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Multiple GIST and pheochromocytoma - A rare association in neurofibromatosis type 1

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Dear Editor,

A 32-year-old male presented to the emergency department with a 3-day history of melena and asthenia. Upon admission, the physical examination revealed conjunctival pallor and four small café-au-lait spots on the arms and back. He had no personal or family health history. Laboratory testing showed normocytic normochromic anemia (hemoglobin [Hb] 10.6 g/dL, compared to 16.0 g/dL two months earlier). Esophagastroduodenoscopy was normal. Subsequently, an ileocolonoscopy was performed, which revealed only blood residues in the terminal ileum. Accordingly, the patient ingested a small bowel capsule (MC1600, Intromedic), which revealed an actively bleeding subepithelial lesion with a central umbilication in the proximal jejunum (Fig. 1A).

An antegrade single balloon enteroscopy was then performed, uncovering three subepithelial lesions in the proximal jejunum measuring 1.0 cm, 1.5 cm and 2.5 cm (Fig. 1 B-D). The latter two lesions were ulcerated and had recent bleeding stigmata; and biopsies were taken. Computed tomography revealed several polypoid intraluminal lesions in the jejunum, with early contrast enhancement (Fig. 1E). Additionally, a 3.6 cm lesion was identified in the left adrenal gland, heterogeneous with a necrotic nucleus (Figure F). The jejunal lesions were identified as low-grade fusocellular GIST, exhibiting diffuse staining for CD117, CD34 and DOG1. Next-generation sequencing studies ruled out KIT and platelet-derived growth factor receptor-α (PDGFRA) mutations. Functional analysis of the adrenal gland revealed elevated urinary metanephrines and chromogranin A, consistent with pheochromocytoma. After multidisciplinary discussion, unilateral adrenalectomy and segmental enterectomy were proposed. Pathology of the surgical specimens confirmed the diagnosis of multifocal gastrointestinal stromal tumors (GIST), the largest was 3.5 cm (Fig. 1G) and pheochromocytoma (5.0 x 4.0 x 3.0 cm) (Fig. 1H). The coexistence of these diagnoses has been rarely reported in neurofibromatosis type 1 (NF1), an autosomal-dominant disorder associated with syndromic GIST in up to 7 % of patients (1) and with pheochromocytoma in up to 5 % (2). Post-surgery, the patient was referred for genetic consultation. The molecular study of the NF1 gene revealed a pathogenic variant with a deletion of a codon (c6789_6792del) in heterozygosity. This is the first report of a young, newly diagnosed case of NF1 presenting with this combination of conditions. Additionally, it underscores the importance of urgently evaluating
ongoing small bowel bleeding (3,4), which is often self-controlled and episodic (5). This case also highlights the need for a high index of suspicion to diagnose syndromic GIST in patients without a prior familial history.

References
Figure 1.