Single Case

Pseudomelanosis Duodeni Appearing after Oral Iron Therapy

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Keywords

Duodenum · Endoscopy · Gastrointestinal tract · Pigmentation disorders

Abstract

Pseudomelanosis duodeni is a rare condition characterized by the endoscopic appearance of diffuse dark pigmentation of the duodenal mucosa. It is typically seen in older women and has been reported to be associated with hypertension, chronic renal disease, diabetes mellitus, gastrointestinal hemorrhage, and the use of medications such as oral iron, furosemide, thiazide, hydralazine, and propranolol. We present a case of pseudomelanosis duodeni appearing after 2 years of oral iron therapy in an 85-year-old woman. Although oral iron supplementation seemed the strongest possible etiology, our patient had multiple comorbidities and was on other medications that have been described as associations. The majority of individuals taking oral iron or under these clinical conditions do not develop this entity; some other factors in patients may be responsible for its occurrence.

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Introduction

Pseudomelanosis duodeni is an unusual endoscopic visualization of dark speckled pigmentation of the duodenal mucosa. It is typically seen in older women and has been reported to be associated with hypertension, chronic renal disease, diabetes mellitus, gastrointestinal hemorrhage, and medications including oral iron, furosemide, thiazide, hydralazine, and propranolol [1–5]. However, underlying cause is not fully elucidated. We report a case of pseudomelanosis duodeni appearing after 2 years of oral iron therapy.

Case Report

An 85-year-old woman with a history of stage III b chronic renal failure, diabetes mellitus, hypertension, atrial fibrillation, spinocerebellar degeneration, and hyperlipidemia referred to our hospital for evaluation of a 2-year history of iron deficiency anemia. She has been taking oral iron with sodium ferrous citrate (50 mg twice daily) for her anemia for the last 2 years. Her other medications including hydrochlorothiazide, digoxin, warfarin, ticlopidine hydrochloride, rabeprazole, glimepiride, sitagliptin, taltirelin, droxidopa, and bezafibrate were prescribed for at least 8 years. Two years prior, esophagogastroduodenoscopy (EGD) was performed and showed no abnormal finding in the duodenum (Fig. 1a, b). With oral iron therapy, her hemoglobin improved from 8.6 to 10.1 g/dL. However, her iron and ferritin were still low level (Table 1).

Although there was no episode of melena or hematochezia, we performed EGD and colonoscopy for the possibility of gastrointestinal lesions including malignant tumors. EGD at this time revealed diffuse dark pigmentation, which were small, round, and homogeneous, in the duodenal bulb (Fig. 2a) and the second portion of the duodenum (Fig. 2b). Since she was taking two kinds of antithrombotic agents (warfarin and ticlopidine hydrochloride), we diagnosed her as having pseudomelanosis duodeni from endoscopic findings and did not perform a biopsy. Colonoscopy showed a 1-cm pedunculated polyp in the sigmoid colon, while no pigmentation was seen. Since her anemia was most likely caused by the polyp, we treated with hot polypectomy and advised follow-up with continuance of oral iron therapy.

Discussion

Pseudomelanosis duodeni was first described by Biscordi and Kleinman in 1976 [5]. Although the exact frequency is unknown, it is usually an incidental finding which may be less recognized due to unawareness of this condition by physicians. Typically, histology demonstrates a fine granular brown material inside the macrophage lysosomes in the lamina propria within the tips of the duodenal villi [7]. While melanosis coli is secondary to the accumulation of lipofuscin in the macrophages [8, 9], the pigment found in pseudomelanosis duodeni reveals to be composed mainly of iron sulfide, although varying amounts of sulfur, calcium, potassium, aluminum, magnesium, and silver are also seen [6, 7, 10]. Prussian blue and Fontana-

Masson stains can be used to detect these pigments in macrophages. Interestingly, staining results may differ due to varying sulfur content and auto-oxidation of iron sulfide to iron oxide [11]; since iron sulfide is known to give a negative reaction whereas iron oxide gives a positive reaction for iron staining.

In the present case, oral iron supplementation seemed to have a strong association for developing this condition since this endoscopic finding appeared after oral iron therapy. To our knowledge, this report is the first to confirm the endoscopic appearance before and after oral iron therapy in a case of pseudomelanosis duodeni. Although our patient had several comorbidities and was on other medications that have been known as associations in the literature, it is unlikely that these drugs are directly related to this occurrence because the patient had been taking them continuously before the appearance of pseudomelanosis duodeni. However, it is known that this pigmentation can be found in the absence of a history of oral iron supplementation [5, 12]. According to Giusto et al. [4], among 17 adult patients with pseudomelanosis duodeni, 13/17 (76%) were on oral iron supplementation, 15/17 (88%) had hypertension, 10/17 (59%) had end-stage renal disease, and 6/17 (35%) had diabetes mellitus. Although the nature and source of the pigment remain unclear, impaired iron transport due to coupling with sulfur is proposed as the mechanism of pigmentation. It has been reported that the source of iron is derived from intramucosal hemorrhage other than oral iron supplementation [13]. Also, certain medications such as antihypertensive drugs are known as the source of sulfur [14, 15]; thus, the source of pigment may not be individual. Moreover, it is unknown why pseudomelanosis duodeni only occurs in certain patients, while most patients taking oral iron or with other associated medical conditions do not demonstrate this entity. Some other patient factors may be related to this impairment of iron transport in the duodenum. The clinical significance and long-term prognosis of pseudomelanosis duodeni is not fully elucidated. Nevertheless, it is considered a benign condition that has not been related to fibrosis, duodenitis, or stricture formation unlike iron or other heavy metal deposition diseases. Hence, any specific therapy or change of medications and endoscopic surveillance have not been determined.

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Statement of Ethics

We have reported this case in compliance with the Declaration of Helsinki. Informed written consent was obtained from the patient's daughter for publication of this case report and any accompanying images.

Conflicts of Interest Statement

All authors have no conflict of interest related to this article.

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Author Contributions

Y.H. performed the endoscopy with the patient's consent. Y.H. wrote the original draft. H.M. and A.F. edited the draft. All the authors read and approved the manuscript.

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Fig. 1. EGD images before oral iron therapy. No significant findings are observed in the duodenal bulb (a) and the second portion of the duodenum (b).

Fig. 2. EGD images after 2 years of oral iron therapy. Diffuse dark pigmentation is seen in the duodenal bulb (a) and the second portion of the duodenum (b). Pigmentation tended to fade towards the anal side (white circle).

Table 1. The laboratory values before and after 2 years of oral iron therapy

Variable	Normal ranges	Before oral iron therapy	After 2 years of oral iron therapy
<i>CBC</i>			
WBC, $\times 10^2/\mu\text{L}$	33–86	86	85
RBC, $10^4/\mu\text{L}$	435–555	237	256
Hb, g/dL	13.7–16.8	8.6	10.1
Ht, %	40.7–50.1	28.6	31.4
MCV, fL	83.6–98.2	99.0	95.4
MCH, pg	27.5–33.2	30.2	30.7
MCHC, g/dL	31.7–35.3	30.1	32.2
Plt, $10^4/\mu\text{L}$	15.8–34.8	20.1	17.8
Ret, %	5.0–20.0	19.2	15.6
<i>Blood chemistry</i>			
BUN, mg/dL	8.0–22.0	17.4	28.1
Creatinine, mg/dL	0.4–0.7	0.93	1.28
Iron, $\mu\text{g/dL}$	40–188	36	54
TIBC, $\mu\text{g/dL}$	246–409	414	325
UIBC, $\mu\text{g/dL}$	137–317	378	271
<i>Serology</i>			
Ferritin, ng/mL	17.9–464	12.9	26.2

CBC, complete blood cell counts; WBC, white blood cells; RBC, red blood cells; Hb, hemoglobin; Ht, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; Plt, platelets; Ret, reticulocytes; BUN, blood urea nitrogen; TIBC, total iron binding capacity; UIBC, unsaturated iron binding capacity.