Scurvy as a Readily Reversible Cause of Pulmonary Hypertension: A Case Report

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Introduction

- Pulmonary arterial hypertension (PAH) has a diverse range of etiologies and carries significant morbidity and mortality burden[1]
- Vitamin C deficiency has been posited to cause reversible PAH[2,3]

Case

Presentation

- A 45-year-old female presented with shortness of breath and malaise
- HR 105 BPM, BP 87/70 mmHg, RR 23 breaths/min, pulse ox 92% on room air
- Physical exam:
  - Ill-appearing female with corkscrew hairs and numerous hematomas and petechia, most prominent on lower extremities (Figure 1B). Lungs clear to auscultation throughout, heart with tachycardia, regular rhythm, no murmurs
- Labs: Lactate 5.3, BNP 8,169 pg/mL
  - Blood smear: Figure 1A
- Imaging and Procedures
  - Transthoracic echocardiogram (TTE):
    - right ventricular (RV) and right atrial (RA) dilation, systolic septal flattening, mid-systolic notching of the RV outflow tract by Doppler, EF 45-50% (Figure 2)
  - Right heart catheterization (RHC):
    - mean pulmonary arterial pressure (PAP) of 34 mmHg, pulmonary vascular resistance (PVR) of 7 WU with pulmonary capillary wedge pressure of 12 mmHg. CO/CI 3.7/2.4

Resolution

- Stabilized on high-flow oxygen, inhaled nitric oxide, and vasopressors → transitioned to sildenafil and macitentan
- She endorsed a diet severely limited in fruits and vegetables and she was started on vitamin C supplementation. Serum vitamin C level later came back non-detectable

Figures

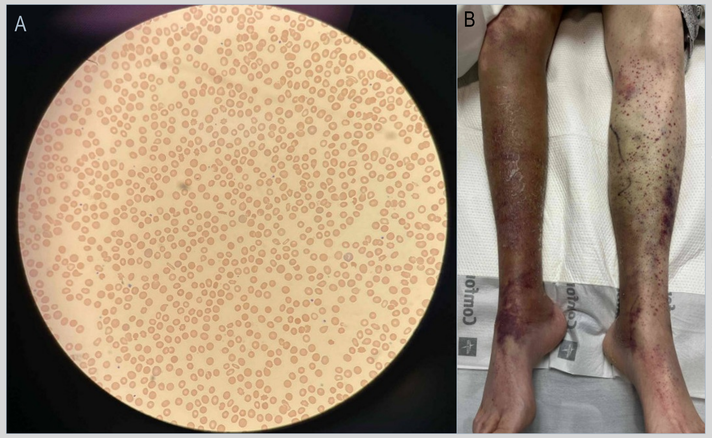

Figure 1: Clinical signs of vitamin C deficiency. (A) Peripheral blood smear demonstrating anisocytosis and poikilocytosis with spur cells, polychromasia, decreased platelets consistent with combined iron deficiency/ vitamin C deficiency/ congestive hepatopathy. (B) Purpura and petechia of bilateral legs, clearing hematoma of right leg. Patient had recent presentation to outside hospital for a fall causing hematoma with blood loss and ensuing anemia. This likely contributed to her decompensation.

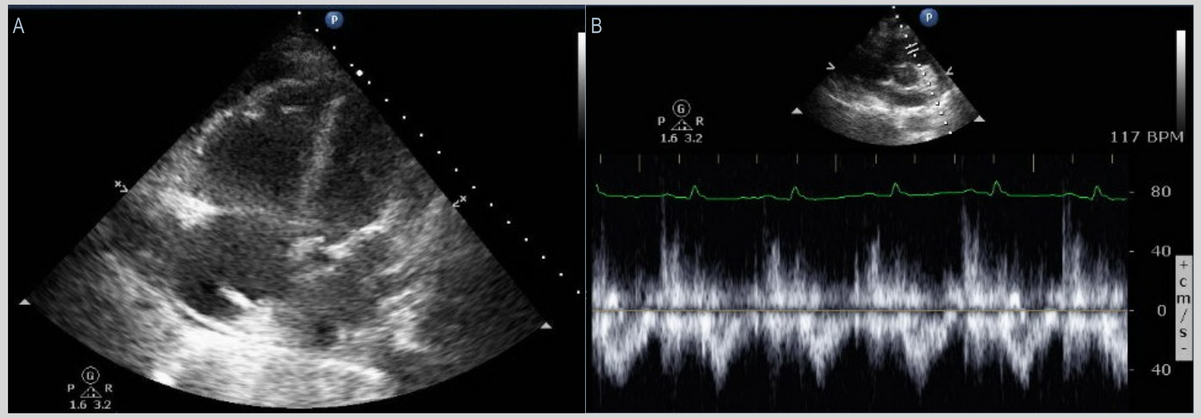

Figure 2: Transthoracic echocardiogram on admission demonstrating (A) dilation of the RV and RA on the apical four-chamber view and (B) mid-systolic notching of the RV outflow tract, consistent with pre-capillary pulmonary arterial hypertension. Patient was receiving inhaled nitric oxide at 5 PPM and sildenafil 20 mg every 8 hours at this time.

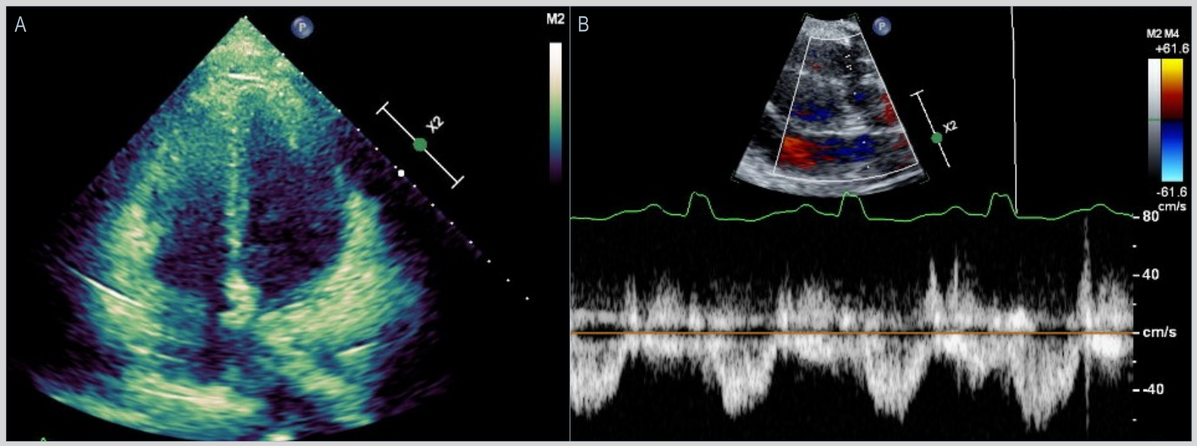

Figure 3: Transthoracic echocardiogram after vitamin C supplementation demonstrating (A) normal RV size and function and (B) absence of mid-systolic notching of the RV outflow tract, consistent with resolution of pre-capillary pulmonary arterial hypertension. Patient was not receiving any anti-pulmonary hypertensive therapies at this time.

Case (cont.)

- Hypotension improved over a few days. She entered a high output state which resolved with discontinuation of sildenafil and macitentan.
  - Repeat TTE demonstrated normal RV size, shape, and function
  - Repeat RHC showed an improved mean PAP (19 mmHg) and PVR (1.5 WU). CO/CI 7.5/4.8.
  - BNP decreased to 180 pg/mL
- Discharged without oxygen or PAH therapy

Discussion

Our patient presented with right heart failure due to PAH and clinical features of scurvy. She rapidly improved after vitamin C supplementation. This correlates with several other case reports attributing PAH to scurvy and describing rapid improvement with Vitamin C.[2]

Most approved anti-PAH agents target the nitric oxide pathway. Vitamin C plays a key role in this pathway and others involved in vasoconstrictive modulation, such as hypoxia inducible factor regulation, thus providing a mechanistic link to PAH. Furthermore, vitamin C deficiencies may be somewhat common, with an estimated prevalence of up to 5% in the U.S. population, making assessment for scurvy worthwhile in patients with newly diagnosed PAH.[2,3]

Conclusion

- Scurvy is a reversible cause of PAH
- Given the prognostic significance of PAH, evaluation for vitamin C deficiency should be strongly considered in at-risk patients with newly diagnosed PAH

References

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2. Hemila H, de Man AME. Vitamin C deficiency can lead to pulmonary hypertension: a systematic review of case reports. *BMC Pulm Med*. 2024;24:140. doi: 10.1186/s12890-024-02941-x

3. d'Uscio LV, Milstien S, Richardson D, Smith L, Katusic ZS. Long-term vitamin C treatment increases vascular tetrahydrobiopterin levels and nitric oxide synthase activity. *Circ Res*. 2003;92:88-95. doi: 10.1161/01.res.0000049166.33035.62