article, editing of the table, critical revision of the article, and final approval.

## Ethical approval

The study researchers have carried out their tasks in compliance with the ethical principles of clinical research established in the Declaration of Helsinki, and with the norms of Good Clinical Practices (International Conference on Harmonization).

The data underlying this short report cannot be shared publicly in order to protect the privacy of the subjects for ethical/privacy reasons. The data, without personal identification of participant subjects, will be shared on reasonable request to the corresponding author.

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## Conflict of interest

Albert Martín-Cardona has received financial support for travelling and educational activities from Abbvie, Biogen, Ferring, Jannsen, MSD, Takeda, Dr Falk Pharma and Tillotts.

Jordi Guardiola has served as a speaker and as consultant for or has received research or education funding from MSD, Abbvie, Kern, Pfizer, Takeda, Janssen, Ferring, Roche and General Electric.

Francisco Rodríguez-Moranta has served as a speaker for Abbvie, Takeda, Pfizer, Jansen, and MSD, and has served as an advisor for Abbvie, Jansen, MSD, and Pfizer.

The rest of the authors declare no conflicts of interest.

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# Iron deficiency anemia as the first manifestation of juvenile polyposis syndrome

## Anemia ferropénica como primera manifestación del síndrome de poliposis juvenil

We present the case of a 41-year-old woman with a history of Wilms' tumour in childhood and a mother who died of colorectal cancer at the age of 28, referred to the gastroenterology department for iron deficiency anaemia refractory to intravenous iron over the course of a year. Initial gastroscopy revealed more than 200 gastric polyps measuring 3—18 mm, grouped in mammillated masses in the subcardial, distal body, incisura and antrum areas. Characterisation with white light and narrow band imaging (NBI) showed erythematous lesions with a smooth surface, friability with adherent fresh blood-stained debris, tubulo-villous appearance and a dense but regular vascular pattern. Endoscopic ultrasound scan showed a marked irregular thickening of the mucosa, without echogenicity changes, infiltration of other layers or adjacent lymphadenopathy. Polypectomy was performed on the larger lesions, with the pathology study reporting they were compatible with hyperplastic polyps (HP). After assessment by a multidisciplinary committee and in agreement with the patient, the decision was made for minimally invasive treatment by endoscopic resection. In the third gastroscopy, histology of some fragments detected adenomatous changes with low-grade dysplasia and a focus of adenocarcinoma. The genetic study detected a mutation in exon 11 of the *SMAD4* gene, compatible with juvenile polyposis syndrome (juvPS). Tumour markers, colonoscopy, capsule endoscopy, angio-CT and extension CT, echocardiography and exploratory laparoscopy did not detect any distant spread or other associated abnormalities. The patient had

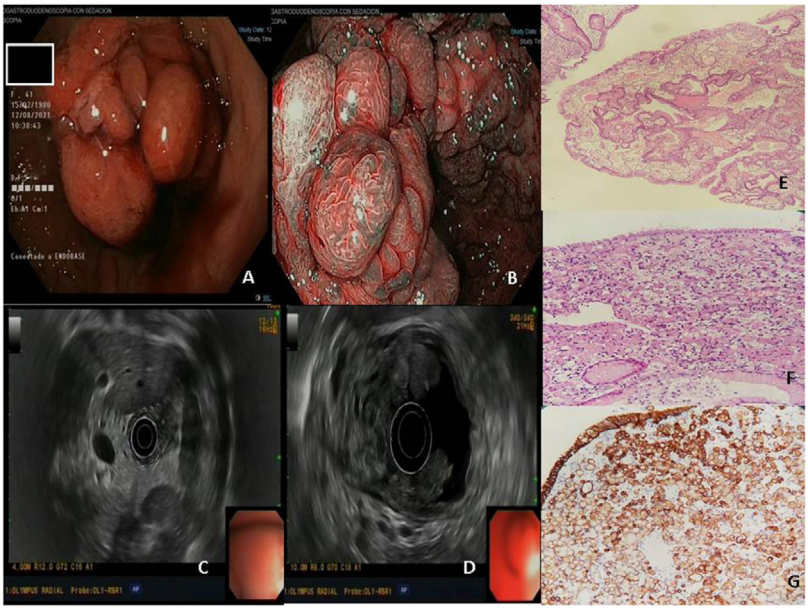


**Figure 1** A and B. Images of white light gastroscopy and NBI respectively, showing hyperplastic gastric polyps. C and D. Linear endoscopy showing marked irregular thickening of the gastric mucosa, with luminal protrusions corresponding to gastric polyps. The last three images correspond to the pathology study of different polypectomy fragments. Image E corresponds to an H-E stain, showing a polypoid formation of hyperplastic glandular epithelium and capillary congestion. Images F (H-E staining) and G (PAN-CK immunohistochemical study) depict neoplastic infiltration by poorly cohesive adenocarcinoma with signet ring cells.

laparoscopic total gastrectomy with lymphadenectomy, with a good outcome.

Gynaecological losses are the most common cause of iron deficiency anaemia in women of childbearing age. Gastrointestinal causes are the second most prevalent, whether through malabsorption or losses from the gastrointestinal tract. In the absence of clinical guidance, double-balloon enteroscopy is indicated as a first diagnostic approach.[1]

HP are the most common gastric polyps. They can be single (75%), multiple or as a component of diffuse hyperplastic polyposis syndrome *(gastric adenocarcinoma and proximal polyposis of the stomach [GAPPS]*; defined as more than 50 HP).[2] They are reported more frequently in areas with a high prevalence of *Helicobacter pylori*.

They sometimes occur in the context of polyposis syndromes such as juvPS, Gardner syndrome or Peutz-Jeghers syndrome.[3] HP related to a syndrome are macroscopically and histologically indistinguishable from sporadic HP and are associated with a higher risk of malignancy.[4]

Of autosomal dominant inheritance, juvPS is characterised by a predisposition to develop juvenile/hamartomatous polyps (juvP) in the gastrointestinal tract. The incidence is estimated at 1:16,000–1:100,000. It may be asymptomatic or onset may be in the form of anaemia, gastrointestinal bleeding or abdominal pain. At least one of the following criteria have to be met for the diagnosis to be made[5]:

- More than five juvP in colon or rectum.
- Multiple juvP in the upper or lower gastrointestinal tract.
- Any number of juvP along with a family history of juvPS.

Diagnosis of juvP is highly complex because of their similarity on pathology examination to other gastrointestinal polyps. They are more common in the colon or rectum and gastric-only involvement is usually associated with the *SMAD4* mutation.[3] Most are benign but they can degenerate, with colorectal cancer being the cancer most commonly associated. The incidence of stomach cancer is as high as 21% in patients with gastric polyps (Fig. 1).

Individuals with clinical criteria for juvPS should be screened for *BMPR1A* and *SMAD4* gene mutations, although only 40% will have a known germline mutation detected. The pathogenic variant of *SMAD4* is associated with pulmonary, hepatic and intracranial arteriovenous malformations, aortic disease, epistaxis and telangiectasias.

Diagnosis of juvPS requires a thorough examination of the gastrointestinal tract, resecting any polyps observed to reduce the risk of bleeding, obstruction or malignancy. Partial/total gastrectomy/colectomy will be necessary in the case of endoscopically uncontrollable polyps (>50–100), severe gastrointestinal bleeding, dysplasia or family history of cancer.

Follow-up by gastroscopy and colonoscopy is recommended every three years starting at 15 years of age, or earlier if the patient has symptoms. If polyps are detected, follow-up will be annual. In patients undergoing surgery, monitoring should be continued of the remaining segments.[5]

Genetic screening of high-risk relatives is necessary if the pathogenic variant involved is known. Otherwise, follow-up should be by colonoscopy.

Our patient developed gastric adenocarcinoma with pT1aG3 signet ring cells, with no perineural or lymphovascular invasion, HER2 negative and no alteration in repair proteins. At this stage (IA), the administration of adjuvant

treatment has shown no benefit, so we have started to perform six-monthly CT scans.

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## Conflicts of interest

The authors declare that they have no conflicts of interest.

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