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## **Oncocytoma in Concert with Mixed Epithelial Stromal Tumor**

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### **Abstract**

Mixed epithelial stromal tumors (MEST) are relatively uncommon neoplasms accounting for only 0.4% of renal cancers, while oncocytomas are more common, accounting for 3-7% of renal neoplasms [1-2]. In the case discussed here, a female in her early 60s presented with non-specific diffuse back pain. Imaging revealed a mass and a cystic lesion on the right kidney. Upon histologic observation of the resected lesions, the solid mass was diagnosed as MEST with oncocytoma. As of now, this is believed to be the only reported case in which MEST was found in concert with oncocytoma.

### **Introduction**

MEST is a biphasic cancer with patients often presenting with hematuria and flank pain [1,3-4]. Due to the differences in naming, an exact number of reported MEST cases has not been identified; however, it is estimated that there have been roughly 100 reported cases with a high predominance in females at a 10:1 female-to-male ratio [5-6]. At the time of diagnosis, ages ranged anywhere from 18 to 78 years old, with an average of 45 years old [6-7]. Typically, cases were benign with a favorable prognosis; however, later presenting cases were noted to have a less favorable outlook due to local recurrence or possible malignant transformation [4-7]. In comparison, oncocytomas are usually found incidentally in the seventh decade of life with a female-to-male ratio of 1:2.5 [2,8]. Much like MEST, oncocytomas have a favorable prognosis [2]. While a great deal has been discovered about MEST and oncocytoma, the connection between the two has yet to be explored. Prior to this case, there have been no reported instances where MEST and oncocytoma were diagnosed together.

### **Case Presentation**

#### **Clinical History**

A female in her early 60s, with a history of hypertension, initially presented with back pain. On 3/2/2022 an MRI of the lumbar spine revealed an incidental cyst measuring 2.9 cm on the right side. CT scan of the abdomen and pelvis with and without contrast showed an enhancing mass originating from the lateral side of the middle region of the right kidney. Dimensions of the mass measured 2.7 x 2.6 x 2.6 cm in length, width, and height, respectively. Findings raised strong suspicion of renal cell carcinoma. Additionally, a cyst measuring 1.0 cm adjacent to the back margin of the main lesion was noted. Another enhancing nodule was observed projecting from the lateral margin of the upper region of the right kidney, with dimensions of 1.4 x 0.7 x 1.0 cm [Figure 1]. As a result, on 7/7/2022, the patient underwent a robotic partial nephrectomy of the right kidney. Microscopy revealed a dense collection of spindle cells around epithelial components and a nested cellular pattern with rounded nuclei and centered nucleoli [Figures 2A,2B,3A,3B]. Immunohistochemistry (IHC) yielded: ER (+), PR (+), CD117 (+), Ki67 <1%, SMA (+), PAX8 (+), AE1/AE3 (+), HMB (-), and CAIX (-) [Figures 4-9]. Based on histopathological features and

IHC stains, the mass was diagnosed as oncocytoma in concert with MEST.

### **Structures**

#### **Discussion**

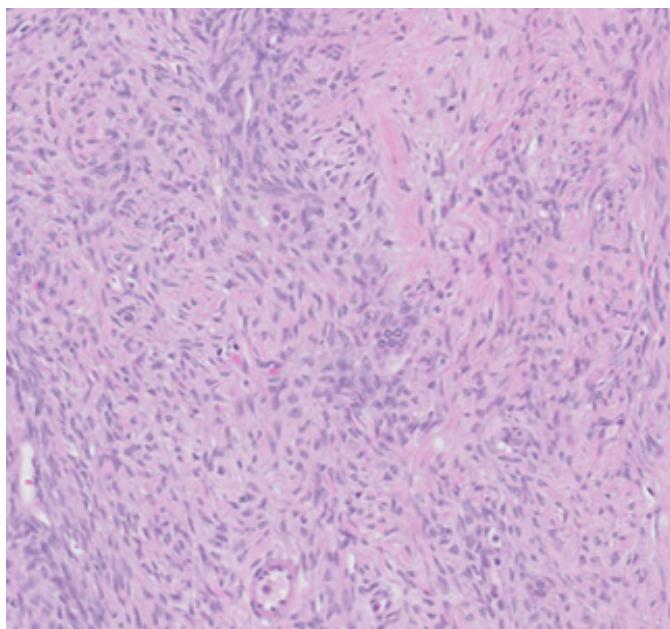
Histologically, MESTs have mesenchymal elements of dense collections of spindle cells studded with simple cuboidal to stratified epithelial tubules of various sizes; often, immunohistochemistry (IHC) staining panel yields: ER(+), CR(+), CD117(+), Ki67 <1%, smooth muscle actin(+), CD10 (+), Inhibin(+), PAX2 and PAX8(+), cytokeratin(+), HMB45(-), S100(-), WT1(-), CD34(-), Melan A(-) [1,3-7,9]. Gross examination of MEST neoplasms often shows a well-defined, yellow-beige-colored lesion with occasional cystic components [5,10]. Oncocytoma somewhat parallels the gross features of MEST, presenting as a well-circumscribed, tan-colored mass; however, a stellate scar feature is often noted [2]. Upon histological examination, oncocytoma displays tubular and nested structures surrounded by eosinophilic cells; the cells generally have uniform nuclei [2]. IHC panels of oncocytoma have been reported to show: CD117/KIT (+), E-cadherin (+), S100A1 (+), PAX8 (+), CK7 (-), AMACR (-), CAIX (-), Vimentin (-), HMB45 (-), CK20 (-) [2,12].



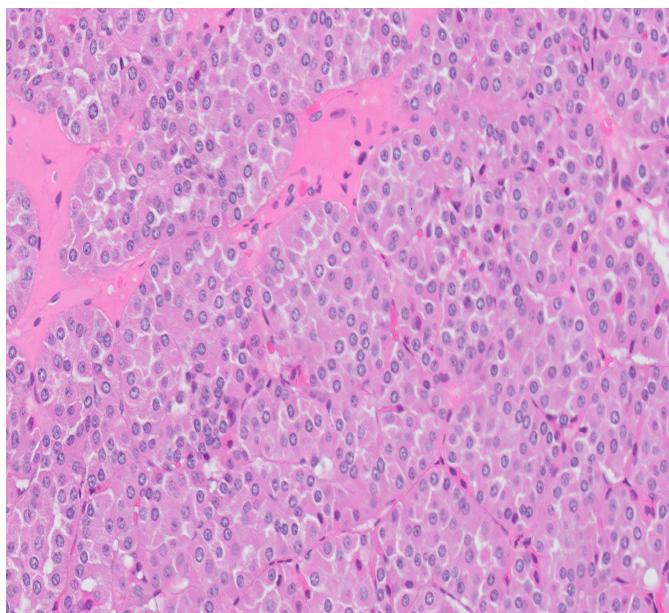
**Figure 1:** Gross specimen from partial nephrectomy of the right kidney.

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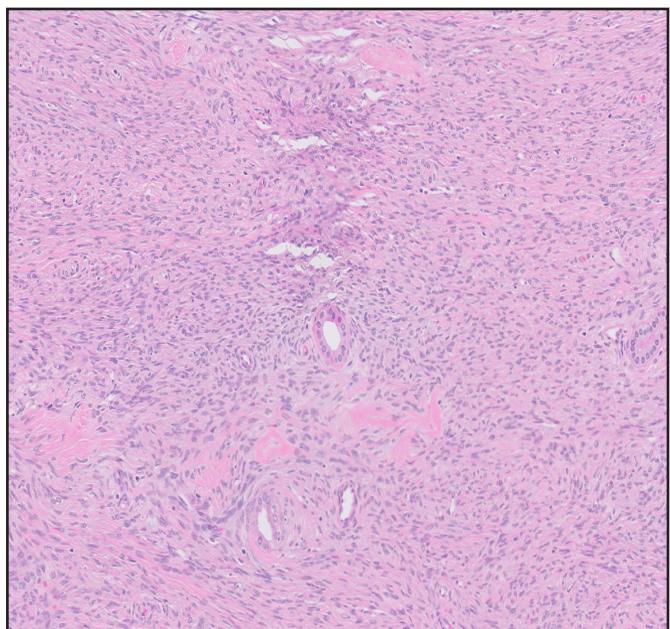
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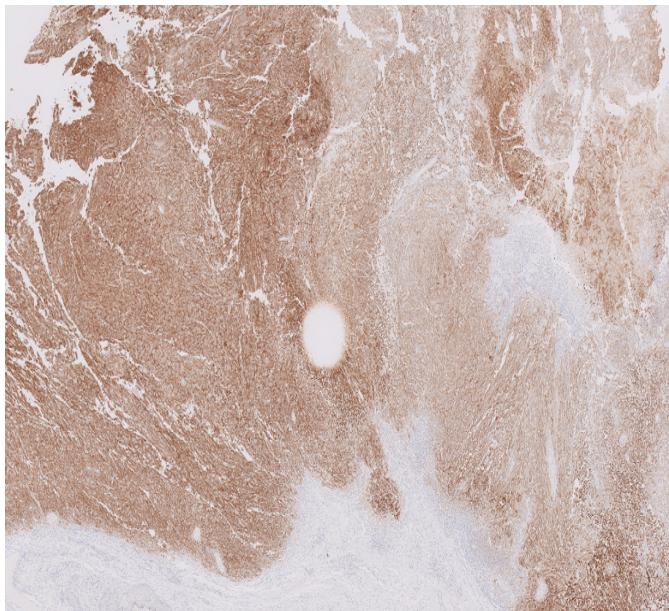
**Figure 2A:** Hematoxylin and Eosin-stained section showing a dense collection of spindle cells around epithelial components.



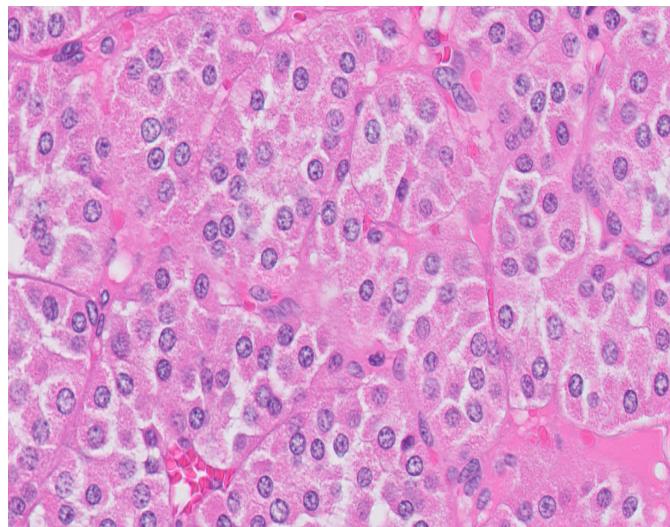
**Figure 3B:** Hematoxylin and Eosin-stained section showing a nested cellular pattern with rounded nuclei and centered nucleoli.



**Figure 2B:** Hematoxylin and Eosin-stained section showing a dense collection of spindle cells around epithelial components.



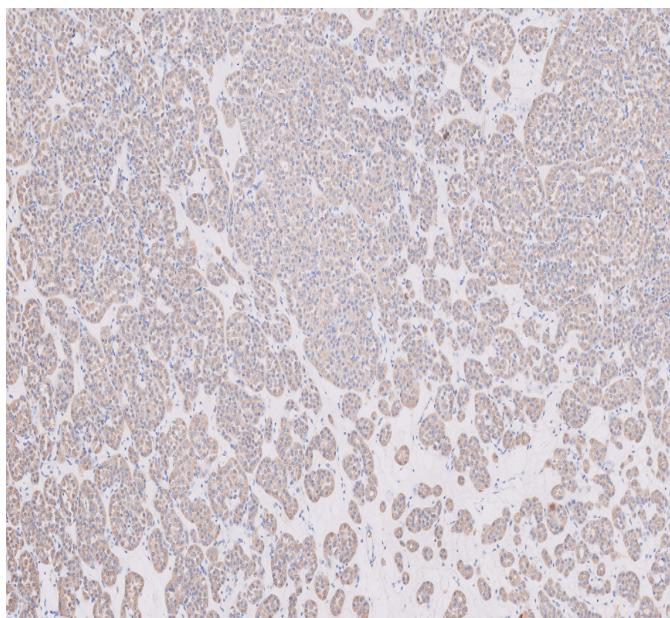
**Figure 4:** HMB 45- stained control section illustrating positive staining.



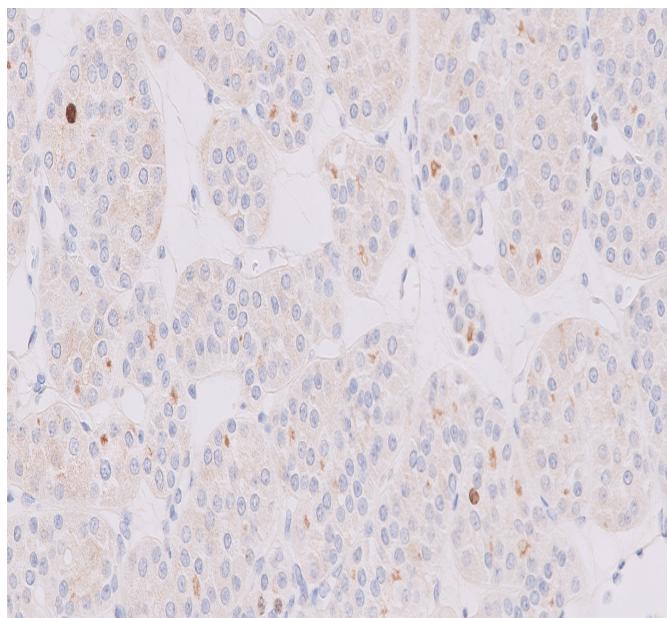
**Figure 3A:** Hematoxylin and Eosin-stained section showing a nested cellular pattern with rounded nuclei and centered nucleoli.



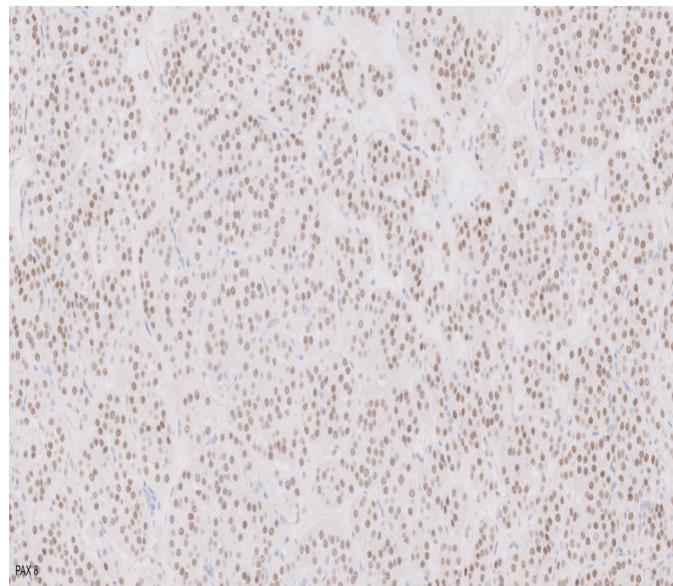
**Figure 5:** HMB 45- stained section of the tumor illustrating a lack of melanoma involvement.



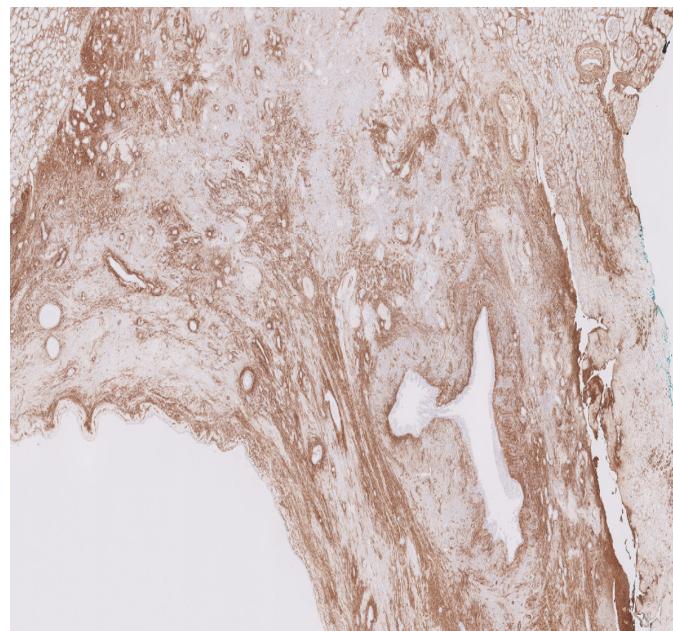
**Figure 6:** AE1/AE3 positively stained section .



**Figure 9:** AKi67- stained section is < 1% .



**Figure 7:** PAX8 staining shows strong nuclear expression.



**Figure 8:** Smooth muscle actin positively stained section.

The neoplasm discussed in this case report had features that aligned with both MEST and oncocytoma, hence the diagnosis. The individual in this study fit the usual demographic and presentation of MEST cases, having been a middle-aged female presenting with generalized back pain. Gross and histological inspection of the resected lesion displayed qualities specific to both MEST and oncocytoma. In Figure 1, the tumor is seen to be a well-circumscribed yellow-tan mass, as seen in most MEST cases; however, it also has a central stellate scar seen quite often in oncocytoma. Histologically, this case showed a MEST-like pattern of a mesenchymal element with epithelial tubules dispersed throughout [Figure 2A, B] and nests of cells surrounded by eosinophilic stained cells [Figure 3A, B] commonly seen in oncocytomas. Analysis of Figures 3-9 resulted in the listed IHC: ER (+), PR (+), CD117(+), Ki67 <1%, SMA (+), PAX8(+), AE1/AE3(+), HMB (-), and CAIX (-). Such results match the IHC panels of MEST and oncocytoma when applicable [1-7,9,12].

Discovery of the oncocytoma in concert with MEST adds novelty to the case presented here. Currently, there are no defined genetic links seen in oncocytoma, though it is speculated that possible mitochondrial defects or the genetic mutations seen in Brit-Hogg-Dube syndrome are at play [2,14]. Conversely, it is thought that MESTs are formed through multifactorial elements, with long-term estrogen replacement therapy being the most noted [4,6,9,15]. Additionally, examined stromal and epithelial components are hypothesized to arise from cells of similar origin because the non-random inactivation pattern of the X chromosome is identical in both [16-17]. Due to the rarity of MEST cases, genetic links have not been extensively studied; most papers claim there to be no genetic association and attribute MEST to sporadic events [1,4,6,9,15]. Two studies, however, offer insight into possible genetic components. One such study identified a translocation t (1;19) in a case of MEST, but since this study, there have been no further reports on such occurrences [10]. Another study investigated a family of three, all of whom were diagnosed with MEST [11]. Upon analysis of the individuals, a CDC73 germline mutation was discovered [11]. Such a mutation, specifically in the loss of heterozygosity in wild-type CDC73, has also been observed in sporadic cases of renal oncocytoma, which opens the discussion for further studies exploring a link between CDC73 gene mutations in relation to MEST and oncocytoma [11,18].

## Conclusion:

While concrete environmental and genetic links related to the development of MEST or oncocytomas remain undiscovered, this case suggests the intriguing possibility of a shared connection between the two cancers. Future cases of MEST and oncocytoma, both independent and synergistic, should investigate potential genomic mutations and external factors that may contribute to their etiology. Doing so will allow for a further understanding of renal cancers, thus leading to the possible development of earlier detection and increasingly efficacious treatments of such neoplasms.

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