A previously healthy 50-year-old woman presented with 3 months of progressively worsening shortness of breath associated with extreme fatigue, anorexia, a 5 to 10 pound weight loss, yellowing of her eyes, heavy menstrual bleeding, and a lower extremity rash. She denied recent trauma.

She had never been admitted to the hospital before and had no history of surgical procedures. She took no medications. There was no significant family history. She was a housewife who had worked in the past as a secretary and had never smoked, drank alcohol, or used recreational drugs.

Physical examination revealed blood pressure 91/56 mm Hg, heart rate 92/min, respiratory rate 20/min, and temperature 37°C. Oxygen saturation was 85% on room air. Her skin and conjunctiva were pale, and scleral icterus was present. Her neck veins were distended to her earlobes when sitting, and there was massive hepatomegaly. A nonconfluent, nonblanching petechial rash was noted on her anterior legs and thighs and buttocks (Figure 1A and 1B), and there was a large ecchymosis on her thighs and buttocks (Figure 2).

Laboratory data showed severe normocytic anemia with hemoglobin 3.4 g/dL, hematocrit 12%, mean corpuscular volume 90 fL, reticulocyte count 9.7%, serum iron 9 µg/dL, total iron binding capacity 271 µg/dL, and ferritin 147 ng/mL. Lactate dehydrogenase was 1117 U/L, haptoglobin (109 g/L) was normal, and direct Coombs was negative. Liver function tests were abnormal with aspartate transaminase 726 U/L, alanine transaminase 670 U/L, alkaline phosphatase 154 U/L, direct bilirubin 1 mg/dL, indirect bilirubin 4.2 mg/dL, and international normalized ratio 2.2. The viral hepatitis panel was nonrevealing. Serum acetaminophen and salicylate levels were undetectable and urine drug screen was negative. anti-neutrophil cytoplasmic antibody tests were negative, and complement levels were normal. Tissue transglutaminase and immunoglobulin A were negative. Serum lactate was 4.2 mmol/L, and B-type natriuretic peptide was elevated (347 pg/mL).

An ECG revealed normal sinus rhythm with low voltage in the anterioinferior leads. A computerized tomography scan of her abdomen–pelvis showed periportal edema with hepatomegaly. A computerized tomography scan of her abdomen–pelvis showed periportal edema with hepatomegaly. These complications were well known to physicians hundreds of years ago, when Scurvy was a devastating illness. It is incredible that James Lind postulated this phenomenon in his article “A Treatise on the Scurvy” about 250 years ago. He wrote in his article:

“The case of scorbutic patients is somewhat singular; that though when at rest they find themselves quite well; yet, upon the least exercise, they are subject to panting and breathlessness.”

On the basis of these clinical observations and autopsies showing disproportionate enlargement of the right ventricle, Lind postulated that exercise leads to increased return of blood to the lung leading to pulmonary hypertension. He wrote:

“Upon using exercise, the velocity of blood is accelerated though lungs, and much greater quantity, which when at rest, was almost stagnating in the veins, is at
once returned into the right cavities of the heart, and from thence into the lungs; the weakened vessels of the lungs not being able so quickly to transmit so great a quantity, causes a laborious breathing and panting.”

A causal relationship between scurvy and pulmonary hypertension is likely as no other cause was identified and her echocardiogram completely normalized with vitamin C replacement, which, in turn, led to improvement in hepatic function.

Our patient’s clinical symptoms were magnified by severe anemia, which was probably caused by a combination of hemorrhage and iron deficiency. Resorption of heme from extravasated red blood cells is the most likely explanation for indirect hyperbilirubinemia.

It can be challenging to differentiate between vitamin C and vitamin B1 deficiency. Cardiac dysfunction in wet beriberi is due to high output failure, and pulmonary hypertension develops from increased blood flow to the lungs and elevated left ventricular end-diastolic pressure. Our patient’s diet, although seriously unbalanced, did provide her with adequate thiamine from cereal and eggs. The patient did not exhibit the neurological deficits associated with thiamine deficiency, and her clinical condition improved without high-dose thiamine administration.

Vitamin C deficiency is thought to cause pulmonary hypertension in 2 ways. First, vitamin C is vasodilatory because it increases synthesis and availability of endothelial nitric oxide. Second, vitamin C and iron are cofactors for the prolyl hydroxylase domain of enzymes regulating the hypoxia-inducible family of transcription factors. Hypoxia-inducible family transcription factors play a role in cellular responses to hypoxia, which includes the development of pulmonary hypertension.

Clinical scurvy is rare in the United States, but the prevalence of vitamin C deficiency is ≈13%. In the United States, vitamin C deficiency occurs mostly in malnourished individuals, alcohol abusers, or those living in poverty or on diets devoid of fruits and vegetables. Pulmonary hypertension secondary to ascorbic deficiency seems to be completely reversible and should be considered in high-risk patients presenting with characteristic features.

Disclosures
None.

References

Figure 1. A and B, The petechial rash spreading from the dorsal aspects of her feet up to her knees.

Figure 2. Spontaneous ecchymosis on her thighs and buttocks.
Figure 3. Computerized tomography abdomen—pelvis—transverse plane—revealing hepatosplenomegaly and enlarged inferior vena cava and portal vein.

Figure 4. A, Long-axis view showing dilated right ventricle. B, Short-axis view—septal flattening indicating pulmonary hypertension. C, Four-chamber view showing right atrial and ventricular enlargement. D, Subcostal view showing dilated, noncollapsing inferior vena cava and hepatic vein.
Figure 5. A, Long-axis view—normal right ventricular chamber size. B, Short-axis view—no more septal flattening. C, No more reverse bowing of the interatrial septum. D and E, Subcostal view showing collapsing inferior vena cava.
Reversible Right Heart Failure in Scurvy Rediscovery of an Old Observation
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