



Body Imaging

Combined juvenile polyposis syndrome and hereditary hemorrhagic telangiectasia (JPS/HHT) with MRI and endoscopic correlation

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ABSTRACT

Juvenile polyposis syndrome (JPS) may coexist with hereditary hemorrhagic telangiectasia (HHT) due to implication of the SMAD4 gene in a subset of both diseases. To the best of our knowledge, we present the first case in the radiologic literature on the MRI findings in a patient with this rare combined diagnosis undergoing workup for burden of disease.

1. Introduction

Juvenile polyposis syndrome (JPS) is an uncommon autosomal dominant inherited condition characterized by the development of multiple hamartomatous (juvenile) polyps throughout the gastrointestinal tract. Polyps may occur anywhere along the gastrointestinal tract, though the colon and rectum are common sites. JPS affect approximately 1 in 100,000 people and affected individuals are at increased lifetime risk of malignancy [1].

Hereditary hemorrhagic telangiectasia (HHT), also known as Osler-Weber-Rendu syndrome, is another uncommon autosomal dominant inherited condition characterized by the development of multiple arteriovenous malformations (AVMs). Its incidence varies geographically, ranging from 1 in 2300 to 1 in 39,000 [2].

A rare combined syndrome exhibiting features of both JPS and HHT has been reported in the literature, with the first case described in 1980 [3]. This presentation is believed to be related to a common genetic pathway between a subset of each syndrome [1]. We report a patient with combined JPS/HHT with MRI correlation, which, to the best of our knowledge, has not been previously reported in the literature.

2. Case report

A 56-year-old African-American male presented with recurrent upper gastrointestinal bleeding resulting in anemia. Past medical history is notable for a known diagnosis of JPS/HHT related to *SMAD4* gene mutation and stage I ampullary adenocarcinoma 4 years earlier. Family history was significant for a mother with HHT who died in the third decade secondary to intracranial hemorrhage and a son with JPS/

HHT who died as a teenager secondary to colon and ampullary carcinomas. Past surgical history includes Whipple procedure for ampullary carcinoma and prior partial colectomy.

MR enterography was performed to evaluate for small bowel disease as part of consideration for gastric resection for treatment of upper gastrointestinal bleeding. Extensive hamartomatous polyps were noted within the stomach, appearing as innumerable large T2 intermediate signal frond-like masses projecting into the gastric lumen. The largest polyp was in the gastric fundus, measuring up to 5 cm, however the bulk of disease was within the gastric antrum, prolapsing into the gastrojejunal anastomosis (Fig. 1A–C). Imaging findings correlated well with findings on upper endoscopy (Fig. 1D–E). No definite small bowel disease was identified.

Multiple arteriovenous malformations were noted involving the liver, with innumerable tortuous disorganized vascular niduses, in keeping with the HHT component of the patient's syndrome (Fig. 2). There was associated enlargement of the celiac trunk, hepatic arteries, portal and splenic veins related to associated vascular shunting. A T1- and T2-isointense rounded lesion was present within the right hepatic lobe with avid arterial hyperenhancement and high T2 signal intensity central scar in keeping with a focal nodular hyperplasia (FNH) (Fig. 3), which has a known association with HHT [4].

3. Discussion

JPS affects approximately 1 in 100,000 people [1]. Diagnostic criteria include one of the following: more than five juvenile polyps in the colon and rectum; multiple juvenile polyps distributed throughout the gastrointestinal tract; or any number of juvenile polyps in a patient with

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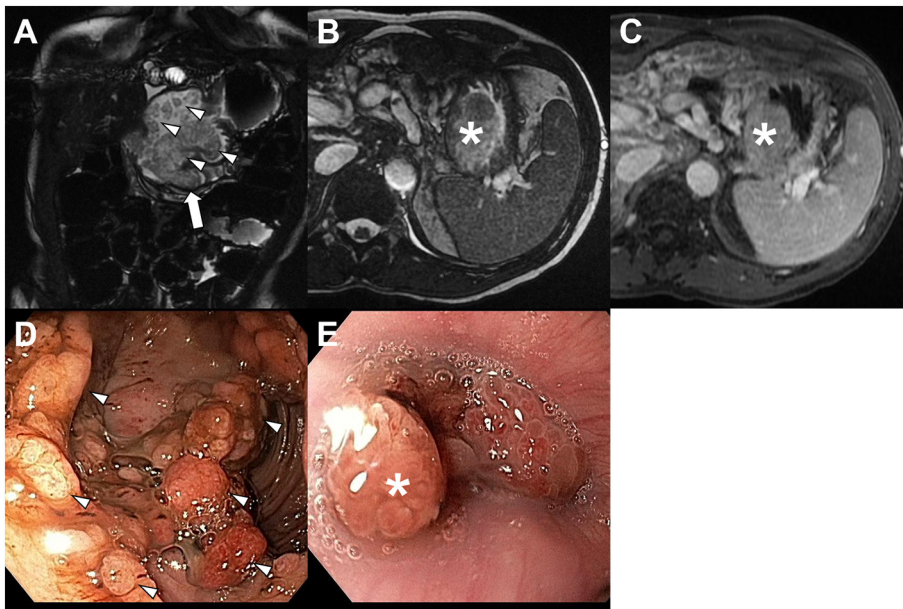


Fig. 1. A 56-year-old male with JPS/HHT. (A) Coronal T2-weighted MRI image demonstrates extensive intermediate signal intensity polyposis within the gastric antrum (arrowheads). Patient is status post Whipple procedure for prior ampullary adenocarcinoma with polyps prolapsing through the gastrojejunal anastomosis into the proximal jejunum (arrow). (B) Axial T2-weighted MRI image at the level of the gastric fundus demonstrates a large T2-intermediate signal polyp (asterisk). (C) Axial fat-suppressed T1-weighted MR image with contrast demonstrates homogeneous enhancement of the fundal polyp (asterisk). (D) Endoscopic image at the level of the gastric antrum shows abundant polyposis (arrowheads), corresponding to the MRI findings in A. (E) Endoscopic image at the level of the gastric fundus shows a large polyp near the gastroesophageal junction (asterisk), corresponding to the MRI findings in B–C.

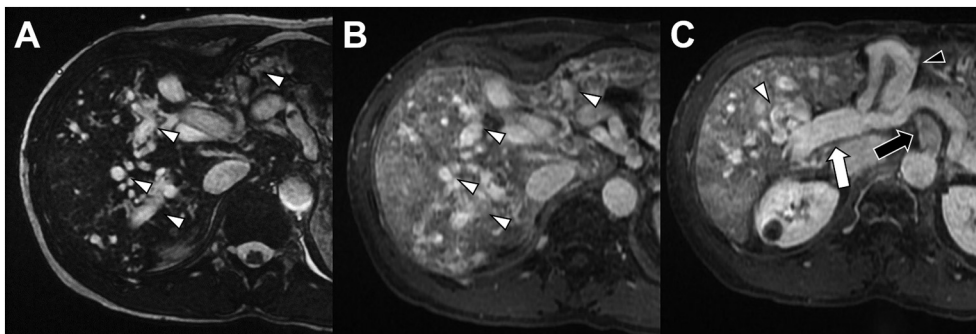


Fig. 2. A 56-year-old male with JPS/HHT. (A) Axial T2-weighted MR image demonstrate innumerable prominent tortuous vessels throughout the liver parenchyma consistent with known AVMs (white arrowheads). (B) Axial fat-suppressed T1-weighted MR image with intravenous contrast shows homogeneous enhancement of the AVMs (white arrowheads) iso-enhancing to the blood pool. (C) Axial fat-suppressed T1-weighted MR image shows marked enlargement and tortuosity of the celiac trunk (black arrow), common hepatic artery (black arrowhead), portal and splenic veins (white arrow), related to shunting from HHT. Arteriovenous malformations are again noted within the liver (white arrowhead). Incidental right renal cyst.

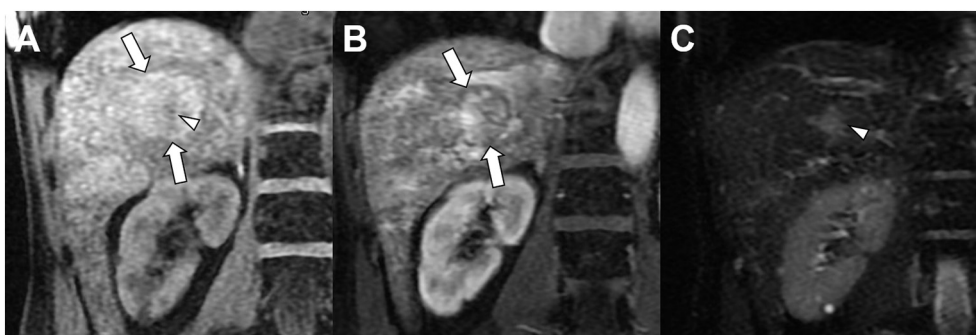


Fig. 3. A 56-year-old male with JPS/HHT. (A) Coronal fat-suppressed T1-weighted image without intravenous contrast shows a rounded lesion within the right hepatic lobe (arrows), which is isointense to background liver with T1-hypointense central scar (arrowhead). (B) Coronal fat-suppressed T1-weighted image with intravenous contrast shows arterial enhancement of the lesion (arrows), which is typical of FNH. (C) Coronal Fat-suppressed T2-weighted image shows T2 hyperintensity of the central scar (arrowhead), which is characteristic of FNH. Multiple right renal cysts are incidentally noted.

family history of juvenile polyposis [1,5]. The polyps in JPS have a distinctive histologic appearance with cystic dilated cuboidal/columnar-lined glands surrounded by edematous lamina propria and inflammatory cells, likely accounting for the intermediate/high T2 signal intensity of the gastric polyps in our patient [6]. While the polyps are considered benign, these patients are at an elevated risk of gastrointestinal malignancy (up to 50%) and may present with other complications of polyposis such as bleeding and anemia [5,6]. Pathogenesis of JPS has been tied to mutations in the *SMAD4* or *BMPRI1A* genes in the

majority of cases.

HHT is slightly more common than JPS, with incidences ranging from 1 in 2300 to 1 in 39,000 depending on the population [2]. Diagnostic criteria include three or more of the following criteria: epistaxis, mucocutaneous telangiectasias, visceral AVMs, and/or a family history of HHT [7]. Larger visceral AVMs typically affect the lungs, liver, and brain whereas smaller AVMs (telangiectasias) are noted cutaneously affecting the face, tongue, oral mucosa, chest, and fingers [7]. At imaging, abdominal manifestations of HHT are typically hepatic,

with vascular malformations of various sizes resulting in arteriovenous and arterioportal shunting [8]. HHT is also associated with a higher incidence of FNH, as seen in our case, with a reported incidence of 2.9% in HHT versus 0.6% in the average population [4,9]. Complications are usually related to bleeding or hemodynamically significant arteriovenous shunting. Enlargement of the hepatic arteries and portal veins is common, as seen in our case, and is related to the degree of shunting with hepatic artery and portal vein caliber correlative with cardiac output [10]. Pathogenesis of HHT has been tied to mutations in the *ACVRL1*, *ENG*, *GDF2*, or *SMAD4* genes.

The combined JPS/HHT phenotype has been linked to subsets of both syndromes which are secondary to mutations in the *SMAD4* gene. In a study of 80 unrelated families with juvenile polyposis syndrome, Aretz et al. found that 35% of cases of JPS were tied to *SMAD4* mutations, of which 22% exhibited features of HHT [11]. Based on these estimates, an incidence for combined JPS/HHT of approximately 1 in 1,250,000 would be expected. In patients with combined JPS/HHT, screening should be performed for *SMAD4* gene mutations. Family history will often reveal additional affected family members, given autosomal dominant inheritance. Genetic counseling for both the patient and family members may be beneficial. Management will typically consist of regular screening colonoscopy and upper endoscopy as well as polypectomy to prevent complications from mechanical bowel obstruction, bleeding, and malignant transformation [5]. Surgical resection may also be considered, depending on the distribution of polyposis, as in our patient. Hepatic AVMs, as in our patient, are typically treated medically; pulmonary and intracranial AVMs may be treated by embolization or surgically, depending on their size and location; and cutaneous telangiectasias may be treated medically or with localized laser ablation or sclerotherapy [7].

In our patient, MRI was able to provide an overview of the burden of disease for both the gastrointestinal polyposis as well as the vascular malformations. MR enterography may be particularly useful in evaluating the small bowel, which is difficult to reach endoscopically. It is also useful in delineating the anatomy in patients who have had prior resections, as in our patient. However, small lesions, which remain visible endoscopically may be undetectable at imaging. Patients with

inherited syndromes of disease may be at risk of other disease phenotypes due to the overlap in the genetic basis for multiple syndromes. Radiologists should be aware of the possibility of such associations, as other syndromic findings outside the classic spectrum of disease may be first detected at imaging.

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