

Differential diagnosis of iron deficiency anemia in a patient with chronic kidney disease and myasthenia gravis

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ABSTRACT

Background: Iron deficiency anemia is the most common cause of anemia worldwide. The differential diagnosis of this entity remains one of the most encountered problems: from thalassemia, neoplasia, malabsorption syndrome to chronic kidney disease under hemodialysis.

Case report: This case report describes clinical and paraclinical features of a 75-year-old patient with multiple comorbidities and iron deficiency anemia. We emphasize on the importance of endoscopic videocapsule examination for the accurate diagnosis of iron deficiency anemia when other methods fail (endoscopy and colonoscopy), thus revealing the source of bleeding in a small bowel benign polyp. Thus, tumors of the small intestine present as a unique challenging diagnosis.

Conclusion: Endoscopic videocapsule, even if expensive, should remain an important tool in the diagnosis of iron deficiency anemia with normal upper GI endoscopy and colonoscopy. Small bowel tumors are seldom considered as a diagnostic hypothesis, but should not be overlooked, especially when alarm symptoms are present (weight loss, melena, hematochesia).

Keywords: anemia, videocapsule, small bowel, tumor

INTRODUCTION

Iron deficiency anemia is the most common form of anemia worldwide, explained by a large number of diseases (1). Neoplasia remains a potential cause and early diagnosis is essential for a good prognosis. When iron deficiency anemia is associated with melena and negative upper and lower endoscopy, the exploration of the small bowel is imperative.

CASE-REPORT

A 75-year old male presented to the emergency room complaining of melena, fatigue and pal-

lor. Even though the fatigue and pallor started 3 weeks prior to presentation, the patient presented melena 2 days before coming to the emergency room. Personal history reveals iron deficiency anemia for one year (for which the patient did not undergo further tests), myasthenia gravis under corticotherapy and treatment with azathioprine, type II diabetes under treatment with oral antidiabetics, cardiac ischemic disease, stage II hypertension, stage IV arteriopathy obliterans, recent gastric polypectomy and right leg and left thumb amputations. On examination, the patient had a BMI of 24 kg/m², body temperature of 36.4°C, respiratory rate 18 per minute, pulse rate 86 per minute, blood pressure 135/60 mmHg. Rectal exam

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showed melena, and the patient presented also right leg and left thumb amputations.

Laboratory results showed severe hypochromic, microcytic, hyposideremic anemia, hyperglycemia, hypoproteinemia and high serum creatinin. Evaluation included normal abdominal ultrasonography, esogastroduodenoscopy (EGD) and colonoscopy, that were within normal range.

At this moment, endoscopic videocapsule was indicated and performed. It showed a 7 small sized polyp and a small pedunculated polyp with a bleeding stigmata in the middle part of the small bowel (Fig. 1); in the terminal ileum, a polipoid, polilobulated, ulcerated mass was found, that occupied more than half of the lumen with slow active bleeding. However this mass did not induce stenosis (Fig. 2).

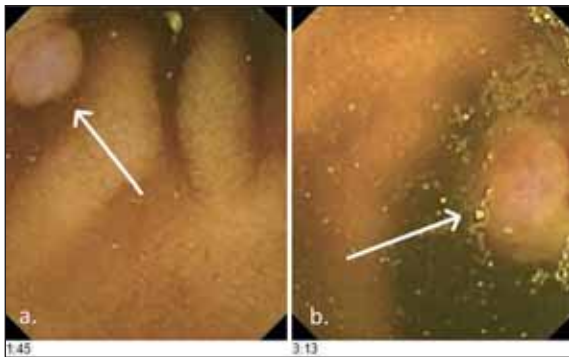


FIGURE 1. Polyps in the middle part of the small bowel: a. small polyp; b. pedunculated polyp with bleeding stigmata

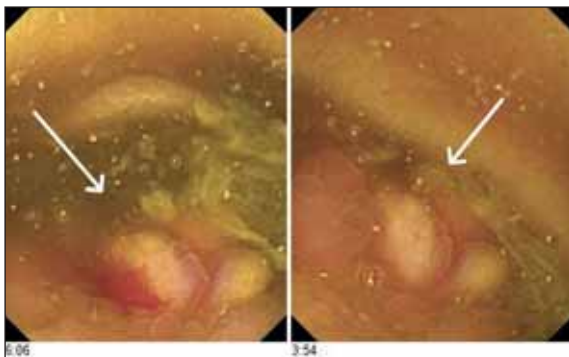


FIGURE 2. Polypoid, polilobulated, ulcerated mass in the terminal ileum, that occupied more than half of the lumen with slow active bleeding

Computerized tomography of the abdomen and pelvis with contrast substance described a polypoid mass in the terminal ileum (3.5/1.8cm), intact peritoneum and normal lymph nodes (Fig. 3).

The patient opted for a surgical treatment that consisted in the removal of the terminal ileum, the appendix, the cecum and in the end an

ileo-colic anastomosis was performed (Fig. 4). The recovery was uneventful and the patient was discharged 4 days postoperatively.



FIGURE 3. Polipoid mass in the terminal ileum (3.5/1.8cm)



FIGURE 4. Intraoperative aspect of the small bowel and polipoid mass

The pathology result revealed an inflammatory fibroid polyp, infirming the malignant suspicion of the mass.

DISCUSSION

Anemia is considered by the World Health Organisation as haemoglobin concentration under 13g/dL in men over 15 years old, below 12g/dL in non-pregnant women over 15 years old and below 11g/dL in pregnant women (2). Iron deficiency anemia occurs when the iron body supplies drop below the limit to support the production of normal erythrocytes. Iron

deficiency is the most encountered deficiency state on a worldwide basis. Multiple causes can explain this entity, as presented in Table 1 (3).

TABLE 1. Etiology of iron deficiency anemia

Etiology of iron deficiency anemia	
Dietary factors	Low intake of sources of heme iron
	Substances that diminish the absorption of ferrous and ferric iron (<i>phytates, phosphates, carbonates, oxalates and tannates</i>)
Hemorrhage	
Congestive heart failure	
Paroxysmal nocturnal haemoglobinuria	
Malabsorption	Celiac disease
	Extensive surgical removal of the proximal bowel
Iron-refractory iron deficiency	
Thalassemia	
Sideroblastic anemia	
Lead poisoning	
Chronic kidney disease under hemodialysis	
Neoplasia	

Myasthenia gravis can associate, in 5-10% of cases, other autoimmune disorders, such as pernicious anemia, thus macrocytic anemia (4). Moreover, chronic renal failure leads to the decrease of production in erythropoietin, therefore a decreased production of red blood cells, often leading to normocytic, normochromic anemia. However, in patients with chronic kidney disease under hemodialysis, iron supply can be limited, leading to hypochromic, microcytic, hypsideremic anemia (5). In our case, despite the multiple comorbidities that can explain the anemia, when associating the symptoms (melena, fatigue and pallor) with hypochromic, microcytic, hypsideremic anemia, a GI bleeding source is the most compelling diagnosis.

Small intestinal benign tumors are rare entities. Even though the small bowel represents 75% of the length and over 90% of the surface area of the gastrointestinal (GI) tract, it is rarely the site for neoplasms, counting for less than 2% of the GI malignancies. The possible subtypes of small bowel benign tumors are: inflammatory polyps, hyperplastic polyps, lipomas, adenomas, hemangiomas and gut (6).

Inflammatory fibroid polyps (IFP) are benign mesenchymal tumors derived from the submucosa of the stomach or the small bowel (seldom encountered in the colon and esophagus). Even though these tumors can distinguish

from gastrointestinal stromal tumors by their morphology, origin (submucosal) and clinical behavior (not aggressive), one common characteristic remains: mutational subtype of PDGFRA gene. Inflammatory fibroid polyps are often undiagnosed for a long time or incidentally found during endoscopy. When they present as large polyps, complications may arise, such as superficial ulcerations, local bleeding (most common clinical symptom also found in our case), intussusception and invagination (7-9).

Despite the fact that our patient was 75 years old, the tumors are mostly encountered in the fifth and sixth decade of life, with a slight predominance in males (10).

Benign small bowel tumors are often asymptomatic. However, in rare cases, these tumors can present with vague and nonspecific symptoms, such as: intermittent pain, constipation, melena, diarrhea, early satiety, palpable mass (in tumors that exceed 6 cm, GI hemorrhage (in larger sized tumors), obstruction, fatigue. In our case, the patient presented fatigue, pallor and melena (GI hemorrhage). Moreover, the tumors can present with complications such as: bowel obstruction, intussusception, volvulus, perforation, GI bleeding (as encountered in our case report). The last can appear in up to 38% of the lesions and can be seen with heme-positive stool or as an acute, active bleeding (6).

Workup lab results can reveal microcytic anemia (as seen in our case). Barium contrast studies can show an upper GI lesion in up to 29% of cases, whilst barium enemas help identify tumors in the distal ileum. One can use selective arteriography not only in diagnosing vascular lesions or embolization of active bleeding, but also in demonstrating aberrant arterial inflow encountered in malignant lesions. Surprisingly, only 29% of cases are diagnosed by computerized tomography. Ultrasound can be useful in demonstrating tumors larger than 4 cm (11). Upper endoscopy can detect tumors of the proximal small bowel in 12-30% of cases and allows for polypectomy in small lesions (12). Capsule endoscopy is considered a breakthrough in the diagnosis of small bowel tumors, as seen in our case report, where other methods (upper and lower endoscopy and ultrasound were negative) failed.

Histologically IFP divide in two types: "intestinal" type, that presents as bland spindle cells arranged in whorls around blood vessels and mucosal glands with fibrillar collagen matrix and the "classic" type (or gastric type). The latter

presents heavy inflammatory infiltrate rich in eosinophilic granulocytes and less collagen than the intestinal type. These tumors present no obvious proliferative activity with a Ki67 under 1%. Immunohistochemically, the spindle cells of IFP are often positive for CD34 (more obvious in gastric type than intestinal type). PDGFRA gene mutation is often found (9).

Surgical treatment remains the treatment of choice in small bowel tumors: exploratory laparotomy with excision of the lesion (13). Enteroscopy would have been an option if the lesion was amenable for endoscopic polypectomy. Moreover incidental found tumors should be

removed to prevent future clinical symptoms or complications. This course of treatment was applied in our patient.

CONCLUSION

Hypochromic, microcytic, hyposideremic anemia can be explained by multiple causes. When associated with gastrointestinal symptoms (melena) and negative upper and lower endoscopy, one should focus on a small bowel bleeding source. Endoscopic videocapsule remains a new and powerful diagnosis tool for this segment of the GI tract.

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