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Scurvy with Distinctive Pulmonary Manifestation: A Case Study

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Abstract

Scurvy, a condition resulting from vitamin C (ascorbic acid) deficiency, was previously thought to be rare in affluent countries, yet its prevalence has increased in recent years even in these regions. This clinical case report of scurvy details an atypical association between severe vitamin C deficiency and pulmonary involvement. This case report highlights an unconventional presentation of scurvy with pulmonary involvement, which, to our knowledge, has not been previously reported if not associated to alveolar hemorrage or pulmonary hypertension in the literature.

This distinctive case necessitates a reassessment of scurvy's pathophysiology and clinical presentations, especially concerning pulmonary manifestations, thereby focusing on previously unclear facets and unidentified mechanisms.

Introduction

Scurvy is caused by a deficiency of vitamin C (ascorbic acid) and was long considered eradicated or uncommon in affluent countries [1]. Recent data, however, indicate a resurgence in its incidence, even in these regions [2]. Predisposing factors encompass dialysis-dependent renal insufficiency, diabetes mellitus, smoking, alcohol dependence, malnutrition, gastrointestinal chronic inflammatory conditions, AIDS, neoplasms, and psychosocial elements such as poverty and psychosis [3].

Classic clinical manifestations, first comprehensively documented in the 18th century by James Lind (1716-1794), a Royal Navy physician, include follicular hyperkeratosis, peri-follicular haemorrhage, gingivitis with bleeding, gum retraction, and dental caries, often linked to inadequate oral hygiene [1,3,4]. Nowadays, these manifestations may not always be present, likely due to improved oral and dental care.

Systemic manifestations encompass fatigue, malaise, anorexia, neuropathy, and vasomotor instability [5]. Joint swelling and musculoskeletal pain, often resulting from intramuscular or periosteal haemorrhages, have been noted, with debilitating effects particularly in paediatric scurvy cases [6].

Vitamin C is the commonest non-toxic essential dietary antioxidant and is a crucial cofactor for the action of 15 enzymes in mammals, with three involved in collagen synthesis [7,8]. Humans, along with monkeys and guinea pigs (Cavia porcellus), are among the few species incapable of synthesizing Vitamin C by the liver [9]. Therefore, dietary intake of Vitamin C is essential for various oxidation reactions, and clinical manifestations of insufficient intake appear within 2-4 months when plasma ascorbic acid concentration is below 0.2 mg/dL (11µmol/L) [5,10]. Disturbed collagen synthesis in scurvy leads to widespread haemorrhages, cutaneous ulcerations, and impaired wound

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healing [11]. Vitamin C deficiency also affects the synthesis of neurotransmitters such as carnitine and catecholamines, contributing to nonspecific symptoms like fatigue, depression, irritability, and anorexia [4,6].

The treatment regimen for scurvy predominantly involves high-dose vitamin C supplementation, coupled with management of the underlying deficiency causes. Paediatric patients are advised 100mg of ascorbic acid thrice daily for one week, followed by a maintenance dose until full recovery. Adults may require 300mg to 1000mg daily for one month [11].

Clinical Case

A 51-year-old man with a complex medical history, including substance abuse, HIV, and HCV infection, presented to the emergency department with worsening dyspnea (NYHA Class III), left upper limb swelling, nausea, and epigastric pain persisting for 2 months.

He is currently receiving antiretroviral therapy consisting of Dolutegravir, Emtricitabine, and Tenofovir.

The patient's general condition at admission was markedly compromised, and physical examination revealed petechiae and hemorrhagic suffusions on the trunk and lower limbs (Figure 1). Laboratory tests showed thrombocytopenia, altered coagulation parameters with reduced factor XIII (37%; normal range: 75 - 155%), and a significant increase in factor VIII (388%; normal range: 50 - 150%).

Biochemical tests fell within normal limits. Chest CT revealed bilateral ground-glass parenchymal opacities, suggestive of interstitial lung disease, atypical pneumonia, or alveolar hemorrhage (see Figures 2a-b).

Further investigations, including bronchoscopy with Broncho Alveolar Lavage (BAL) and cultures, did not yield a conclusive diagnosis. Transthoracic echocardiography did not reveal any direct or indirect signs of pulmonary hypertension.

A detailed medical history uncovered the patient's poor diet, excessive alcohol consumption, and avoidance of fruits and vegetables for months.

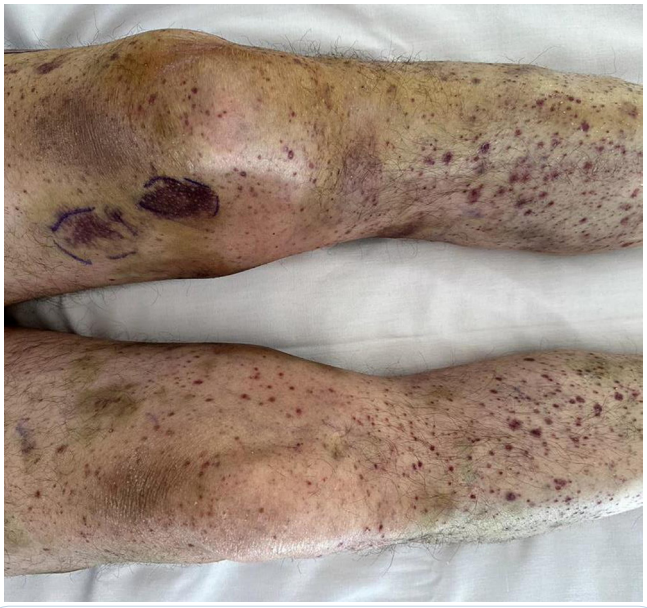

Figure 1: Lower limbs petechiae and hemorrhagic suffusions.

A vitamin C assay confirmed severe deficiency (<2.3 µmol/L; reference range: 23.0-85.0 µmol/L), leading to the diagnosis of scurvy. Treatment with supplemental ascorbic acid resulted in clinical improvement: Dyspnea disappeared

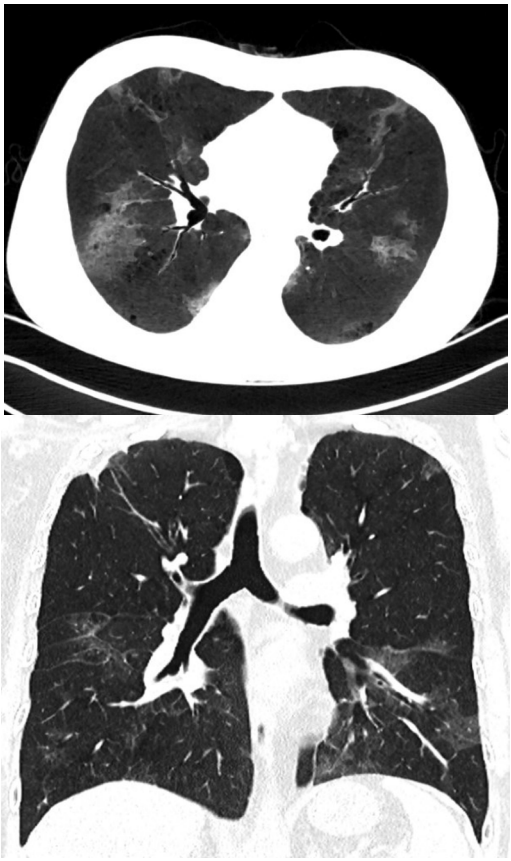

Figure 2a-b: CT chest with bilateral central and peripheral ground-glass parenchymal opacities, suggestive of possible interstitial lung disease, atypical pneumonia, or alveolar hemorrhage.

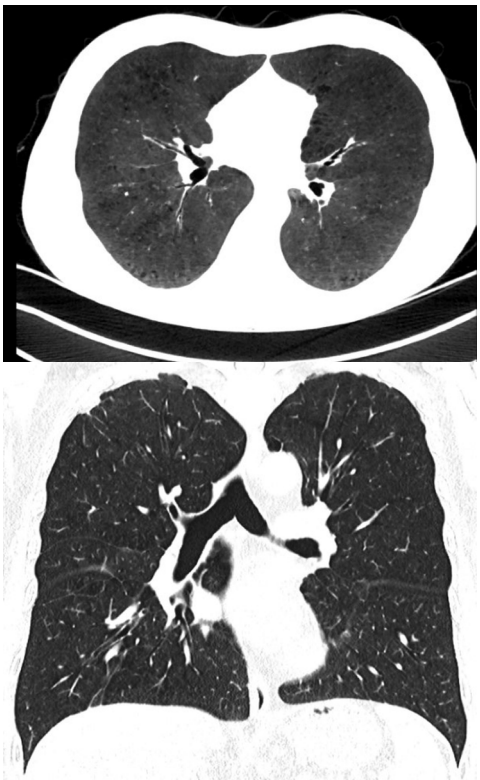

Figure 3a-b: Complete resolution of parenchymal ground glass opacities after 1 month of Vitamin C therapy.

Followed by the resolution of laboratory abnormalities, including the radiological pulmonary findings initially observed (Figure 3a-b).

Discussion

This case of severe scurvy, in addition to presenting classic symptoms, was characterised by widespread and substantial haemorrhagic suffusions, and a distinctive clinical presentation involving the lungs. The chest CT, conducted because of dyspnea upon admission, revealed bilateral ground-glass opacities, with pronounced involvement of the lower pulmonary lobes. These alterations resemble those observed in atypical and viral pneumonias, such as COVID-19. However, no microorganisms were identified, and bronchoalveolar lavage results were normal, particularly excluding SARS-CoV-2 infection and any sign of alveolar haemorrhage. Several cases of pulmonary arterial hypertension (PAH) reported in the literature demonstrate an association between vitamin C deficiency and PAH [13]. Low endothelial nitric oxide levels in the pulmonary vasculature, combined with inappropriate activation of hypoxia-inducible transcription factors, are believed to be the primary contributors to increased microvascular permeability and the exaggerated pulmonary vasoconstrictive response observed in patients with scurvy-induced PAH [8-14].

Generally, it is supposed that Vitamin C, with its antioxidant properties, plays a crucial role in regulating the pulmonary system, particularly in reducing the heightened microvasculature permeability characteristic of acute lung inflammation [7]. There is limited experimental evidence for the potentially beneficial effects of vitamin C in models of increased vascular permeability [14,15]. The ability of ascorbic acid to counter lung inflammation and fibrosis has been demonstrated in animal studies, where it attenuated fibrosis and tissue damage in rat lungs exposed to endotoxin [15]. In this study, 24 rats were divided into three groups: Group I (control), Group II (receiving lipopolysaccharide LPS), and Group III (receiving both LPS and vitamin C). After 30 days, lung tissue samples were collected for histological analysis. Group II showed signs of pneumocyte degeneration, widened interstitial spaces, increased collagen deposition, macrophage infiltration, and irregularities in the capillary basement membrane with increased fibrosis. In contrast, Group III exhibited less pronounced pathological changes, emphasising ascorbic acid's efficacy in countering LPS-induced lung inflammation and fibrosis by scavenging reactive oxygen species and promoting antioxidant enzyme activity. Consequently, vitamin C can reduce the heightened microvascular permeability characterising acute lung inflammation following endotoxin infusion, such as LPS [7,15].

Recent research has explored the potential benefits of Vitamin C in mitigating lung inflammation and fibrosis, as seen in severe SARS-CoV-2 infections characterised by a severe inflammatory response with a cytokine storm. Ascorbic acid helps maintain the integrity of the epithelial barrier, mitigating oxidative stress through its antioxidant properties. Recently, it has been used as a co-treatment for severe COVID-19 pneumonia, contributing to a reduction in inflammation-induced damage and facilitating a quicker recovery [16]. Similarly, a daily supplement of 400 mg of Vitamin C is associated with clinical improvement in patients with COPD, enhancing lung function and serum antioxidant levels [14-16]. In addition, plasma concentration of vitamin C was found to be reduced in patients with sepsis and multi-organ failure [7].

Based on this data, we hypothesise that vitamin C plays a crucial role in regulating the pulmonary system through its antioxidant activity, which may explain the ground-glass opacities observed in our case, attributed to heightened microvascular permeability characterising acute lung inflammation.

Conclusion

This case report underscores the importance of considering scurvy as a potential diagnosis, even in affluent countries, where it was once thought to be rare. The association between scurvy and pulmonary involvement, as demonstrated in this case, highlights the need for further research to understand the mechanisms underlying this link and the potential role of vitamin C in lung health.

Learning points

The case presented illustrates an atypical form of scurvy with pulmonary involvement.

Little is known about the pathophysiological mechanisms underlying the pulmonary manifestations in scurvy.

The pulmonary involvement of scurvy may presents similar characteristics compared to atypical pneumonia or SARS-CoV-2 infection.

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