A case of hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu disease) with multiple polyps arising in the cecum and appendix

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Abstract

We present the case of a 32-year-old female with cecal and appendiceal polyps that were removed by laparoscopy-assisted surgery. She also had recurrent nosebleeds due to telangiectases in the nasal mucosa and arteriovenous malformations in the lung, all of which contributed to the diagnosis of hereditary hemorrhagic telangiectasia. (Acta gastroenterol. belg., **2011**, 74, **352-354**).

Key words : Osler-Weber-Rendu disease, hereditary hemorrhagic telangiectasia, juvenile polyposis, colon cancer.

Introduction

Hereditary hemorrhagic telangiectasia (HHT), also known as Osler-Weber-Rendu disease, is an autosomal dominant inherited disease of vascular malformation affecting at least 1 in 10,000 men and women (1). Characteristics include spontaneous recurrent epistaxis, cutaneous telangiectasia, visceral arteriovenous malformations (AVMs) and a positive family history (2,3).

It is now known that a subpopulation of HHT patients has a combined syndrome of juvenile polyposis and HHT (JPHT) (4,5), which is associated with mutations in MADH4 (SMAD4) (6). However there have only been a few reports in English regarding colonic adenomatous polyps and adenocarcinoma in HHT patients (7,8).

We herein report a case of HHT with cecal and appendiceal polyps that included adenomas on histological examination, and discuss the clinical and genetic features in diverse types of HHTs by reviewing the literature.

Case report

A 32-year-old female visited a clinic in her neighborhood because her annual health check showed positive occult blood in her stool. Since barium enema and colonoscopy showed polyps in the cecum, she was referred to our surgical department for further examination. Laboratory tests showed normal findings except for iron-deficiency anemia (10.1 g/dL of hemoglobin). Double contrast barium enema examination showed a polypoid tumor, 3 centimeters in diameter, in the cecum below the ileocecal valve (Fig. 1). Colonoscopy revealed two cecal polyps (Fig. 2), but the orifice of the appendix vermiformis could not be identified. Pathological examination of biopsy specimens revealed that the larger polyp was a tubular adenoma with severe atypia, and the other an inflammatory polyp. A computed tomography (CT) scan of the chest revealed bilateral pulmonary arteriovenous malformations (AVMs) (Fig. 3). Magnetic resonance images (MRI) disclosed old infarctions, hemorrhages, and a small aneurysm in the cerebrum. Further questioning of the patient with regard to her symptoms and family history revealed that she and her father had recurrent nosebleeds and that he also had multiple colonic polyps. On examination by an otolaryngologist, the patient was found to have telangiectases in her nasal mucosa. In consideration of the above, our patient fulfilled the criteria for and was diagnosed with HHT.

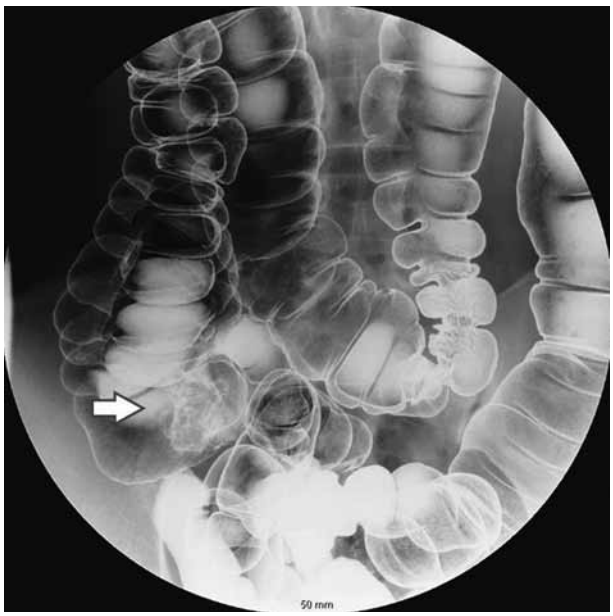

Fig. 1. — A barium enema revealed a polypoid tumor (arrow), measuring 3 centimeters in diameter, at the bottom of the cecum.

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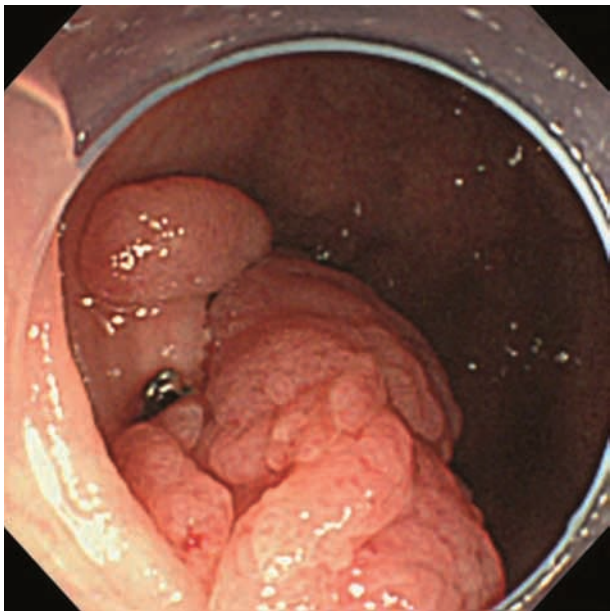

Fig. 2. — Endoscopic appearance of a polypoidal lesion in the cecum.

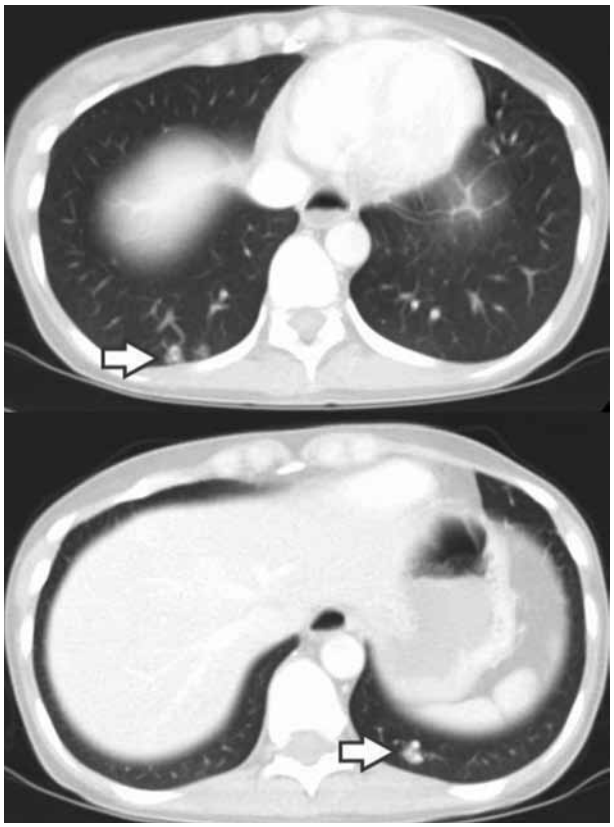

Fig. 3. — A computed tomography scan revealed bilateral pulmonary arteriovenous malformations (arrows).

We performed a laparoscopy-assisted ileocecal resection with regional lymph node dissection in the case of possible malignancy. The resected specimen was found to bear 7 polyps in the cecum and appendix. The largest tumor was 3 × 2 cm in size and arose from the orifice of the appendix (Fig. 4 ; arrow). Histologically the tumor consisted of tubular adenoma cells with severe atypia (Fig. 5). The other small polyps were either tubular adenomas or inflammatory polyps.

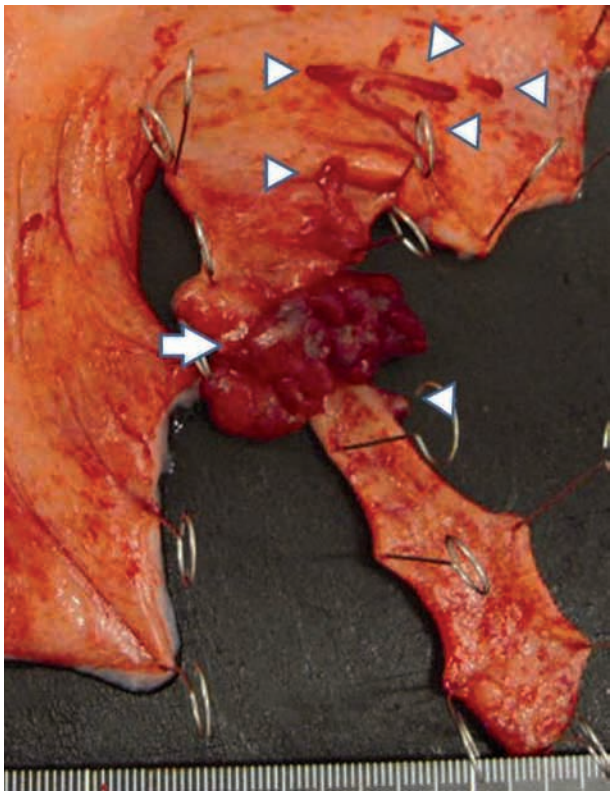

Fig. 4. — Gross appearance of the resected specimen. The largest tumor (arrow) corresponds to the main tumor found in the preoperative image studies as shown in Fig.1 and 2. In addition, 6 polyps (arrowheads) were present in the cecum and the appendix distal to the main tumor.

The patient's post-operative recovery was uncomplicated. She is currently doing well two and a half years after surgery, and is regularly checked at the outpatient clinic in our hospital.

Discussion

HHT is a rare fibrovascular dysplasia that makes vascular walls vulnerable to trauma and rupture, causing bleeding of the skin and mucosa. International consensus diagnostic criteria (Curaçao criteria) for HHT have been developed based on four findings : (1) spontaneous recurrent nosebleeds, (2) multiple mucocutaneous telangiectases, (3) visceral involvement and (4) an affected first-degree relative. *Definite* HHT can be diagnosed when three or more criteria are present and *suspected* HHT when two criteria are present ; otherwise the case is categorized as *unlikely* HHT (9).

Genetically, HHT is heterogeneous and can be divided into subtypes (10). In HHT1, the genetic mutation at chromosome 9q3 has been identified as involving endoglin. This encodes an integral membrane glycoprotein that

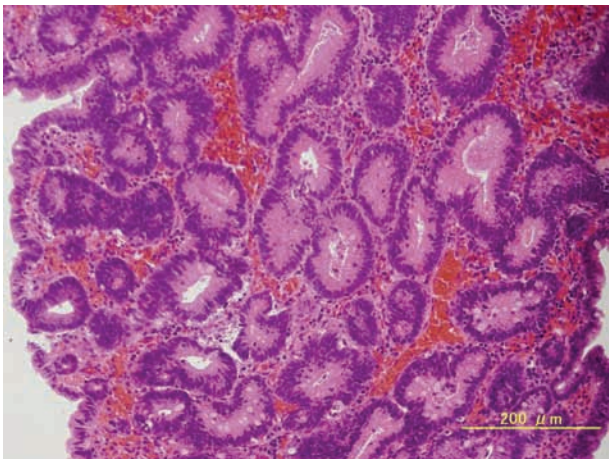

Fig. 5. — Microscopic examination of the largest tumor shows tubular adenoma with severe atypia (hematoxylin and eosin). The bar indicates 200 μm.

binds TGF β. HHT2 is caused by an abnormality in the gene on chromosome 12q13 encoding activin A receptor typeII-like 1, a cell surface receptor of the TGF β superfamily. The loci for HHT3 (11) and HHT4 (12) were recently identified by linkage analysis. Moreover, Gallione *et al.* reported that HHT patients with juvenile polyposis (JPHT) showed several types of mutations in MADH4 (SMAD4) (6).

Elinav *et al.* reported in 2004 that, irrespective of the presence or absence of JPHT, HHT itself has a possible association with malignancies, including colon cancer (7). In their study, 6 of 24 patients with HHT developed colonic neoplasm or adenomatous polyposis, leading them to propose that a full visualization of the colon is indicated for HHT patients with anemia. The colonic polyps arising in our patient were histologically adenomatous and inflammatory polyps. Furthermore, her blood sample was subjected to sequence analysis of the MADH4 gene after written informed consent was obtained. We confirmed that she had no genetic alteration in exons 8, 9 and 11 of MADH4, which cover all the previously reported mutations (data not shown) (6). These findings suggested that cases with HHT and adenomatous polyps fall into a new disease entity that is distinct from JPHT and that awaits the identification of causative gene(s).

In conclusion, our patient reminds us that the gastrointestinal tract manifestations of HHT are not limited to gastrointestinal telangiectasia but can also include gastrointestinal polyps. Based on the current case report, a workup for gastrointestinal polyps and their potential malignancy should be considered in all patients with HHT.

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