PATHOLOGIC DIAGNOSIS: *ALK* Rearranged RCC with Mucinous tubular and spindle cell morphology

DISCUSSION:

Anaplastic lymphoma kinase rearrangement-associated renal cell carcinoma (*ALK-RCC*) is a very rare tumor that accounts for <1% of all renal neoplasms, first described by Debelenko et al in 2011. Their report described a pediatric case with sickle cell trait, and the fusion partner of *ALK* gene was *VCL* gene. The first adult case were reported in 2012 by Sugawara et al. It has been recently included in group of moleculary well-defined renal tumors in the new WHO classification in 2022. *ALK* gene fusions harbour chromosome translocations resulting in gene fusions involving the *anaplastic lymphoma kinase* gene (*ALK*) at chromosome 2p23. *ALK* fusions convert the *ALK* receptor tyrosine kinase into novel fusion proteins that constitutively drive downstream growth-promoting pathways. Most of the tumors reported have been small and organ-confined at presentation (pT1). Tumors have solid to solid-cystic appearance with variegated cut surface.

Most *ALK-RCC* cases display mixed architectural patterns, including papillary, tubular, trabecular, tubulocystic, and solid patterns. The tumor cells typically showed eosinophilic cytoplasm and various degrees of mucin deposition . When fusion partner is *VCL*, the tumors are usually well-circumscribed, with chronic inflammation at periphery, occurring in young patients with sickle cell trait. The tumor cells are polygonal with abundant eosinophilic cytoplasm and vacuolization and sickle-shaped erythrocytes are seen in extravasated blood than in blood vessels. ALK-rearranged RCCs with fusion partners other than *VCL (e.g. TPM3, EML4, STRN, HOOK1)* are more heterogenous showing cytoplasmic vacuolization but often have papillary or cribriform architecture and mucinous stroma. Intracytoplasmic mucin, psammoma bodies, and rhabdoid morphology may be seen.

In view of its heterogeneous and diverse morphologies, the differential diagnosis of *ALK-RCC* varies widely, involving renal medullary carcinoma, collecting duct carcinoma, papillary RCC, MiT family translocation RCC, clear cell RCC with rhabdoid features, metanephric adenoma, thyroid-like follicular RCC, and mucinous tubular and spindle-cell carcinoma (MTSCC). We present a case of *ALK-RCC* with