spindle cell-type GISTs, the most common mesenchymal neoplasm of the stomach, are positive for c-kit/CD117 and DOG1 as well as CD34. Approximately 5% of GISTs are negative for c-kit/CD117 and are subsequently called c-kit negative GISTs.[9] The lack of c-kit/CD117 staining in these GISTs can be confused with a gastric perineurioma, which is always c-kit/CD117 negative. Alternatively, the c-kit positive mast cells in perineurioma could be mistaken for true positivity in GIST. The typical perineurial morphological features of fascicular growth pattern and elongated cells with wavy tapered nuclei together with positive perineurial markers and negative GIST markers should point to the correct diagnosis.

Gastric neural or nerve sheath tumours are also not uncommon differential diagnoses for gastric perineuriomas. Schwannomas of the gastrointestinal tract consist of spindled cells that exhibit focal palisading and mild nuclear pleomorphism.[10] They are usually located in the muscularis propria of the stomach. They have prominent peripheral lymphoid cuffs and often have lymphoplasmacytic cells dispersed throughout the lesion. Most gastrointestinal schwannomas lack typical Antoni A and B areas and true nuclear palisading;[11] however, some tumours have foci of nuclear crowding resembling palisading. Perhaps a more common neural tumour that is in the differential diagnosis with perineurioma is mucosal Schwann cell hamartoma which presents as small polypoid lesions composed of spindle cell proliferation displacing glands and pits apart. Mucosal benign epithelioid nerve sheath tumour is another potential mimic of perineurioma but is characterised by more epithelioid cell morphology and intranuclear pseudoinclusions. Ganglioneuroma is different from perineurioma because of the presence of scattered ganglion cells. All of these neural/peripheral nerve sheath tumours are diffusely positive for S100, which sets them apart from perineuriomas.

Inflammatory fibroid polyps (IFP, Vanek tumour) are more commonly seen in the stomach and are one of the top differential diagnoses with gastric perineurioma. They are thought to be of fibroblastic/myofibroblastic origin and have a predilection for the stomach. These lesions have now been shown to be clonal neoplasms with PDGFR-A mutations.[12] IFPs are also submucosal centred lesions with mucosal extension. They have a characteristic perivascular spindle cell proliferation, commonly termed 'onion skin' as well as a prominent eosinophilic background. A short fascicular growth pattern is present in about one-third of the cases. Eosinophils are present in the majority of IFPs, which is a helpful feature in differentiating from perineuriomas; however, rare IFPs have sparse eosinophils but prominent hyalinisation. The majority of IFPs express CD34, however 14% (6/44) are negative for CD34.[12] Nevertheless, the classic perivascular onion skin-like features, rich eosinophils, positive CD34 and negative perineurial markers are typical for IFPs.

In summary, we report a rare case of gastric perineurioma presenting as a sessile gastric body polyp in a patient complaining of reflux-type symptoms and nausea in addition to epigastric pain. The correct diagnosis of gastric perineurioma is essential since this lesion follows a benign prognosis and thus should be differentiated from other more aggressive and common gastric mesenchymal neoplasms such as GIST. An appropriate diagnostic approach would be carefully reviewing the morphology and using IHC stains to confirm the perineurial differentiation.

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Primary renal sclerosing epithelioid fibrosarcoma: a case report and review of the literature

Sir,
Sclerosing epithelioid fibrosarcoma (SEF) is a rare soft tissue tumour with similar morphological and molecular characteristics to low-grade fibromyxoid sarcoma (LGFMS). SEF is commonly seen in the lower extremities and is composed of epithelioid cells in nests and cords in a sclerotic background.[1] While LGFMS may exhibit a prolonged clinical course with late recurrences or metastases, SEF has a more aggressive clinical course.[2] The majority of LGFMS harbour a *FUS/CREB3L2* or *FUS/CREB3L1* fusion gene with *EWSR1/CREB3L1* fusion reported less frequently.[3,4] In contrast, the *EWSR1/CREB3L1* fusion is most common in SEF followed

by *EWSR1/CREB3L2* and less commonly *FUS* gene rearrangement.[2,5] MUC4, a high-molecular weight transmembrane glycoprotein, is over-expressed in most LGFMS and SEF and is a sensitive and specific immunohistochemistry marker for these neoplasms.[6]

Several other tumours with epithelioid morphology can mimic SEF; hence, its diagnosis can be challenging. The presence of the *EWSR1/CREB3L1* fusion gene as a surrogate marker for SEF has recently given this entity more recognition. Primary renal SEF is extremely rare and only a few cases have been reported in literature (Table 1).[7–9] In the current study, a case of a genetically confirmed primary renal SEF with a review of the literature is presented.

A 30-year-old male presented to his local physician with sharp and persistent left flank pain, shortness of breath, and nausea. Three days prior to admission to the hospital, the patient reported experiencing haematuria, but denied having a fever or other urinary or gastrointestinal symptoms. His past medical history was otherwise non-contributory. A non-contrast computed tomography (CT) scan of the abdomen showed a well-circumscribed 5.3 cm expansile solid mass in the inferior pole of the left kidney. Within 2 months the mass grew to 13.7 cm with focal micro-calcifications and invasion into the collecting system. There was no evidence of lymph node or distant metastasis. The patient underwent a left radical nephrectomy and a diagnosis of sarcoma not otherwise specified was rendered. Post-surgery, the patient was lost to follow-up until 2.5 years later when he presented with abdominal pain. A CT-scan of the abdomen demonstrated a 15.1 cm mass in the nephrectomy fossa with mesenteric and perihepatic lymphadenopathy.

Gross examination of the original nephrectomy specimen revealed a nodular mass measuring 15.0 × 11.0 × 11.0 cm occupying the lower pole with foci of necrosis. Although the mass abutted the renal capsule, there was no evidence of overt invasion. The tumour had also distorted the renal pelvis with no infiltration into the urothelial structure. Histopathologically, the neoplasm was composed of sheets, nests, and cords of epithelioid cells with inconspicuous nucleoli and eosinophilic to clear cytoplasm in a background of hyaline sclerosis. Foci of calcification and tumour necrosis were also present (Fig. 1).

The tumour cells were diffusely immunoreactive for vimentin, Bcl2, MUC4, and focally for CD99 and negative for pankeratin, EMA, CD10, CD117, RCC, desmin, CD45, S-100 protein, CD56, WT-1, and myogenin. INI-1 immunostaining was retained. Ki-67 showed a proliferation index of 15−20%.

Fluorescence *in situ* hybridisation (FISH) analysis using an *EWSR1* break-apart probe (Abbott Molecular, USA) showed loss of the 3′ (telomeric) signal in 98% of the 200 interphase cells analysed (Fig. 2A). Reverse transcription-polymerase chain reaction (RT-PCR) studies for potential select *EWSR1* partners (*FLI1, ERG*, and *WT1*) were negative. RNA was also extracted from representative tissue for targeted next generation sequencing testing using the Archer FusionPlex Solid Tumour Kit (Caris Life Sciences, USA). A fusion between exon 8 of the *EWSR1* gene and exon 6 of the *CREB3L1* gene that maintained an open reading frame was detected. This fusion is predicted to create a functional *EWSR1/ CREB3L1* fusion gene. Specifically, the breakpoint occurring within *CREB3L1* exon 6 included extra inserted nucleotide(s) (Fig. 2C). This finding was confirmed by RT-PCR and Sanger sequencing.

Subsequent FISH analysis using a custom *EWSR1/ CREB3L1* dual colour, dual fusion probe set as previously described[10] showed fusion signal in 83% of the 53 interphase cells analysed (Fig. 2B).

The recurrent tumour was found to be unresectable and the patient was treated with systemic chemotherapy, which included cyclophosphamide (1200 mg/m^2), doxorubicin (75 mg/m^2), and vincristine (2 mg) alternating with ifosfamide/mesna (1800 mg/m^2) and etoposide (100 mg/m^2), given every 21 days. After 4 cycles of chemotherapy, restaging with CT scan of the abdomen showed stable disease with no additional lymphadenopathy or metastasis.

The cAMP response element-binding (CREB) and CREB-like proteins are transcription factors that are involved with cell proliferation, survival and differentiation.[10] EWSR1 and FUS proteins belong to FET protein family that regulates gene expression and mRNA/micro-RNA processing.[11] Translocations involving these two gene families are seen in several mesenchymal tumours including clear cell sarcoma,[12] primary pulmonary myxoid sarcoma,[12] LGFMS,[3] and SEF, among others.[5]

Primary renal SEF is an extremely rare tumour and only a few cases have been reported to date (Table 1). There is no

Table 1 Primary renal sclerosing epithelioid fibrosarcoma

Ref	Age/Sex	Size (cm)	Relapse/Met	Follow-Up	MUC4 IHC	*EWSR1* break apart FISH	*EWSR1/CREB3L1 (FISH)*
Current study	30/Male	13.7	Relapsed/LN	Alive (3 years F/U)	Positive	Loss of 3' *EWSR1* probe signal	Positive
Arbajian *et al.*[2]	41/Female	9	Lung	DOD	Positive	Loss of 3' *EWSR1* probe signal	ND
Argani *et al.*[7]	17/Male	25	Bone/liver	DOD	Positive	ND	Positive
Argani *et al.*[7]	61/Female	5	Bone/Lung/LN	DOD	Positive	ND	Positive
Ohlmann *et al.*[9]	24/Female	22	Bone/Lung	DOD	Positive	ND	ND
Ohlmann *et al.*[9]	43/Male	4.2	None	Alive (8 months F/U)	Positive	Positive for rearrangement (split signals)	ND
Ertoy Baydar *et al.*[8]	16/Female	7	Bone/Lung	Alive (30 months F/U)	Positive	Loss of 3' *EWSR1* probe signal	Positive
Ertoy Baydar *et al.*[8]	57/Female	7.5	None	Alive (10 months F/U)	Positive	ND	Positive

DOD, died of disease; F/U, follow-up; LN, lymph node; ND, not done.