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CASE REPORT

Iron deficiency anemia due to excessive green tea drinking

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Key Clinical Message

Tea interferes with iron absorption and can lead to iron deficiency anemia when consumed in large quantities. The rechallenge effect of green tea on anemia in a middle-aged man emphasizes the potential causal role of this beverage. Lifestyle and dietary habits are important diagnostic considerations in diseases of this type.

Keywords

Green tea, iron deficiency anemia.

Introduction

Iron deficiency anemia is a prevalent disease worldwide. It is usually caused by chronic blood loss and insufficient intake or malabsorption of iron in food. Making a diagnosis depends on not only symptom evaluation and laboratory examination, but also careful investigation of patient behavior, for example, whether they force themselves to eat non-nutritive material (pica) [1]. On the other hand, ingestion of large amounts of normal food or beverages containing substances that impair iron absorption may be overlooked as a cause of iron deficiency. We aim to present the clinical course of iron deficiency anemia induced by excessive green tea consumption in a middle-aged patient.

Case Report

A 48-year-old businessman with a long history of regularly treated hypertension and type 2 diabetes mellitus was referred for evaluation of persistent anemia first observed by a general practitioner during an examination for progressive exertional dyspnea 1 month prior. He was employed as the sales and marketing manager of a mold production and processing company. He was previously diagnosed with "low-grade" thalassemia, but was allowed to donate blood several times in his twenties while in military service. Despite recent fatigue, he denied fever, dark-colored urine, persistent diarrhea, abdominal bloating or pain, tarry or fatty stool, change of bowel movement, and weight loss. He was not a vegetarian. Physical examination revealed pale conjunctiva and finger nail beds without cheilosis or koilonychias. Blood tests showed a microcytic anemia at initial presentation (Table 1). Hypochromic microcytic red cells with anisocytosis and poikilocytosis were detected in the peripheral blood smear (Fig. 1). The white cells had a normal differential distribution. Alpha-thalassemia trait was identified by positive hemoglobin H staining, but no beta thalassemia pattern was observed in hemoglobin electrophoresis (Table 1). Iron deficiency status was demonstrated by decreased levels of serum ferritin, serum iron, and transferrin saturation with an elevated total iron-binding capacity (Table 1). The serum lead concentration was within normal limits. He was not a carrier of hepatitis B or C virus. Biochemical study did not disclose any liver, renal, or thyroid dysfunction. There was neither microhematuria nor pyuria.

Table 1. Blood routine, iron status, and hemoglobin analysis.

WBC	HB	MCV	PLT
4000/μL	6.2 g/dL	50.2 fl	201,000/μL
Ferritin (23.9~336.2)	Serum Iron (45~182)	TIBC (255~450)	Transferrin saturation (20~50)
1.6 ng/mL	10 μg/dL	513 μg/dL	1.95%
Reticulocyte	HB A	HB A2	HB H
3.8%	98.2%	1.8%	Positive

(): Reference range in our laboratory. WBC, white blood cell; HB, hemoglobin; MCV, mean corpuscular volume; PLT, platelet; TIBC, total iron-binding capacity.

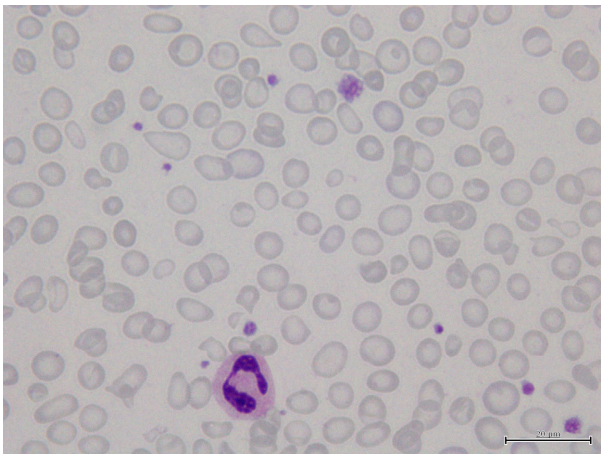

Figure 1. Patient peripheral blood smear at presentation.

Despite low levels of serum tumor markers CEA and CA19-9, we performed gastroscopy and colonoscopy examinations. These revealed no significant bleeding source in the upper and lower gastrointestinal tracts, except for minimal reflux esophagitis, slight superficial gastritis in the antrum, and mild internal hemorrhoids. Endoscopic features of duodenal mucosa atrophy related to celiac disease, such as reduction, scalloping, or mosaic pattern of duodenal folds, were not detected. To rule out possible small intestine tumors, an abdominal CT scan with intravenous and oral nonionic iodine contrast was performed, but abnormal findings were limited to mild splenomegaly with a long axis of approximately 137 mm. There were no features of celiac disease, such as a fluid-filled and progressively more flaccid and dilated small bowel, flocculation, or telescoping. The cause of his iron deficiency remained unexplained until we obtained a beverage history. He told us that he observed the Taiwanese tradition of green tea consumption while negotiating with clients during his daily business activities. Because he was very aggressive in

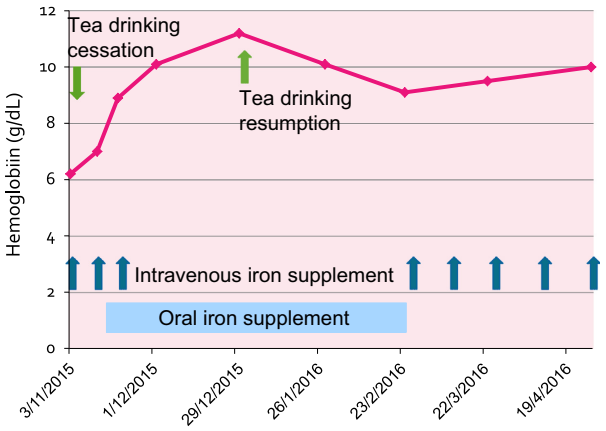

Figure 2. Hemoglobin change during treatment course. *Y*-axis: Hemoglobin level. *X*-axis: Date. Downward green arrow: time of tea drinking cessation. Upward green arrow: time of tea drinking resumption. Upward blue arrow: intravenous iron injection. Shallow blue bar: period of oral iron supplement.

building and expanding his career, he spoke with different clients throughout the entire work day. Under these conditions, he drank green tea almost uninterruptedly during the day from Monday to Friday. The amount of green tea he consumed was estimated to be more than 1500 mL each weekday over the past twenty years.

Figure 2 illustrates the patient's clinical course of treatment and hemoglobin change. Initially, we administered an intravenous injection of 400 mg elemental iron in the form of ferric hydroxide sucrose complex once a week and encouraged immediate abstention from tea consumption. Daily oral supplementation with 400 mg elemental iron in the form of ferric hydroxide polymaltose complex was added soon after the patient promised to stop drinking tea. Because hemoglobin levels steadily increased following treatment, intravenous iron injection was discontinued after three doses, and the patient was prescribed a daily oral iron supplement for long-term maintenance therapy. However, the hemoglobin level decreased again after achieving a peak value of 11.2 g/dL at approximately 2 months of treatment, in spite of continuous oral iron supplementation. The patient admitted resuming his tea drinking habit when he was aware of the improvement in his anemia. He seemed to be addicted to the stimulating effects of green tea during business activity and would not agree to abandon his accustomed lifestyle for a second time. This resulted in resumption of intravenous iron injection at an interval of 2–3 weeks in place of oral treatment. The patient's hemoglobin level gradually rebounded to 11.2 g/dL at follow-up on 22 June 2016. Although not shown in the figure, his serum ferritin level was highly correlated with the level of hemoglobin throughout the course of treatment.

Discussion

The fact that iron absorption can be reduced by tea consumption has been recognized for many years [2, 3], with the inhibitory effects predominantly facilitated by the marked iron-binding properties of the phenolic compounds bearing catechol groups in tea [4]. Although traditional views hold that polyphenols affect nonheme iron absorption only, recent experiments on human intestinal monolayer cells have provided evidence that dietary polyphenolic compounds could interfere with absorption of both heme and nonheme iron across these cells and demonstrated a dose-dependent inhibitory effect of polyphenols on heme iron absorption [5, 6]. This may explain the extraordinary influence of tea drinking on our patient's iron status despite an otherwise normal diet. This negative effect on iron absorption might be beneficial for patients at risk of iron overloading, as shown in previous clinical studies demonstrating that tea drinking decreased iron accumulation in thalassemia and hereditary hemochromatosis [7, 8].

While a review of clinical and epidemiologic data did not suggest the necessity of restricting tea drinking in healthy people not at risk of iron deficiency, especially in conjunction with a Western-style diet [9, 10], iron deficiency anemia and poor oral iron therapeutic effects due to excessive tea consumption have been reported [11, 12]. Hemoglobin levels rose significantly only after withdrawing from tea consumption in these two reported cases, demonstrating clearly the importance of recognition and removal of the deleterious element in addition to supplementation. Our patient's case further confirms the relationship between tea and reduced iron absorption, not only by the improvement of iron deficiency anemia following abstinence from tea, but also by the recurrence of anemia upon a rechallenge of tea during continuous oral iron supplementation. The anemia resolved again when an intravenous iron supplement was substituted for oral iron tablets. This clinical scenario reinforces the importance of cultural and dietary factors in investigating underlying causes of iron deficiency in daily practice.

Most available guidelines for the diagnosis and management of iron deficiency anemia are intended for healthcare practitioners in Western countries where iron is generally sufficient in food and a culture of habitual tea drinking is less popular. Looking for the possibility of tea consumption's interference on iron absorption is usually not mentioned in the recommendations for evaluation of iron deficiency. For example, malabsorption of iron induced by abundant tea drinking was not considered as a dietary risk factor in the recently published British guidelines [13]. Although tea is listed as one of the possible reasons for inadequate response to oral iron therapy in the Australian guidelines [14], questions regarding dietary habits such as tea drinking are not a component of the assessment flowchart aiming to investigate the etiology of iron deficiency.

We adhere to the guidelines that patients without a clear physiological explanation for iron deficiency, especially men and postmenopausal women, should undergo endoscopic investigation to exclude an underlying source of gastrointestinal bleeding, particularly ulcer, cancer, and angiodysplasia. For patients without a detectable bleeding source in the gastrointestinal, urologic, or gynecologic systems, causes of decreased intestinal iron absorption should become the focus of further evaluation. In addition to factors mentioned in the literature, such as inflammation, celiac disease, atrophic gastritis, *Helicobacter pylori* infection, nutritional deficit, intestinal resection, and bariatric surgery with gastric bypass [15], we would like to recommend that excessive tea drinking should not be missed as a potential causative factor. Additionally, we recommend advising children to restrict tea consumption, as a recent epidemiologic study found that regular intake of tea/coffee along with major meals led to a significantly increased odds ratio for iron deficiency anemia among schoolchildren from southern Kerala, India [16]. Because a recent systematic review indicated that most guidelines for iron deficiency anemia recommended oral administration as the first line of treatment [17], a lack of awareness of tea drinking as a potential main cause of iron malabsorption would be problematic. The clinical course in our patient is consistent with this undesirable possibility.

Nevertheless, reporting this case is not intended to negate the value of tea drinking. Epigallocatechin gallate, which constitutes more than 50% of the total amount of catechins contained in green tea, is considered a potent antioxidant substance [18]. The 2015 Dutch dietary guidelines recommended drinking three cups of tea daily based on cohort studies indicating that consumption of tea was associated with a lower risk of stroke and diabetes [19]. However, drinking too much green tea may lead to iron deficiency, as demonstrated in this case report.

Conflict of Interests

The author declares that there is no conflict of interests.

Informed Consent

A written informed consent for patient information was provided by the patient.

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