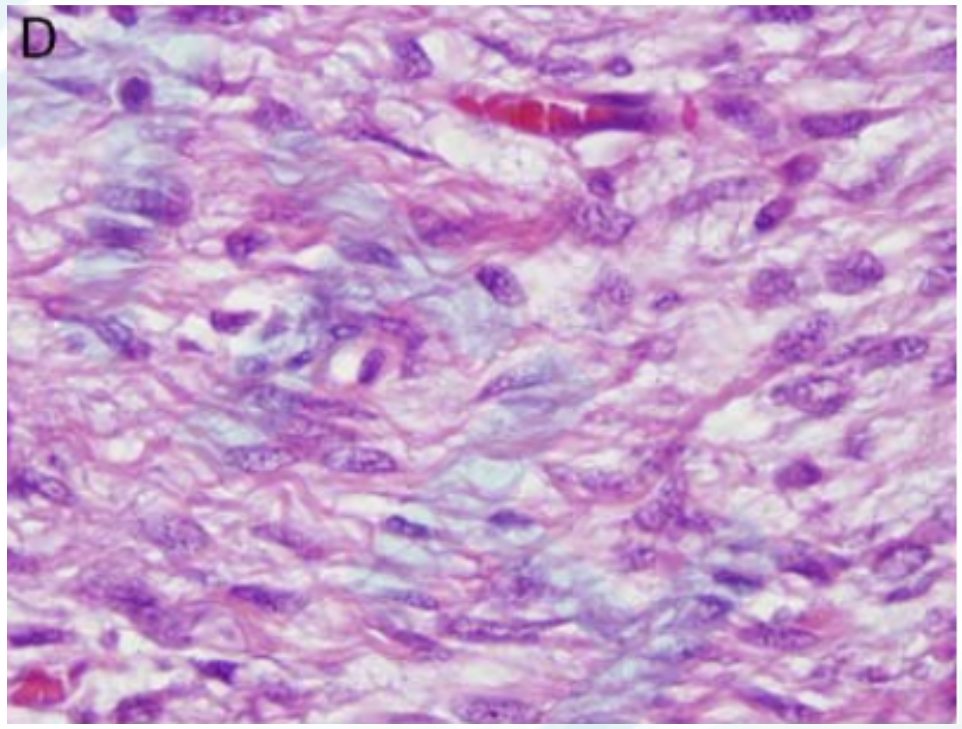
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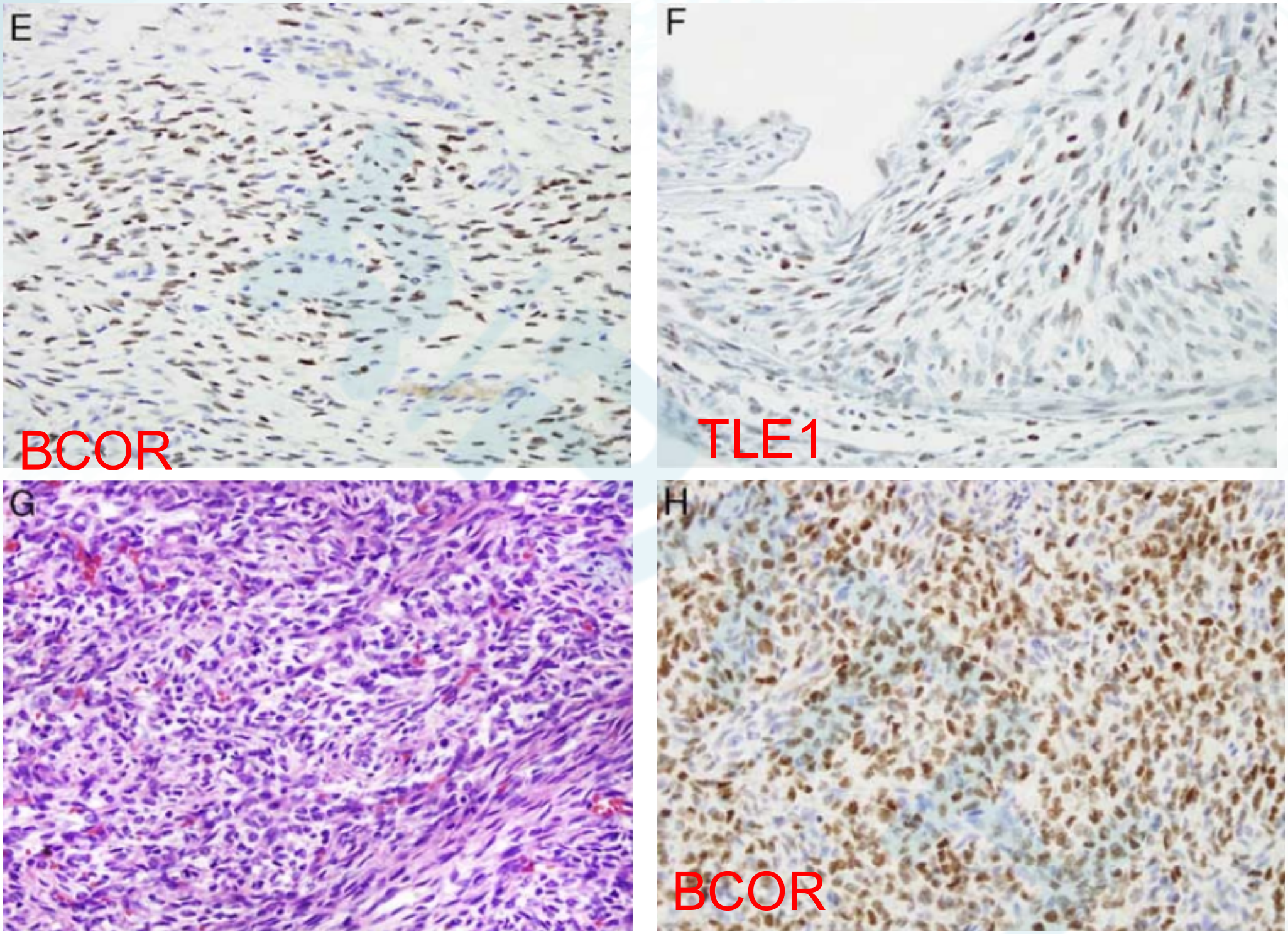
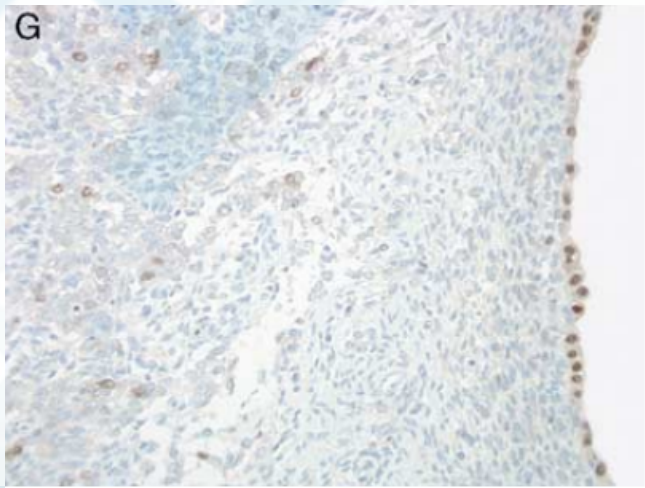


FIGURE 2. Case 2: the original 13 cm renal neoplasm was extensively cystic (A) and the septa were relatively hypocellular in most areas (B), raising the differential diagnosis of cystic nephroma. Focally, more cellular areas in the septa demonstrated the branching capillary vasculature that suggested CCSK (C) and the cord cells between septa demonstrated bland, finely dispersed chromatin (D). The cord cells demonstrated nuclear labeling for BCOR (E), SATB2 (not shown) and TLE1 (F). The abdominal recurrence 15 months later was a highly cellular nonpleomorphic spindle cell neoplasm which again had a suggestion of biphasic cord cell-septal cell appearance that is characteristic of CCSK (G). The cord cells demonstrated diffuse immunoreactivity for BCOR while the septal cells did not (H), highlighting this distinction.

IHC结果

- Both cases demonstrate similar immunohistochemical profiles
- BCOR (+)-----cord cells, BCOR (-)-----septal cells, similar to the pattern previously described in CCSK.
- Bcl2, CD56, SATB2, cyclin D1, and TLE1(+)
- Desmin, S100 , Cytokeratin AE1/3, and CD34(-)
- In both the primary and recurrent tumor in case 2,PAX8(-).
- In case 1,PAX8 focal weak nuclear staining of cord cells,but this was less intense than that of the entrapped native renal tubules that provided an internal control .



FISH

- FISH demonstrated an inversion-fusion pattern between BCOR and CCNB3 in both cases, including both the bland cystic primary renal neoplasm in case 2 and its high grade abdominal recurrence。

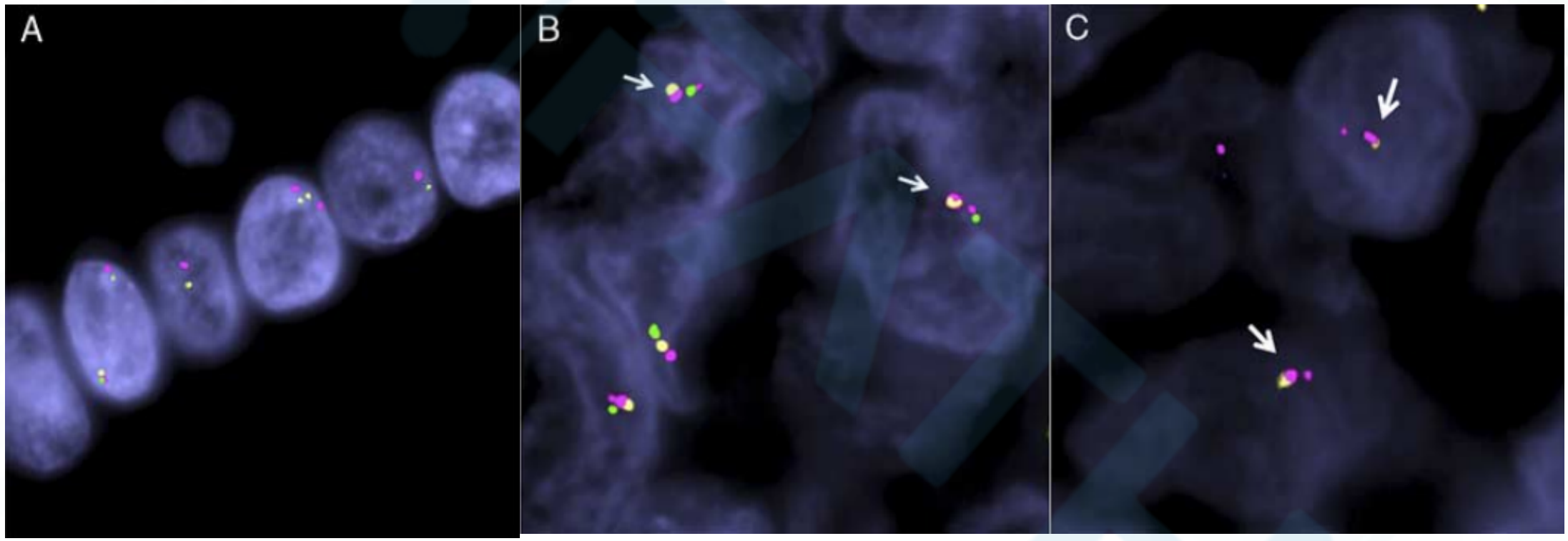


FIGURE 3. Demonstration of *BCOR-CCNB3* gene fusion by FISH. A, Normal cells analyzed with FISH probes. The green-orange probes represent *BCOR* and the red flanking probe represents *CCNB3*. Note the normal, small gap between the 2 genes, which corresponds to 9Mb. B, Case 1: the 2 neoplastic cells illustrated show a *BCOR-CCNB3* fusion/inversion. The *CCNB3* (red) shows a split signal into a larger fragment (centromeric *CCNB3*) and a smaller signal (telomeric *CCNB3*); while the *BCOR* shows a break of the green (telomeric) and orange (centromeric) signals. The end-result is a fusion between the centromeric *BCOR* signal (orange) to the centromeric *CCNB3* (larger red) (arrows), along with fusion of telomeric *BCOR* signal (green) to telomeric *CCNB3* signal (smaller red). C, Case 2: the 2 neoplastic cells illustrated show *CCNB3* inversion reflected by the red probe split into 2 signals (larger, centromeric and smaller, telomeric) and a *BCOR* unbalanced break, with deletion of telomeric end (no green signal). The resulting fusion is composed of centromeric 5′*BCOR* (orange) to centromeric 3′*CCNB3* (larger red) (red-yellow signals fused together, arrows).

Control Group

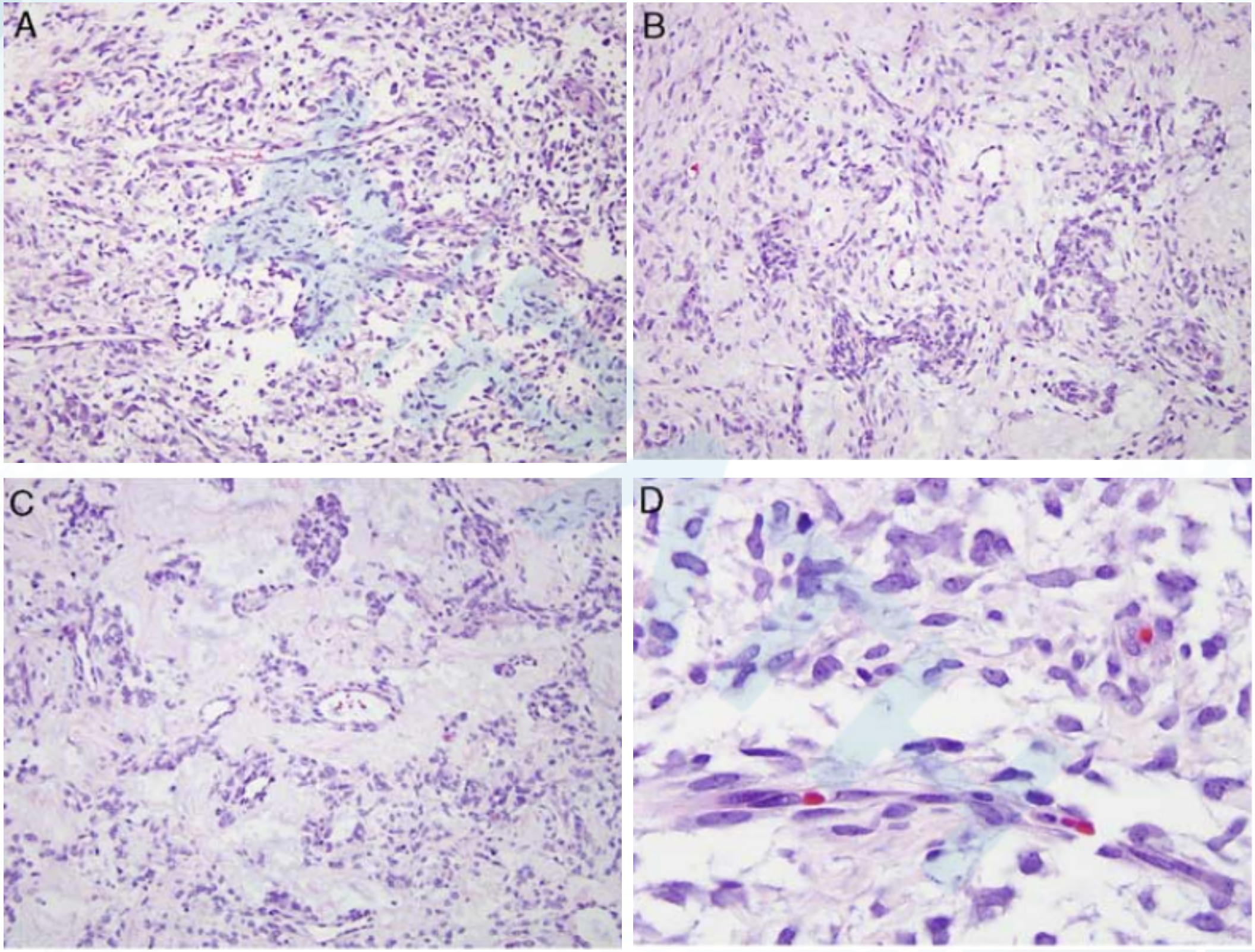
BCOR-related Soft Tissue Sarcomas

23 URCS/PMMTI featured bland round, epithelioid to spindled “cord cells”with open chromatin and prominent “septal cells” overl ap significantly with CCSK 。 21 of the 22 cases BCOR(+)-cord cells, BCOR(-) - septal cells, similar to the pattern noted in renal CCSK.

Also of note, 1 case was predominantly composed of a high grade spindle cell component more typical of the BCOR-CCNB3 sarcomas, while focal areas of spindling were noted in one third of cases.

- 24 BCOR-CCNB3 bone and soft tissue sarcomas demonstrated undifferentiated round to spindle cell features that resembled the cellular spindle pattern of CCSK, in which the“cord cells”ac quire a more spindled appearance that resembles monophasic spindle cell synovial sarcoma.
- 12 cases, BCOR(+)-cord cells, BCOR(-) - septal cells.
- Also of note, a subset focally low grade myxoid areas which overlapped with URCS/PMMTI and the myxoid, hypocellular pattern of CCSK.
- In one case PAX8 demonstrated weak labeling in cord cells similar to that seen in renal BCOR-CCNB3 case 1.

- Cycling D1(+)--- 6 of 7 BCOR-CCNB3 bone/soft tissue sarcomas and all 4 URCS/PMMTI.
- CD99 (+)---7of 9 BCOR-ITD URCS/PMMTI and 5 of 9 soft tissue BCOR-CCNB3 sarcomas, a diffuse cytoplasmic.
- TLE1 (+)---BCOR-CCNB3 bone/soft tissue sarcomas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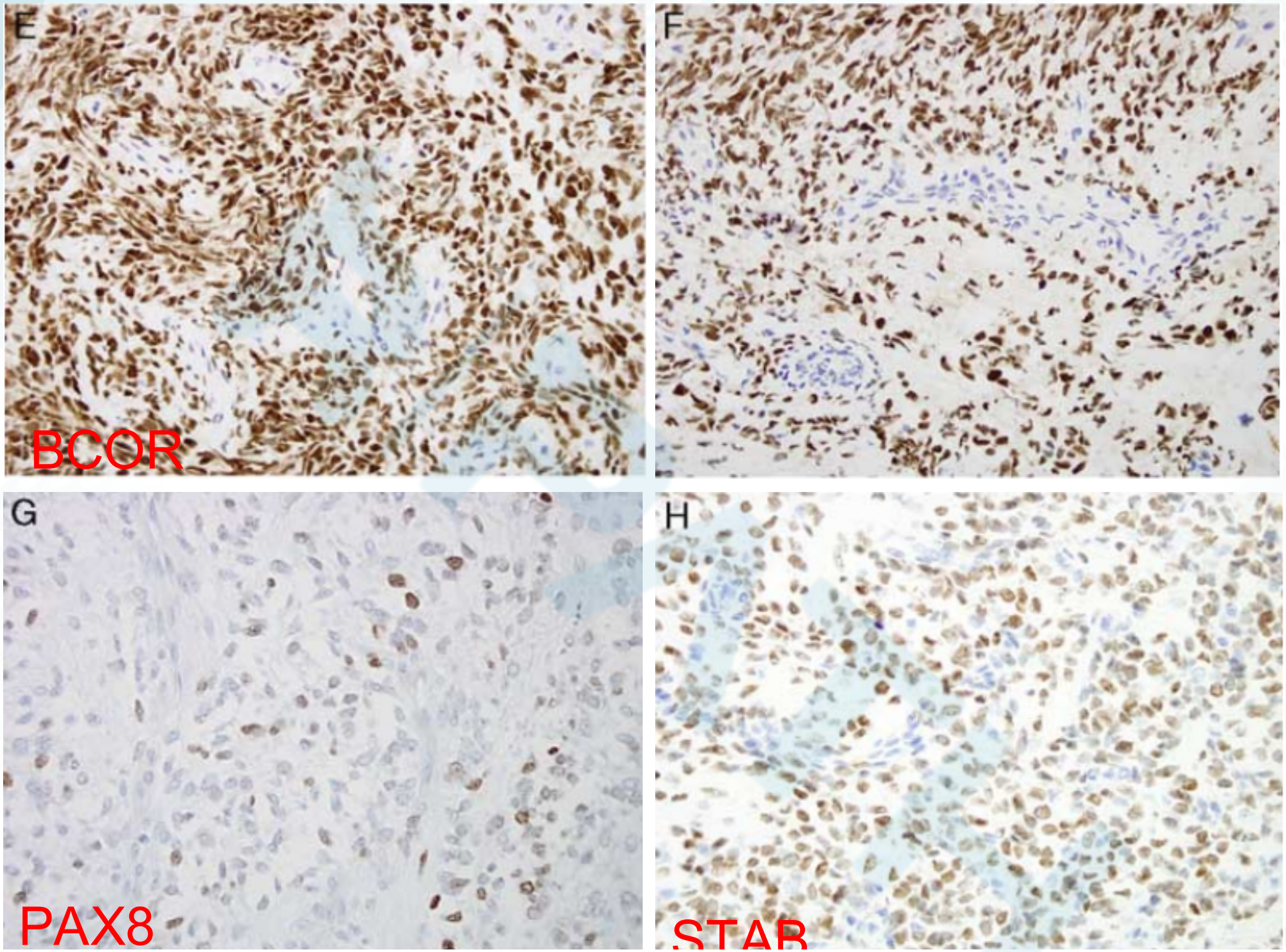

FIGURE 4. *BCOR-CCNB3* soft tissue sarcoma from comparison group. *BCOR-CCNB3* soft tissue sarcomas demonstrated morphologic features that overlap with CCSK, including a branching capillary vasculature pattern separating epithelioid to spindled cord cells that are set in a myxoid stroma (A). The cord cells appear to have clear cell cytoplasm, but in fact this represents extracellular matrix separating the cells (B). Stromal hyalinization mimics the sclerosing pattern of CCSK (C). The chromatin is fine and evenly dispersed similar to that of CCSK (D). Immunohistochemistry for BCOR highlights the neoplastic cord cells, with absence of labeling in the septal cells (E, F), similar to that seen in CCSK. The cord cells demonstrate weak staining for PAX8 (G) and strong staining for SATB2 (H).

- **CCSK**
- All 9 CCSK cases demonstrated typical morphologic features, specifically cord cells with fine chromatin and indistinct cytoplasm set in a myxoid stroma and separated by a regular branching capillary vasculature lined by septal cells.
- All 9 cases --- BCOR(+) in the cord cells, 3 of 7 cases ---SATB2(+), All 5--- cyclin D1(+). 4 of 5 cases ---TLE1(+), 1 of 5 tested CCSK---PAX8(+).

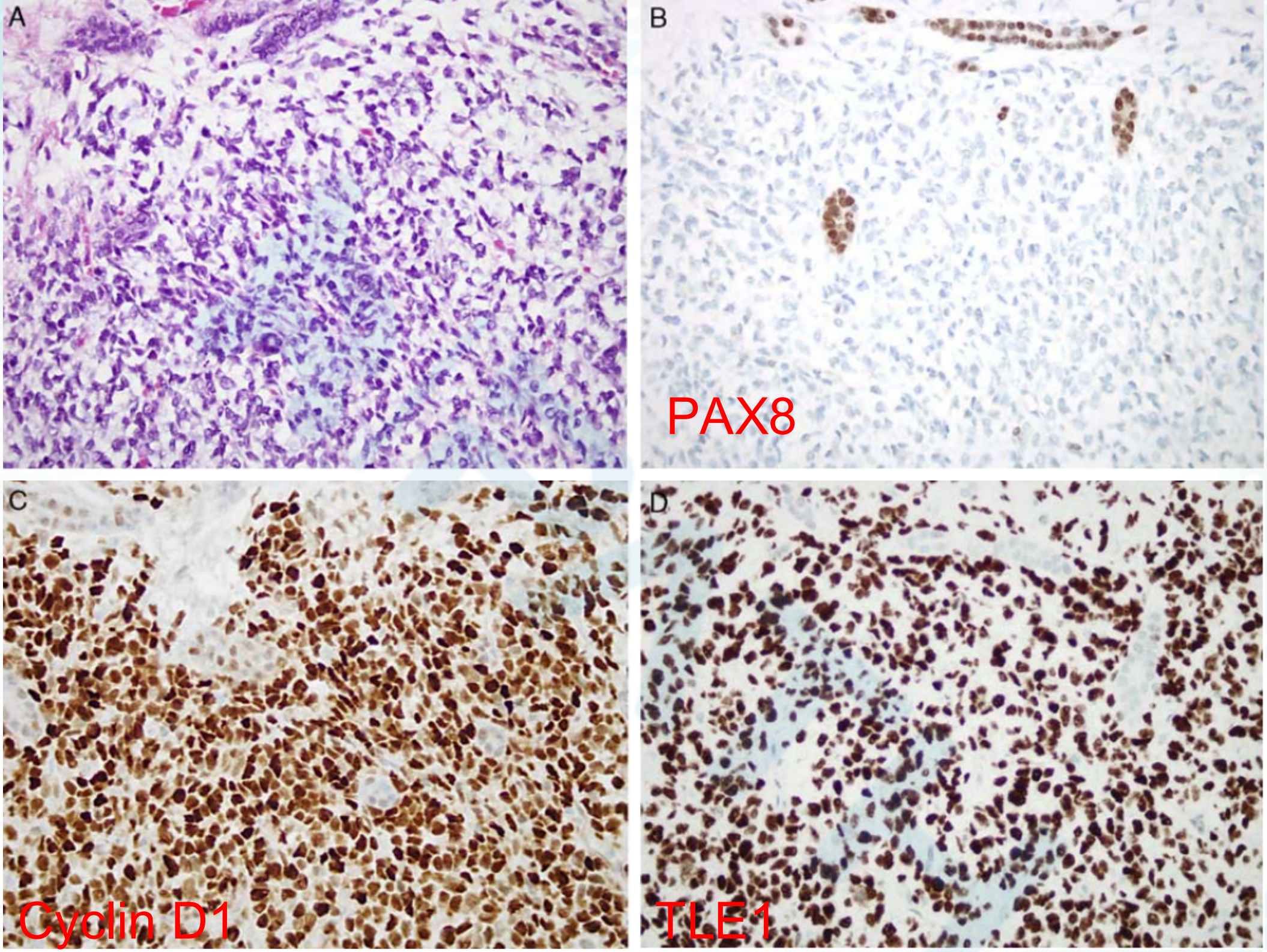

FIGURE 5. Immunoprofile of CCSK. A, This CCSK from the control group demonstrates myxoid extracellular material separating cord cells, and branching capillary vasculature. Note the entrapped renal tubules at the upper and middle portions of the image. B, Like most cases, this CCSK was negative for PAX8. Note the entrapped native renal tubules serving as an internal control. C, The CCSK shows strong diffuse nuclear labeling for cyclin D1, while there is minimal weak labeling of the entrapped renal tubules. D, The neoplasm demonstrates strong diffuse nuclear labeling for TLE1.

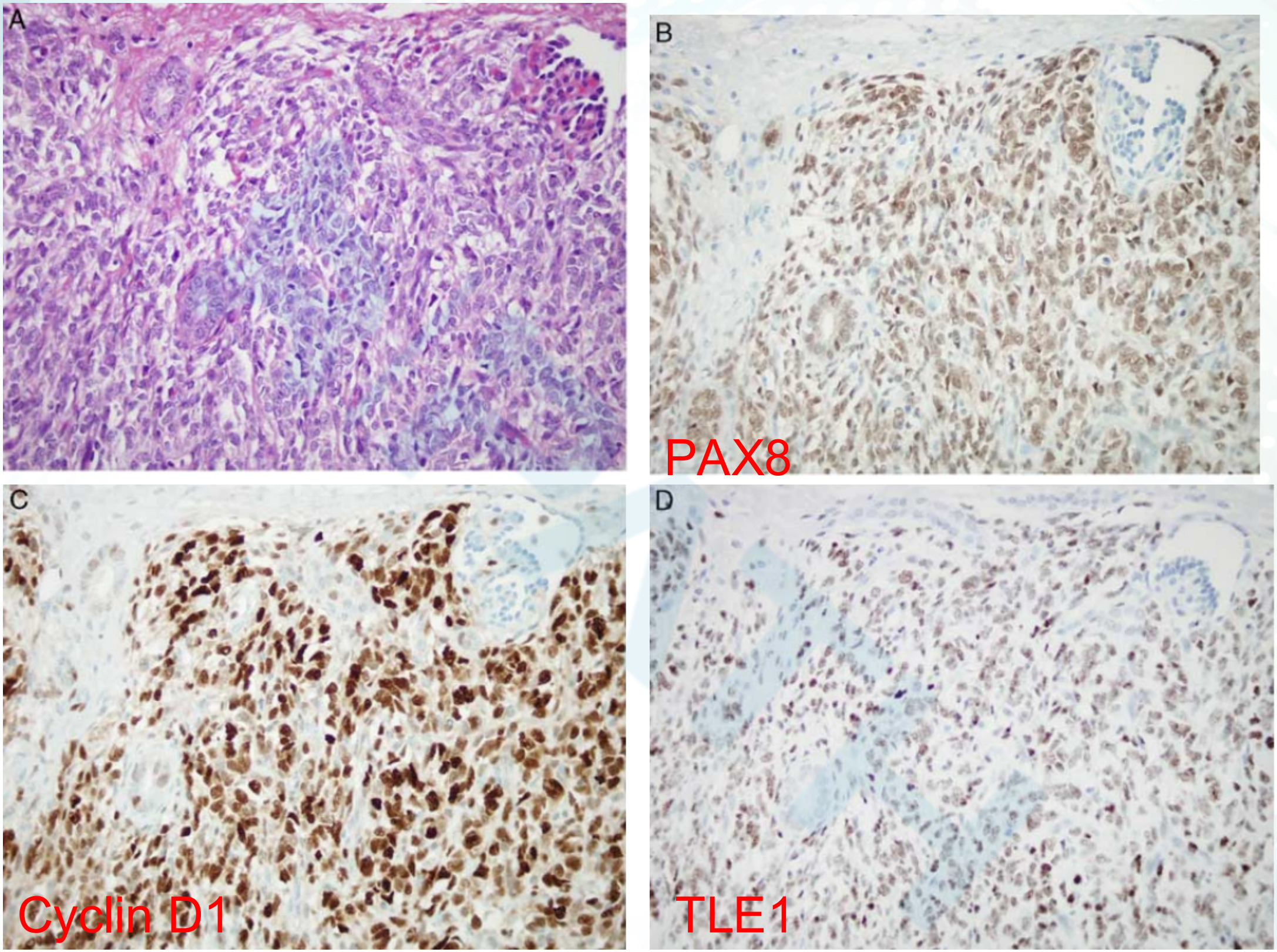

FIGURE 6. Immunoprofile of CCSK. A, This typical CCSK from the control group demonstrates bland epithelioid cord cells separated by a branching capillary vasculature. Note the entrapped glomerulus at the upper right, and the entrapped native renal tubules to the left and center of the field. B, In this case, the neoplastic cord cells and native renal tubules show strong nuclear labeling for PAX8. C, The neoplastic cord cells demonstrate strong, diffuse nuclear labeling for cyclin D1, while there is minimal labeling of entrapped nephrons. D, The neoplasm demonstrates diffuse nuclear labeling for TLE1.

- **Primary Renal Synovial Sarcoma**
- 7 genetically confirmed primary renal synovial sarcomas, 4 of 7 spindle cell synovial sarcoma arising in the kidney.
- 4 of 7 cases BCOR (+) , 4 of 5 cases TLE1(+),3 of 5 cases cyclin D1(+),2 of 5 cases focal weak/ equivocal staining for SATB2, the other 3 were completely negative.

讨论

- We report 2 primary renal sarcomas demonstrating BCOR-CCNB3 gene fusion.
- In the absence of molecular findings, these cases were originally considered to be unclassified sarcomas with a differential diagnosis including CCSK and primary renal synovial sarcoma.
- As neoplasms with BCOR-CCNB3 gene fusion, similar to sarcomas with BCOR-ITD, are associated with a BCOR-driven transcriptional profile, we interrogated the possible relationship of these neoplasms to CCSK.

BCOR-CCNB3 Primary renal sarcomas and CCSK

- **These cases were somewhat unusual for CCSK**
- they affected slightly older children (ages 11 and 12 y) compared with the mean CCSK age of 3
- demonstrated predominant spindle morphology and extensive dilation of native renal tubules resulting in extensive cystic change.
- In one case, the combination of hypocellular neoplastic cells within the septa and extensive cystic change created a mimic of a benign mixed epithelial stromal tumor or cystic nephroma.

- **However, while somewhat unusual, the BCOR-CCNB3 renal sarcomas are certainly compatible with CCSK.**
- The patient ages of the BCOR-CCNB3 renal sarcomas are well within the spectrum of CCSK, which in the largest study in the literature (351 cases) occurred in an age range of 2 months to 14 years.
- Predominant spindle cell morphology and extensive cystic change mimicking cystic nephroma, have also previously been described and illustrated in CCSK.

Argani P, Perlman EJ, Breslow NE, et al. Clear cell sarcoma of the kidney: a review of 351 cases from the National Wilms Tumor Study Group Pathology Center. *Am J Surg Pathol*. 2000;24:4–18.

- BCOR-CCNB3 renal sarcomas --- TLE1 (+) ;typical CCSK in our control group --- TLE1 (+), *a sensitive marker of synovial sarcoma*
- BCOR-CCNB3 renal sarcomas ---BCOR, cyclin D1, and SATB2 (+), *markers of CCSK*
- Overall taking together the common morphologic features of these neoplasms including the biphasic BCOR(+) cord cells and BCOR(-) septal cells, along with cyclin D1, TLE1,SATB2 in the cord cells(+), CD99, desmin, cytokeratin, S100, and CD34(-) , the pathologic of BCOR-CCNB3 renal sarcomas features fall within the broad spectrum of CCSK.

URCS/PMMTI(BCOR-ITD) and BCOR-CCNB3 bone/soft tissue sarcomas

- Despite their common transcriptional profile driven by a consistent upregulation of BCOR mRNA expression, some differences exist.
- First, CCNB3 overexpression both at the mRNA and protein levels is seen only in BCOR-CCNB3 bone/soft tissue sarcomas and not in URCS/PMMTI
- Second, the age at presentation is different; URCS/PMMTI in infants, while BCOR-CCNB3 soft tissue sarcomas typically affect teenagers and young adults.
- Third, most URCS/PMMTI have a alternating compact round cellular areas with hypocellular myxoid components, whereas BCOR-CCNB3 sarcomas are uniformly highly cellular, rounded and often spindled neoplasms which overlap with Ewing sarcoma and synovial sarcoma.

- Despite these differences, our review of a large series of URCS/PMMTI and BCOR-CCNB3 sarcomas of bone and soft tissue found significant areas of overlap.
- Specifically, PMMTI-like areas can be seen at the edge of BCOR-CCNB3 undifferentiated sarcomas of bone and soft tissue, and URCS/PMMTI often have higher grade areas that overlap with BCOR-CCNB3 sarcomas.
- Previous studies from our group have high-lighted morphologic similarities between the URCS/PMMTI and CCSK.

BCOR-CCNB3 sarcomas of bone/soft tissue and kidney with CCSK

- In this study, we note the similarity of BCOR-CCNB3 sarcomas of bone/soft tissue and kidney with CCSK.
- This is high-lighted by presence of cellular septa within the BCOR-CCNB3 soft tissue sarcomas which are very similar to those seen within CCSK.
- In both instances, the cellular septa do not label for BCOR, suggesting that these cellular septa represent aflorid pericyte-rich reactive proliferations associated with these BCOR-CCNB3 driven neoplasms.

- Hence, just as in soft tissue where the BCOR-CCNB3 sarcomas overlap with the URCS/PMMTI with BCOR ITD, the primary renal sarcomas with the BCOR-CCNB3 gene fusion overlap with CCSK showing BCOR-ITD.

- We note that a single neoplasm with the BCOR-CCNB3 gene fusion was recently reported in abstract form within a series reported as CCSK.
- We propose that CCSK, URCS/PMMTI, and BCOR-CNB3 sarcomas of kidney and bone/soft tissue can be thought of as a "BCOR-alteration family"of renal and extrarenal neoplasms with a common genetic signature and overlapping (but not identical) linicopathologic features.

TABLE 2. *BCOR*-Alteration Family of Neoplasms

CCSK
BCOR-CCNB3 sarcomas of kidney and bone/soft tissue
URCS/PMMTI

Primary renal synovial sarcomas and BCOR-CCNB3 renal sarcoma

- The predominantly spindle appearance of the BCOR-CCNB3 renal sarcomas created significant overlap with synovial sarcoma.
- Morphologic and immunohistochemical overlap of BCOR-CCNB3 soft tissue sarcomas with synovial sarcoma has been reported, as has overlap between CCSK and renal synovial sarcoma.
- Along these lines, BCOR overexpression in (49%) of soft tissue synovial sarcomas, though BCOR expression had not been addressed in primary renal synovial sarcomas until now.

- In this study, we document that primary renal synovial sarcomas similarly overexpress BCOR in (60%) of cases. also express cyclin D1, (*a sensitive marker of CCSK*) and TLE1(a sensitive marker of *soft tissue synovial sarcoma*) furthering the potential overlap with BCOR-CCNB3 renal sarcoma.
- While analysis of BCOR gene status and the SS18-SSX gene fusions (*typically resolve the differential diagnosis of CCSK and renal synovial sarcoma*) there may also be significant overlap at the genetic level.

TABLE 1. Comparison of *BCOR*-related Neoplasms and Renal Synovial Sarcoma

	Typical CCSK	*BCOR-CCNB3* Renal Sarcomas	URCS/PMMTI	*BCOR-CCNB3* Bone/Soft Tissue Sarcoma	Renal Synovial Sarcoma
Usual age (y)	3 (mean)	11.5 (mean)	< 1	Teens	43 (median)
Morphology	Round/spindle cells separated by branching capillary vasculature in myxoid stroma; numerous variant patterns	Variably cellular spindle cell sarcoma associated with entrapped dilated renal tubules	Round to spindled primitive cells in myxoid background	Cellular round/ spindle cell sarcoma	Cellular spindle/round cell sarcoma often associated with entrapped dilated renal tubules
Genetics	*BCOR* ITD (90%); *YWHAE-NUTM2B/E* fusion (< 10%)	*BCOR-CCNB3* fusion	*BCOR* ITD	*BCOR-CCNB3* fusion	*SS18-SSX* fusion
PAX8	20% positive	50% focal positive	NA	50% positive*	Usually negative†
BCOR	Positive‡	Positive	Positive	Positive	50% positive
Cyclin D1	Positive§	Positive	Positive	Positive	60% positive (weak)
SATB2	42% positive‡	Positive	75% positive‡	100% positive‡	Minimal/negative
TLE1	80% positive	Positive	NA	Positive‖	Positive

*Data from Ludwig et al.[24] 1/1 *BCOR-CCNB3* soft tissue sarcoma in the current study was focally positive for PAX8.
†Data from Karafin et al.[25]
‡Includes data from Kao et al.[5]
§Includes data from Mirkovic et al[3] and Jet Aw et al.[4]
‖Data from Yamada et al.[26] 2/2 *BCOR-CCNB3* soft tissue sarcomas in the current study were positive for TLE1.
NA indicates not available.

SATB2 表达情况

- SATB2 is less frequently expressed in renal synovial sarcoma than in typical CCSK or the renal BCOR-CCNB 3 sarcomas, providing one useful discriminatory immunohistochemical marker.

PAX8表达

- Case1,PAX8 focal labeling, unusual for CCSK, previously PAX8(-) in CCSK.
- we found that PAX8 (+) in a minority of CCSK,focally expressed in bone/soft tissue BCOR-CCNB3 sarcomas。
- Furthermore, a recent study found that PAX8 is expressed in over 50% of BCOR-CCNB3 soft tissue sarcomas and PAX8 immunoreactivity also been described in primitive round cell sarcomas such as alveolar rhabdomyosarcoma and rhabdoid tumor
- Hence, in the setting of primitive round/spindle cell neoplasms, PAX8 is not specificfor renal parenchymal versus mesenchymal origin.

治疗

- Our fi nding of overlap between BCOR-CCNB3 fusion-positive sarcomas of the kidney and bone/soft tissue with CCSK has potential therapeutic implications.
- BCOR-CCNB3 sarcomas were initially recognized as “ Ewing sarcomas,” and been treated with Ewing sarcoma chemotherapy regimens, though some evidence exists that their behavior may be more indolent.

- Given the overlapping morphology of BCOR-CCNB3 sarcomas with CCSK and their overlapping transcriptional profile
- It seems logical to consider treating the BCOR-CCNB3 bone/soft tissue sarcomas with CCSK-based therapy regimens (*which emphasize Doxorubicin and do not include Ifosfamide*) rather than Ewing sarcoma–based regimens *(which include both Doxorubicin and Ifosfamide*).
- The former chemotherapy regimen is overall less toxic, and at least in CCSK has demonstrated signifi cant clinical benefi t.

总结

- BCOR-CCNB3 renal sarcomas may account for a subset of cases currently classified as CCSK but which lack BCOR-ITD or YWHAE-NUTM2B/Egene fusions.
- Ourfindings support the concept of a BCOR-alteration family of renal and extrarenal neoplasms having a highly related genetic profile and similar (though not identical) clinicopathologic features, including CCSK, BCOR-CCNB3 sarcomas, and URCS/PMMTI.

THANKS