

## A Case of Pica-like, Nutrient-induced, Severe Iron-deficiency Anemia

To the Editor:

Data from the Third National Health and Nutrition Examination Survey (1988-1994) indicate that iron deficiency is present in 1% to 2% of adults in industrialized countries.<sup>1</sup> Foods and medications can impair iron absorption. We recently observed a patient with severe iron-deficient anemia mimicking impaired iron absorption in the absence of gastrointestinal pathology.

### CASE SUMMARY

A 44-year-old woman was referred to our outpatient clinic because of recurrent symptoms of iron deficiency. One year

ago, she was treated with oral iron (100 mg/d) because of severe iron-deficiency anemia with a hemoglobin level of 7.0 g/dL. Guaiac-based fecal occult blood test results were negative. Endoscopies of the whole gastrointestinal tract, including a small bowel biopsy for exclusion of celiac disease, revealed no abnormalities. A gynecologic examination excluded uterine bleeding. Oral iron therapy was terminated after remission of symptoms 3 months later when hemoglobin had increased to 14.6 g/dL. Nonetheless, reviewing the patient's file suggested that repletion of her iron stores was not yet accomplished at that time.

On referral, she reported fatigue, headache, a burning tongue, and exercise intolerance. She appeared to be in a normal nutritional condition. Her skin was pale, and inspection of her oral cavity revealed atrophic glossitis. Pulse rate and blood pressure were normal. Blood tests indicated a hemoglobin level of 10.0 g/dL with a low mean cell volume (70 fl) and a low mean corpuscular hemoglobin (21 pg). Erythrocyte count was not decreased ( $4.8 \times 10^{12}/L$ ), suggesting long-lasting iron-deficient hemostasis rather than bleeding. The most recent laboratory values of serum iron, transferrin saturation, ferritin, and blood counts are shown in **Table 1**.

When asked about her food pattern, our patient recounted a daily intake of 100 to 150 g of blue raisins for more than 2 years. She craved sweet raisins because she was doing

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**Table 1** Blood Count and Biochemical Laboratory Findings

	May 23, 2013 3 Weeks After Definite Cessation of Raisin Consumption	May 3, 2013 1 Week After Reexposure to Raisins	April 26, 2013 1 Week After Cessation of Raisin Consumption
CRP, mg/dL		<0.5	<0.5
Hemoglobin, g/dL	12.2	10.1	10.0
Erythrocytes, $\times 10^{12}/L$	5.2	4.7	4.8
Mean cell volume, fl	76	71	70
Mean corpuscular hemoglobin, pg	23	21	21
Hematocrit, %	40	33	33
Reticulocytes, %	0.9	1.0	2.9
Leukocytes, $\times 10^9/L$	4.6	4.3	4.0
Platelets, $\times 10^9/L$	262	366	297
Serum iron, $\mu g/dL$	17	11	15
Transferrin, mg/dL	315	322	335
Transferrin saturation, %	7	4	4
Ferritin, ng/mL	17	11	15
Oral iron absorption test			
Serum iron at 1 h, $\mu g/dL$		178	165
Serum iron at 2 h, $\mu g/dL$		168	313

CRP = C-reactive protein.

regular endurance training. After cessation of raisin intake for 1 week, an oral iron absorption test using 225 mg of iron(II)-glycine-sulfate (equivalent to 40 mg of Fe<sup>2+</sup>) revealed no abnormalities. Thereafter, she was requested to continue with her previous food pattern, and enteric iron absorption was reexamined 1 week later after daily ingestion of 100 to 150 g of blue raisins. The oral absorption test at that time indicated a markedly lower serum iron at 2 hours. In addition, reticulocyte count decreased during reexposure to raisins, whereas the degree of iron-deficiency anemia was similar. Three weeks after definite cessation of raisin consumption, anemia had resolved to subnormal hemoglobin levels without any oral iron supplementation (**Table 1**).

## DISCUSSION

Grape products, including raisins, contain high concentrations of specific natural phenolic compounds.<sup>2</sup> Polyphenols released through the indigestible carbohydrate matrix of the fruit skin bind to iron and form a nontransportable complex that cannot enter the bloodstream. It was shown that bioactive dietary polyphenols inhibit heme iron absorption in a dose-dependent manner.<sup>3</sup> Thus, we suspected that consumption of raisins in larger quantities would interfere with the bioavailability of dietary iron,<sup>4</sup> similar to pica syndrome. For testing of our hypothesis, we administered a lower than standard dose of iron in the absorption tests, because we were aware from our patient's history that oral iron supplementation was capable of offsetting the dietary deficiencies.

## CONCLUSIONS

To our knowledge, this is the first clinical case indicating that blue raisins decrease the absorption of iron from foods. Although our observation comprises a rare cause of iron-deficiency anemia, natural bioactive polyphenols may offer an adjunct dietetic treatment in patients with hereditary hemochromatosis, who experience iron overload because of an accelerated rate of intestinal iron absorption.<sup>5</sup>

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