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Synchronous Gastrointestinal Stromal Tumorof Jejunum and Low-Grade Oncocytic Tumor of Kidney: A Unique Association Managed in the Same Sitting

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Gastrointestinal stromal tumor (GIST) is the most common primary mesenchymal tumor of the gastrointestinal tract. Most cases of GIST are sporadic and about 5% are associated with genetic syndromes[1]. Here, we report a case of synchronous GIST and low-gradeoncocytic tumor (LOT) of the kidney managed in the same sitting. Although GIST has been reported with other primary malignancies, including renal cell carcinoma (RCC), this reported dyad of GIST and LOT is the first such in the literature.

Case Report

A gentleman in late 40s presented with melena, generalized weakness, and fatigue for one year. He was admitted twice to a hospital elsewhere for blood transfusion in past one year. There was no history of abdominal pain, distension, altered bowel habit, and hematuria. He had no family history of malignancy. He had a Karnofsky score of 90%. On examination,he had pallor, whereas his vitals were within normal limits and his abdominal examination was unremarkable. Lab investigation showed that his hemoglobin (Hb) was 7.8 g/dl, total leucocyte count (TLC) 4,190/cumm, Platelet count 1.93 lakh/cumm, and his renal function tests (RFT) and liver function tests (LFT) were within the normal range. Peripheral smear and iron studies were suggestive of microcytic hypochromic anemia. Upper GI endoscopy and sigmoidoscopy were normal. Contrast-enhanced computed tomography (CECT) Abdomen demonstrated a 4x2.7 cm well-defined lobulated arterial phase hyper-enhancing endo-exoenteric mass in mid jejunum suggestive of GIST and a 3.1x2.7x2.7 cm partly exophytic, cortical based rounded heterogeneously enhancing mass lesion arising from the upper pole of left kidney suggestive of a mitotic etiology (**Figure 1**). The patient underwent exploratory laparotomy with resection of the jejunal mass with a 5 cm margin with isoperistaltic side-to-side jejunojejunostomy and left partial nephrectomy. The postoperative course was uneventful, and the patient was discharged with stable vitals on postoperative day 6.

Gross examination of the resected specimen showed a 5x4x4 cm polypoidal mass protruding from the serosal aspect ofthe jejunum. This mass was greyish-white, lobulated, and fleshy on the cut surface (**Figure 2**). Microscopically, sections showed features of GIST, spindle cell type with a mitotic count of 0-1/5 sq mm. No necrosis was seen. Tumor cells were immunopositive for CD117, DOG1, CD34, and SMA. SDHB immunoexpression was retained (**Figure 3**). The tumor was suggested low-risk GIST as per Miettinen and Lasota risk stratification system based on tumor size and mitotic count. The nephrectomy specimen measured 4x4x2.7 cm. The overlying capsule was congested but intact. The cut surface demonstrated a relatively well-circumscribed tumorof 4x3x2.5 cm in dimensions with areas of hemorrhage (**Figure 4**). The tumor was 0.1 cm from the overlying capsule and 0.4 cm from the resected surface. There were small areas of normal-appearing renal parenchyma at the periphery. Sections examined were suggestive of LOT (**Figure 5**). No nuclear pleomorphism was noted. No mitosis or necrosis was identified. However, areas of fresh hemorrhage and focal edematous degeneration were

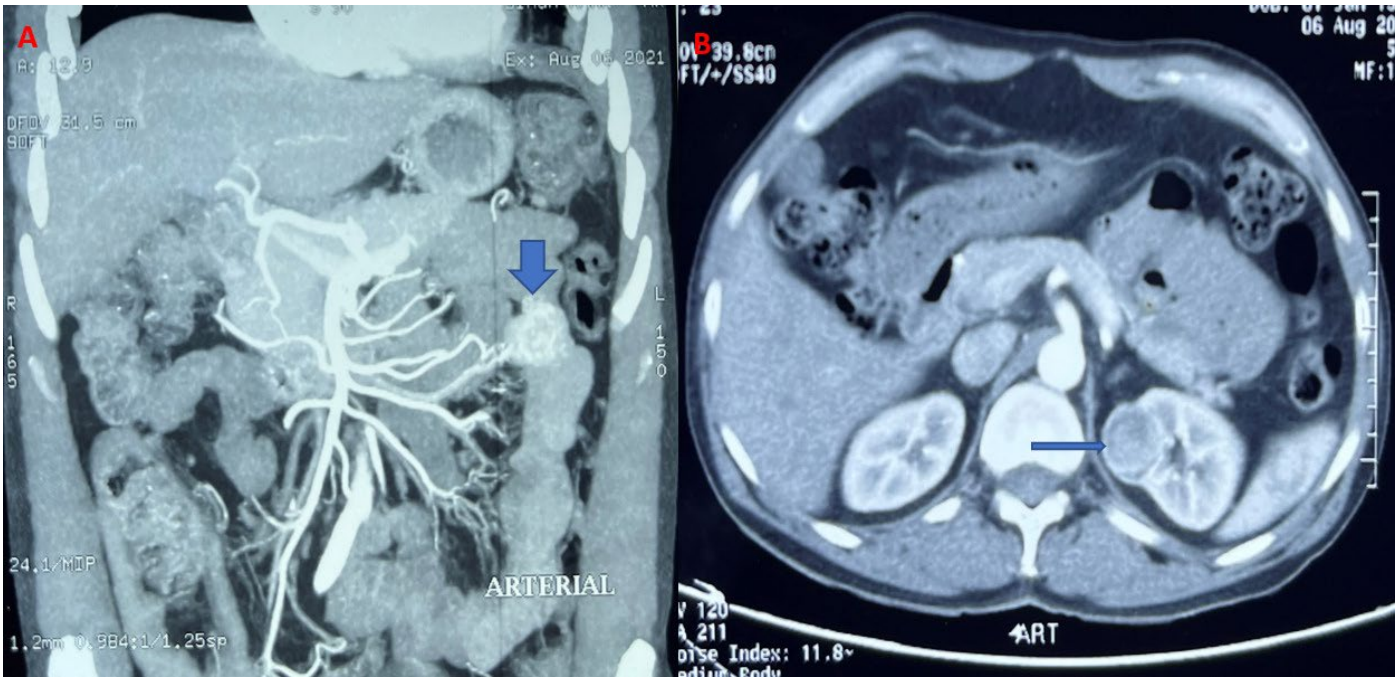

Figure 1: CECT (A): The coronal section demonstrates well-defined lobulated arterial phase hyper-enhancing endo-exoenteric mass in jejunum (broad arrow) suggestive of GIST. (B): Axial section demonstrates cortical based rounded heterogeneously enhancing mass lesion arising from the upper pole of left kidney (narrow arrow).

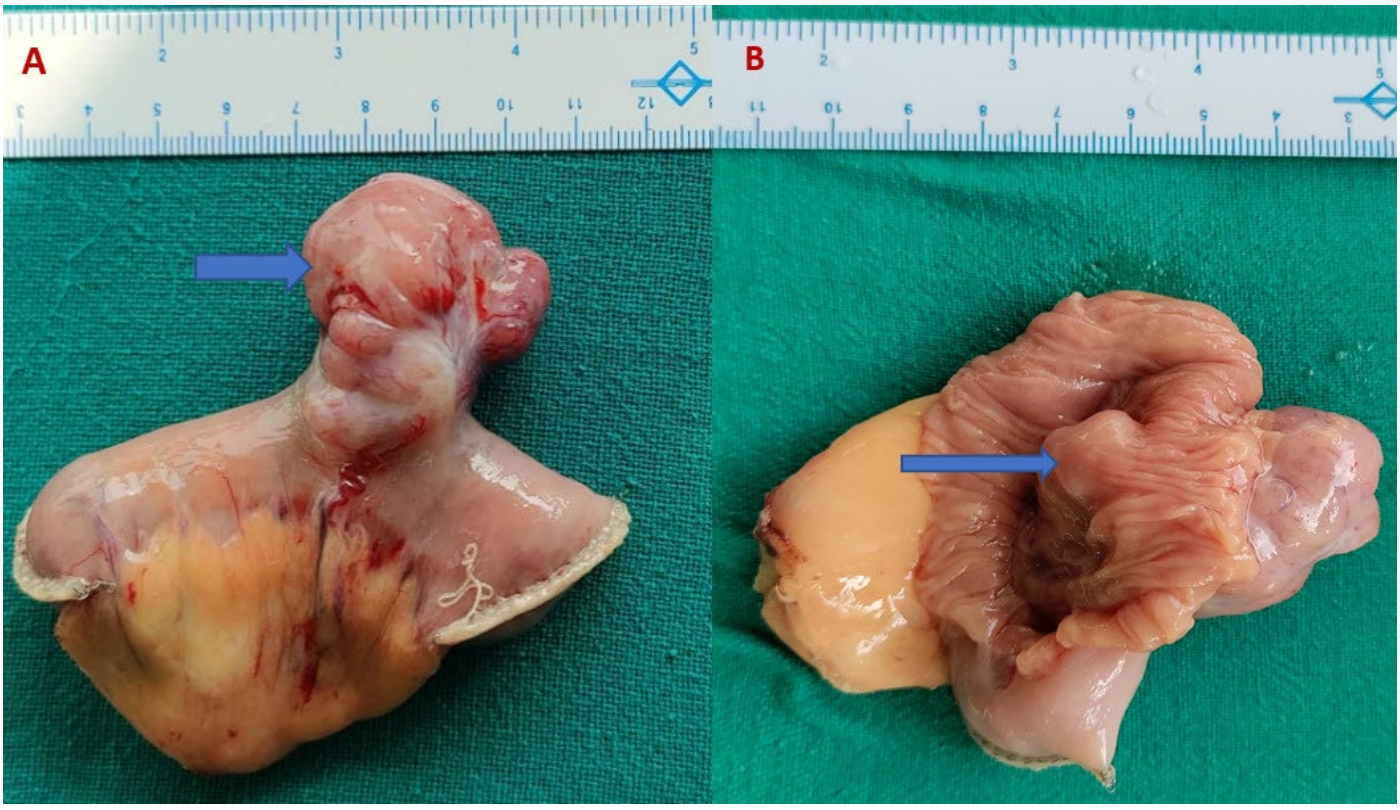

Figure 2: Specimen (A and B) showspolypoidal mass protruding from the serosal aspect of the jejunum (arrow marked).

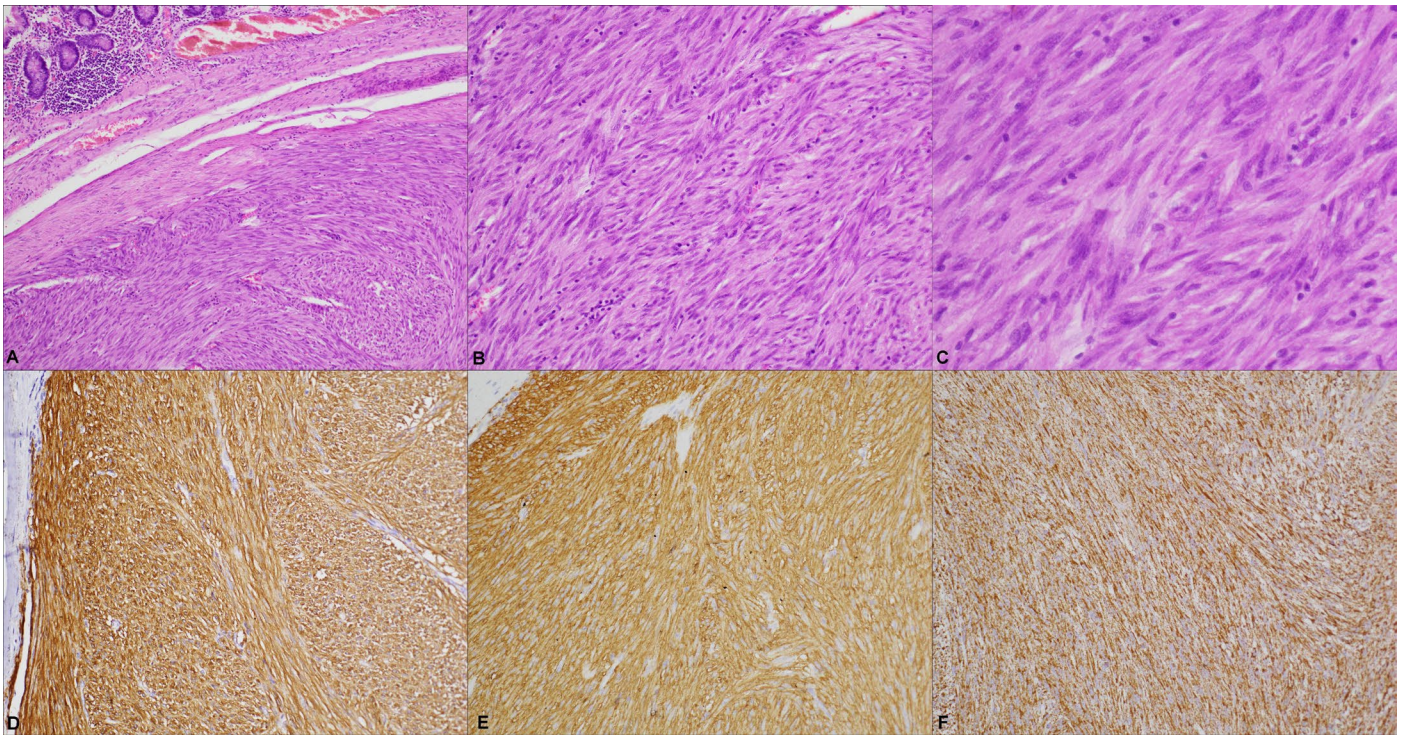

Figure 3: The tumor is seen to arise from the jejunal wall (A: H&E, X100) and is composed of spindle shaped tumor cells arranged in intersecting fascicles (B: H&E, X200 and C: H&E, X400). The tumor cells show immunopositivity for CD117 (D, X200) and DOG1 (E, X200). Immunoexpression for SDHB is retained (F, X200).

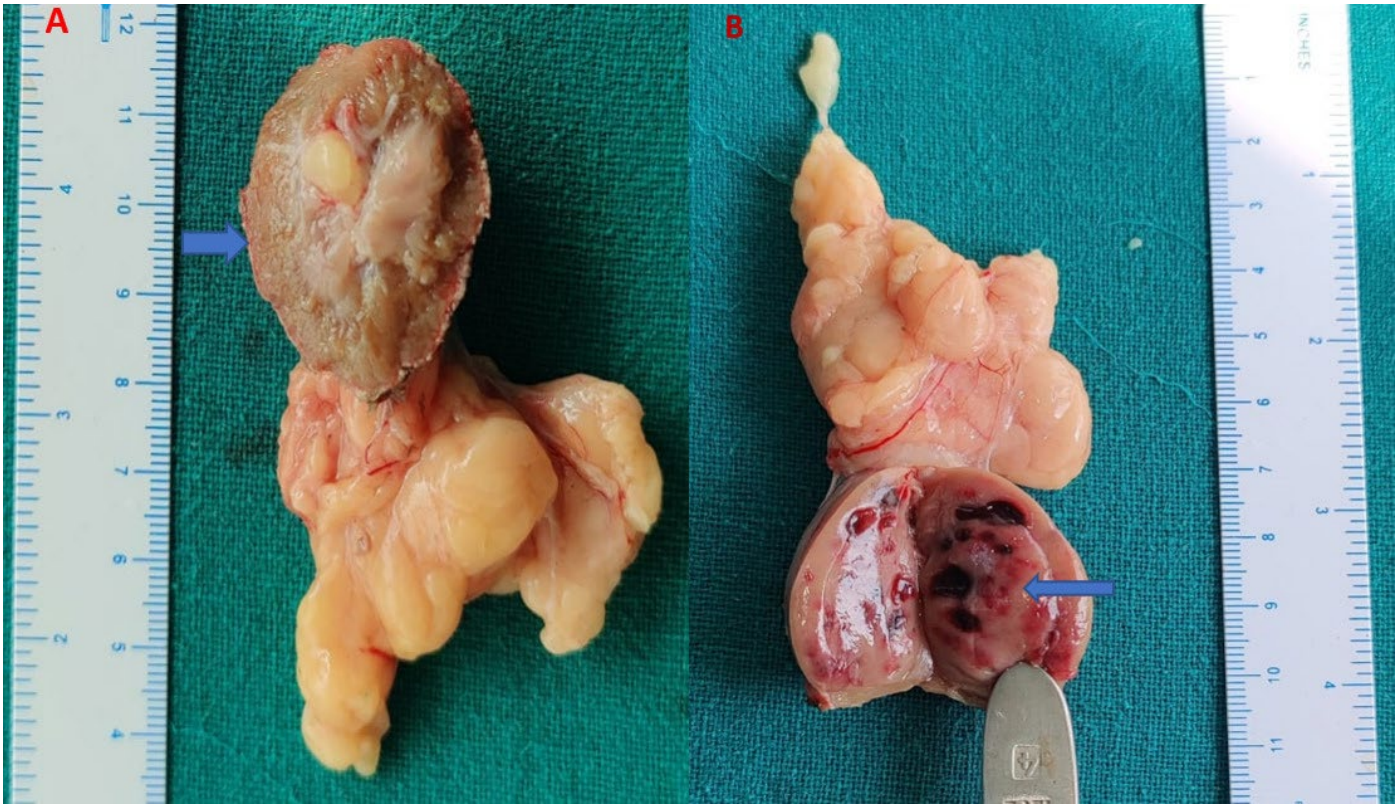

Figure 4: Partial nephrectomy specimen demonstrates renal tumor (arrow marked).

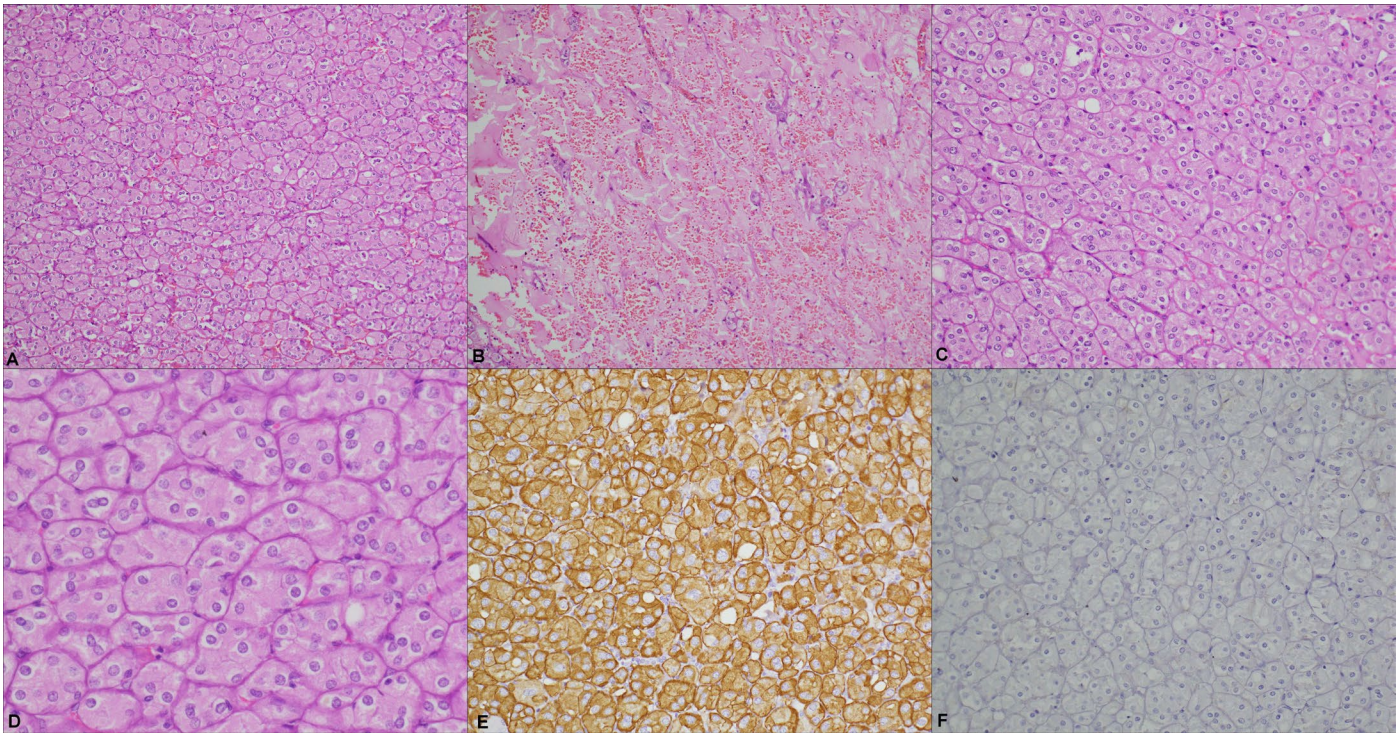

Figure 5: The renal tumor shows compact nested architecture (A: H&E, X100). Also, there are loose edematous areas with hemorrhage in the tumor (B: H&E, X100). The tumor cells contain abundant granular eosinophilic cytoplasm and central round nuclei (C: H&E, X200) with perinuclear halos and inconspicuous to tiny nucleoli at places (D: H&E, X400). The tumor cells stain immunopositive for CK7 (E, X200) while they are immunonegative for CD117 (F, X200).

seen. The tumor cells were immunopositive for pan-cytokeratin, CK7, PAX8, and BerEp4, while negative for CD117, AMACR, S100, CAIX, CK20, CD19, HMB45, and Vimentin. E cadherin and SDHB immunoexpression were retained. Tumor genomic DNA was extracted from representative formalin fixed paraffin embedded tissue block of GIST and used for genetic analysis using next generation sequencing illumina platform. c.1727T>C mutation (missense) leading to p.Leu576Pro was detected in exon 11 of KIT gene.

At 6 months and 1 year of follow-up, clinical examination and CECT abdomen were normal and did not suggest any recurrent disease.

Discussion

GIST is mainly a sporadic tumor, although 5% are associated with various genetic syndromes which include Carney triad (GIST and pulmonary chondroma), Carney-Stratakis syndrome (GIST and paraganglioma), and Neurofibromatosis type 1 (NF1)[1,2]. GISTs are characterized by a mutation in the gene c-KIT but may also have associated mutations in platelet-derived growth factor alpha (PDGFRA), succinate dehydrogenase complex, and BRAF gene; rarely they can have associated mutation in the RAS family gene. GISTs are mostly found in the stomach (60%) and small intestine (20-30%) but can be found at any level of the gastrointestinal tract and rarely in the omentum, mesentery, and peritoneum[2]. Immunohistochemistry shows 95% of GISTs to be positive for CD117 (KIT), and70% positive for CD34. Other markers include DOG-1, SMA (smooth muscle actin), S-100 protein, desmin, and keratin[3]. Microscopically, GIST is of three main types: spindle cell type (70%), epithelioid type (20%), and mixed type (10%)[2]. The standard treatment for localized GISTs is surgery. Neoadjuvant therapy with tyrosine kinase inhibitors (TKIs) should be considered in patients with large tumors in whom immediate resection is not possible, whereas adjuvant TKIs should be considered a standard treatment

in all patients who underwent resection of primary GIST and have a significantly high risk of recurrence.

GISTs have shown an association with other primary malignancies including renal cell carcinomas. Like GISTs, 5-8% of RCCs are known to occur due to hereditary etiology. Previous reports and case series of a few patients have described synchronous RCC and GIST and attempted to hypothesize an association between them. These studies have shown the occurrence of synchronous GIST and RCC due to germline mutations in SDHA, SDHC, and translocation of Xp11[2]. Additional reports and series have identified the association of GIST with papillary RCC over other RCC histologies[4]. The association between RCCand GIST is supported by the common genetic and molecular pathway involving tyrosine kinase, resulting in these malignancies and favorable clinical outcomes of both tumors by inhibiting a common pathway (tyrosine kinase) suggesting a common relationship[5]. A case series by Mendonca SJ et.al consisting of 9 cases of GIST and RCC suggested the possibility of a familial syndrome owing to unique clinical findings, besides the co-occurring GIST and RCC[5]. The study showed most patients (55.6%) had other malignancies in addition to RCC and GIST. Furthermore, papillary RCC was found in 44% of patients with GIST which was higher than expected relative frequency (12-14%) in the overall RCC population, also GIST was found to originate from small bowel in 44% of patients relative to expected frequency in the overall population (20-30%)[5]. Such repeated association of specific tumors is a pointer to novel oncogene defects, further studies are required in a larger population to identify a specific genetic mutation or a hereditary syndrome for these co-occurring tumors. Despite these reported associations, we did not find an association of jejunal GIST with a low-gradeoncocytic tumor of the kidney in our literature search, which we report here.

The low-grade oncocytic renal tumor is an uncommon, eosinophilic renal neoplasm constituting 4% of tumors diagnosed historically as oncocytomas[6]. Such tumors were previously diagnosed as an 'eosinophilic variant' of chromophobe RCC or as unclassified RCC. Morphologically, they have overlapping features with oncocytoma and chromophobe renal cell carcinoma. Morphologically, diffuse expression of CK7 is diagnostic of chromophobe RCC whereas oncocytomas show scattered positivity of tumor cells. LOT in contrast to oncocytoma and chromophobe RCC shows diffuse immunoreactivity for CK7 while being negative for CD117, whereas both chromophobe RCC and oncocytoma are positive for CD117[6]. In a study largest for LOT, 29 cases of LOT were identified in three clinical settings; sporadic, tuberous-sclerosis complex (TSC) associated, and end-stage renal disease (ESRD), but no cases having association with GIST were found[6]. TSC and ESRD-associated LOT showed multifocality. All the tumors had an indolent course, and no metastasis was reported. These tumors also had retained SDHB and FH immunoexpression and were negative for cytokeratin, cathepsin K and p63. Oncocytoma has a cytogenetic abnormality in the form of loss of chromosome 1, X, or Y in 10% of cases, and chromophobe RCC shows losses of chromosomes 1, 2, 6, 10, 13, and 17 in approximately 50% of cases, whereas LOT lacks common cytogenetic abnormality seen in both[7]. Recent studies suggest, FOX1, amarker specific for intercalated cells of the distal nephron, from which oncocytoma and chromophobe RCC originate[8]. In this context, the absence of CD117 expression by LOT suggests that although these tumors share similar morphological features with oncocytoma or chromophobe RCC, their cell of origin is different. LOT is associated with an indolent course and mainly managed with partial nephrectomy, so its distinction from oncocytoma may not be clinically critical, however, its definition and recognition are of significant clinical importance to not mislabel them as chromophobe RCC. Although LOT isreported in association with TSC and ESRD, to our knowledge we are the first to report its association with GIST, and the clinical significance, specific genetic mutation of such association needs to be explored in larger studies.

Conclusion

GISTs are known to occur with other primary malignancies including RCC, predominantly the papillary variant. We describe the first report to our knowledge of an adult with synchronous jejunal GIST and LOT managed by resection of jejunal and renal mass. This association is important to be aware of as syndromic tumors need to be excluded in multiple primary malignancy cases.

Abbreviations

GIST: Gastrointestinal Stromal Tumor
RCC: Renal Cell Carcinoma
LOT: Low Grade Oncocytic Tumor
CECT: Contrast Enhanced Computed Tomography
TKI: Tyrosine Kinase Inhibitors
TSC: Tuberous Sclerosis Complex

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Peripancreatic Tuberculous Lymphadenopathy: The Great Masquerader

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Infection with *Mycobacterium tuberculosis* (TB) can cause a wide range of symptoms. Although miliary tuberculosis frequently involves the liver, spleen, colon, and mesenteric lymph nodes, tuberculosis that exclusively affects the peripancreatic lymph nodes is a rare clinical condition[1]. On imaging, it is frequently mistaken for cancer or pancreatitis. This might necessitate unnecessary surgery. It is crucial to diagnose this condition prior to surgery because it is a curable disease[2]. We present a case series of 3 suchpatients diagnosed with space-occupying lesion of the pancreas on imaging and found to have peripancreatic tuberculous lymphadenopathy on endoscopic ultrasound (EUS) examination.

Case Series

Clinical details of all three patients have been described in **Table 1** (Case series of patients with peripancreatic tuberculous lymphadenopathy). Computed tomography (CT), EUS and histopathology findings of the three patients have been illustrated in **Figures1,2,3,4** respectively.

Discussion

Abdominal TB can present in an isolated nodal form as abdominal lymphadenopathy.[1] The lymphatics of the ileocecal region, jejunum, ileum, and right side of the colon drain the ingested infectious material, which accounts for the common involvement of the mesenteric root,