

CASE REPORT

A rare presentation of an ancient disease: scurvy presenting as orthostatic hypotension

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SUMMARY

A 49-year-old man presented to hospital with severe orthostatic hypotension, gingival dysplasia and a purpuric rash involving his extremities. The orthostatic hypotension failed to respond to fluids and, on the basis of physical examination and dietary history, the patient was given a preliminary diagnosis of scurvy (ascorbic acid deficiency). Serum ascorbic acid levels were undetectable and the orthostasis was resolved within 24 h of ascorbic acid replacement. The pathogenesis of orthostatic hypotension in the setting of scurvy appears to involve impaired catecholamine synthesis and attenuated vasomotor response to α -adrenergic stimulation. We believe that this case describes a rare presentation of scurvy and highlights a previously under-reported connection between scurvy and vasomotor instability.

BACKGROUND

Scurvy results from a deficiency of ascorbic acid. Clinical features manifest as early as 3 months after the onset of dietary insufficiency and often begin to improve within 24 h of supplementation.¹ While vasomotor instability and shock have been documented in the later stages of disease, postural hypotension and presyncope are unusual presenting symptoms. We describe a rare presentation of scurvy and highlight an underappreciated connection between ascorbic acid, catecholamine synthesis and vasomotor tone.

CASE PRESENTATION

A 49-year-old man presented to hospital after a fall. He reported being well until 3 weeks earlier, when he developed lightheadedness and palpitations upon rising. He had a history of schizophrenia and remote head trauma. On the day of presentation, his family physician observed a systolic BP of 70 mm Hg while seated. In the emergency department (ED), the patient reported presyncope, exertional dyspnoea, generalised myalgias and arthralgias, easy bruising and a rash that began 2 weeks earlier on his shins and progressed to involve the distal upper extremities. His only medication was quetiapine, which he started 10 months earlier. He consumed up to 2 L of beer daily and his diet consisted primarily of plain spaghetti with few fruits and vegetables. On examination his supine BP was 158/103 mm Hg and heart rate was 95 bpm. On standing he became lightheaded, his BP fell to 116/89 and heart rate rose to 130 bpm. Examination revealed gingival dysplasia,

purpura on the shins and distal upper extremities, and large ecchymoses on both upper thighs.

INVESTIGATIONS

Laboratory investigations revealed slightly low haemoglobin (125 g/L) and serum sodium (126 mEq/L) concentrations, while all other indices were unremarkable, including adrenocorticotrophic hormone (ACTH) and morning cortisol. CT scan of the head showed an area of encephalomalacia in the inferior left frontal lobe consistent with old trauma. A chest radiograph and ECG were unremarkable.

TREATMENT

The patient received 2 L of intravenous crystalloid in the emergency room (ER) with no improvement in his postural hypotension. On the basis of his physical examination and dietary history, a presumptive diagnosis of scurvy was made and a serum ascorbic acid level was collected. Thereafter, ascorbic acid 500 mg orally daily was begun empirically, along with a multivitamin.

OUTCOME AND FOLLOW-UP

Within 24 h the patient's muscle weakness improved dramatically. On discharge 2 days later his orthostasis, myalgias and arthralgias had fully resolved. The patient was seen in follow-up one month later. The ascorbic acid level drawn in hospital returned at $<5 \mu\text{mol/L}$ (normal $>25 \mu\text{mol/L}$). His BP was 130/90 and heart rate was 95 bpm with no orthostatic changes. The patient continued to take ascorbic acid and remained symptom free.

DISCUSSION

Scurvy is an uncommon illness in the developed world because of an abundance of fruits and vegetables as well as the widespread use of multivitamins. However, perhaps we underestimate the prevalence of vitamin C deficiency; results from the Third National Health and Nutrition Examination Survey (NHANES III) data suggest that 14% of men and 10% of women are vitamin C deficient.² Scurvy is a disease that is still present among those with significant risk factors: poor diet, poor dentition, gastrointestinal problems, patients with symptoms of cancer, psychiatric and behavioural disorders and those suffering from alcoholism.

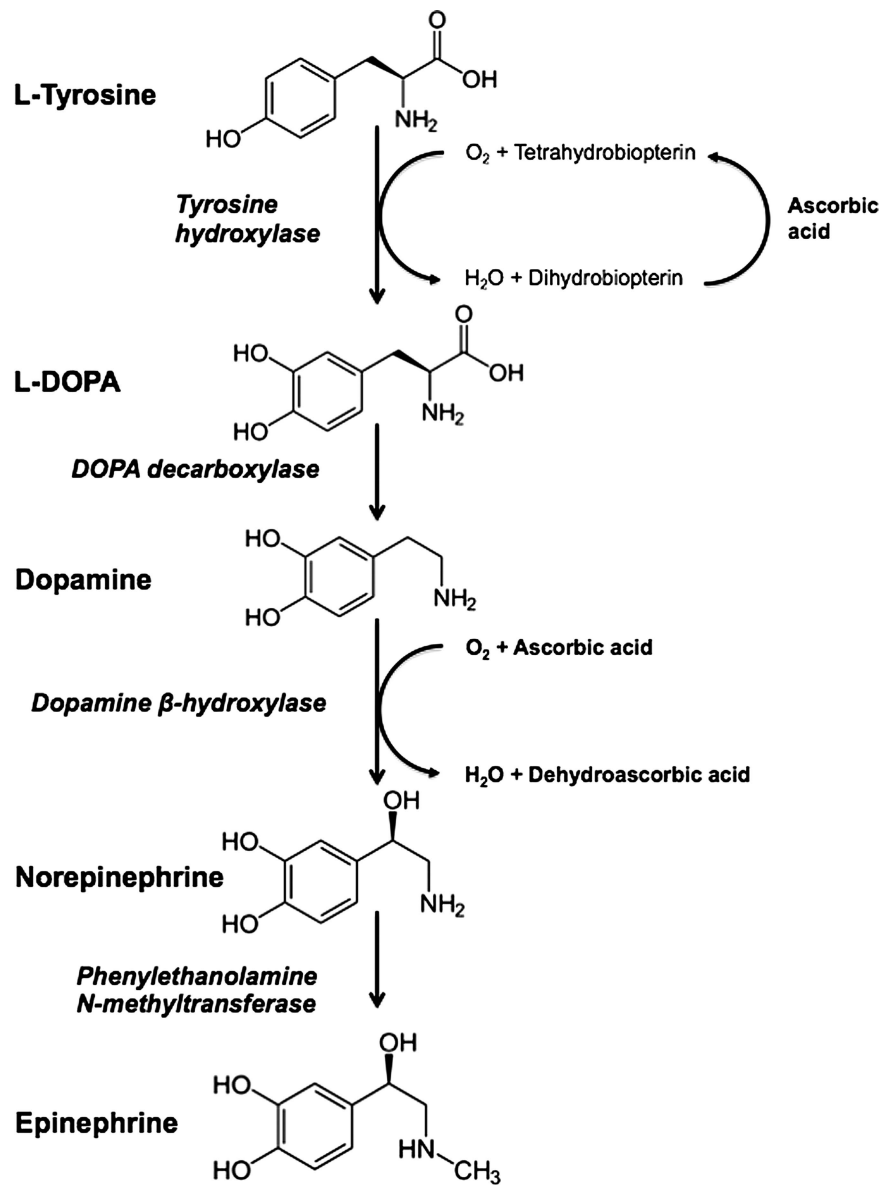
The pathogenesis of orthostatic hypotension in scurvy appears to involve impaired catecholamine synthesis and attenuated vasomotor response to α -adrenergic stimulation. The synthesis of epinephrine requires ascorbic acid at two steps (figure 1).



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Figure 1 The biosynthesis of catecholamines. Ascorbic acid facilitates the reduction of the trihydrobiopterin radical generated by the hydroxylation of tyrosine by tyrosine hydroxylase and acts as a cofactor for dopamine β hydroxylase.



In the first, ascorbic acid helps recycle the essential cofactor tetrahydrobiopterin by reduction of the trihydrobiopterin radical generated by hydroxylation of tyrosine by tyrosine hydroxylase.³ Ascorbic acid also directly augments the synthesis of tyrosine hydroxylase by stimulating messenger RNA (mRNA) production.² Thereafter, the conversion of dopamine to norepinephrine by dopamine β-hydroxylase (DBH) requires ascorbic acid as a cofactor.³ Our patient was able to mount a compensatory tachycardia in response to hypotension, suggesting that catecholamine synthesis was at least partially preserved. Ascorbic acid also facilitates α-adrenergic vasoconstriction.^{4 5} In vitro experiments show that ascorbic acid binds to the α-adrenergic receptor, enhancing its activation by epinephrine.⁴ Hypotension may therefore be a consequence of impaired α-adrenergic vasoconstriction, even in the presence of catecholamines.

Clinicians should be aware of the association between ascorbic acid, catecholamine synthesis and vasomotor tone; they should also consider the diagnosis of scurvy in patients who present with orthostatic hypotension, particularly when other features such as unexplained purpura are present.

Learning points

- ▶ Scurvy is a rare disease in the developed world, but it is an illness to consider in patients with significant risk factors: poor diet, poor dentition, gastrointestinal problems, patients with symptoms of cancer, psychiatric disorders and alcoholism.
- ▶ Ascorbic acid is an important cofactor at two steps in the catecholamine biosynthesis pathway that converts tyrosine to epinephrine.
- ▶ Ascorbic acid can bind directly to the α-adrenergic receptor and enhance epinephrine-mediated vasoconstriction.
- ▶ Scurvy is a diagnosis to consider in patients who present with orthostatic hypotension and other systemic findings such as unexplained purpura.

Competing interests None.

Patient consent Obtained.

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