Respir Case Rep 2024;13(2):78-81 DOI: 10.5505/respircase.2024.73604

Diet-treatable Cause of Hemoptysis: Lane Hamilton Syndrome

Diyet ile Tedavi Edilebilen Hemoptizi: Lane Hamilton Sendromu

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Abstract

Idiopathic pulmonary hemosiderosis is a rare cause of alveolar hemorrhage that is referred to as Lane Hamilton Syndrome when co-occurring with coeliac disease. Although the underlying cause is still unknown, the improvements brought by a gluten-free diet point to a shared pathogenesis. An 18-year-old female underwent bronchoscopy after presenting with complaints of recurrent hemoptysis attacks, revealing hemosiderin-laden macrophages pointing to alveolar hemorrhage. The presence of anti-endomysium IgA in the serum, substantiated by an endoscopic biopsy, was indicative of Celiac Disease. Her symptoms improved dramatically upon starting a gluten-free diet, but the patient subsequently died from an alveolar hemorrhage due to non-compliance with the diet.

Keywords: *Hemorrhage, gluten, anemia, immunocomplex, bronchoalveolar lavage.*

Öz

İdiyopatik pulmoner hemosideroz nadir görülen bir alveolar hemoraji nedenidir ve çölyak hastalığı ile birlikte görüldüğünde Lane Hamilton Sendromu olarak adlandırılır. Altta yatan neden hala bilinmemekle birlikte, glutensiz diyetle iyileşmeleri ortak bir patogeneze işaret etmektedir. Tekrarlayan hemoptizi ataklarıyla başvuran 18 yaşında bir kadın hastaya bronkoskopi yapılmış ve alveolar hemorajiyi doğrulayan hemosiderin yüklü makrofajlar görülmüştür. Serumda anti-endomisyum IgA varlığı nedeniyle yapılan endoskopik biyopsi ile Çölyak Hastalığı tanısı doğrulandı. Başlangıçta glutensiz diyetle semptomları dramatik bir şekilde düzelen hasta ilerleyen dönemde diyet uyumsuzluğu nedeniyle alveolar hemoraji atağından kaybedildi.

Anahtar Kelimeler: *Kanama, gluten, anemi, immünkompleks, bronkoalveolar lavaj.*

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Submitted (Başvuru tarihi): 12.11.2023 ***Accepted (Kabul tarihi):*** 29.01.2024

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Hemoptysis is an uncommon but significant symptom that typically prompts the patient to seek medical attention. Diffuse alveolar hemorrhage (DAH), one of the causes of hemoptysis, usually occurs due to infections, vasculitis, connective tissue diseases, cardiac pathologies and coagulopathies, although sometimes no underlying cause can be found, which is referred to as idiopathic pulmonary hemosiderosis (IPH). It is clinically characterized by iron deficiency anemia, hemoptysis and pulmonary infiltrates on lung imaging, with no specific underlying identifiable cause (1).

Celiac Disease (CD) is a clinically variable autoimmune bowel disorder whose symptoms are triggered by the consumption of foods containing gluten. Although the majority of cases experience gastrointestinal (GI) symptoms, including unexplained abdominal pain, indigestion, non-dietary weight loss, diarrhea or constipation, extra-GI symptoms such as fatigue, recurrent migraines and dermatitis herpetiformis are also common (2).

IPH and CD may co-occur, which is referred to as Lane Hamilton Syndrome (LHS), and the management of these two life-threatening diseases, surprisingly, does not involve drugs, but rather diet. This paper presents the case of a young adult with LHS.

CASE

An 18-year-old non-smoker female presented to us with a complaint of hemoptysis for the past two weeks. The patient's history included recurrent hemoptysis for about 4 years, for which she was treated with multiple antibiotics and tranexamic acid during attacks, but without a definitive diagnosis, and also complaints of palpitations, shortness of breath, appetite loss, abdominal discomfort and weight loss.

On examination, the patient appeared pale, weak and apathetic, while other physical examination findings were normal. A complete blood count revealed the following values: hemoglobin: 8.6 g/dL (hematocrit: 22%), white blood cells: 6000/mm^3 and platelets: 213,000/mm^3. The blood smear was notable for hypochromic and microcytic erythrocytes, but without polychromatophilia.

Further evaluations for iron deficiency anemia demonstrated an iron level of 27 µg/dL (50–120), ferritin 75 ng/mL (13–150), and a total iron-binding capacity of 431µg/dL (250–450). There was no gross or microscopic bleeding in the urine or stool, other laboratory examination findings were within normal limits and there was no previous medical history.

Prominent interstitial markings and focal areas of ill-defined nodular opacities were identified on a chest radiograph. Figure 1 shows pulmonary opacities compatible with alveolar hemorrhage on chest computed tomography (CT). Bronchoalveolar lavage (BAL) confirmed hemosiderin-laden macrophages consistent with pulmonary hemosiderosis (Figure 2).

After complaining of abdominal discomfort, she was assessed to rule out celiac disease (CD). Serum anti-endomysium IgA was positive, and a duodenal biopsy demonstrated duodenal pili findings and total villous atrophy compatible with CD, and the patient was subsequently diagnosed with Lane-Hamilton Syndrome (LHS) and advised to go on a gluten-free diet (GFD). For the first 6 months she benefited from the diet and experienced no hemoptysis, but her failure to adhere to the diet led to her death a year later from an attack of alveolar hemorrhage.

DISCUSSION

LHS is a rare condition characterized by the coexistence of a rare but life-threatening disease, IPH, and a common but frequently neglected condition, CD. Although they are believed to share a common immune pathogenesis, the actual background remains unknown. A literature review conducted by Tryfon et al. (2) assessing all patient reports since 1971 – the year LHS was first defined – to 2020, identified 80 cases, including 44 children and 36 adults, who had been diagnosed with LHS. Our patient developed symptoms during childhood, but was not diagnosed until her early adult years and died from the condition.

IPH is one of the most challenging conditions of the respiratory system to diagnose due to the presence of hemoptysis, a symptom that almost always results in hospital admission, anemia, which must be investigated, and diffuse lung infiltrations (1). Typically, adolescents and young adults are affected. Despite the presence of diffuse alveolar hemorrhage in the pathogenesis of the disease; hemoptysis is not always seen clinically, and patients usually present with dyspnea and cough (3). This could be due to the diverse range of the disease, as well as the fact that children do not expectorate and instead swallow bloody sputum. Although our patient presented with a complaint of hemoptysis, there are previous pneumonia-like episodes with or without hemoptysis that could lend credence to the hypothesis.

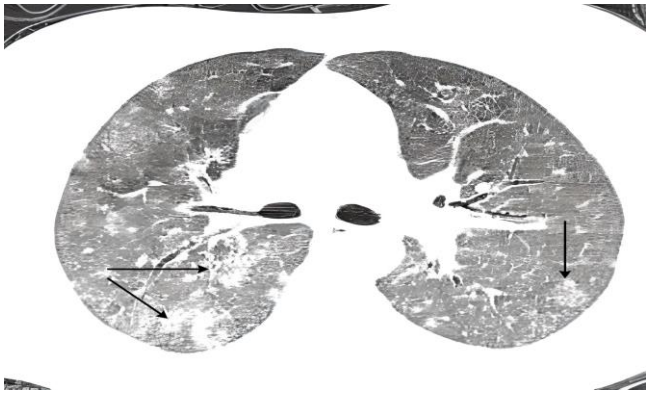

Figure 1: Ill-defined nodular opacities suggestive of alveolar hemorrhage

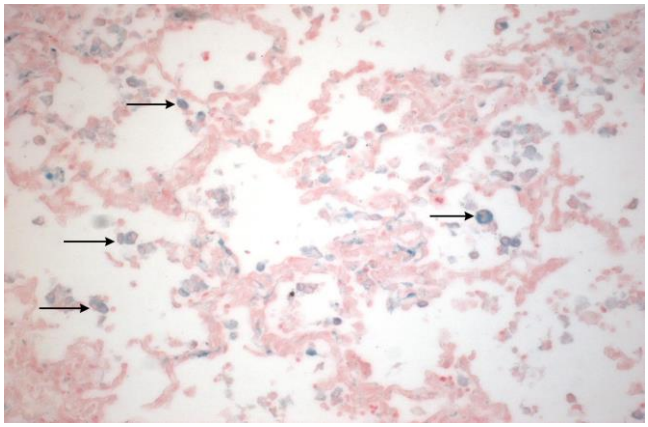

Figure 2: Hemosiderin-laden macrophages stained with Prussian blue at X500

The radiologic appearance of IPH includes bilateral diffuse ground glass opacities with no definite cause. In such cases, bronchoalveolar lavage should be carried out to rule out infections and to reveal hemosiderin-rich macrophages, as in the presented case. Recurrences of these alveolar hemorrhages indicate chronic blood loss from the lungs, which explains the remaining member of the IPH triad, iron deficiency anemia (4). However, as was the case in our patient, the presence of severe anemia in patients with intermittent and bland hemorrhage should alert clinicians to other causes that may contribute to anemia.

Celiac disease is an autoimmune disease that is diagnosed in childhood rather than adulthood, like IPH. Marine et al. (5) report the prevalence of CD to be around five times higher in children than in adults, with a predominance for females. Diagnosis is based on the determination of increased intraepithelial lymphocytes, atrophic mucosa, enhanced epithelial apoptosis and crypt hyperplasia from a small intestine biopsy in patients with positive serology (anti-gliadin antibody, anti-endomysial antibody IgA, tissue transglutaminase, deamidated gliadin peptide) (6). It typically manifests with recurrent diarrhea or constipation, malabsorption, unexpected weight loss, abdominal pain, and the clinical signs and symptoms of iron deficiency anemia.

Most patients are admitted to hospital with complaints related to IPH rather than CD, with hemoptysis, exertional dyspnea, cough, chest pain, fatigue and pallor being common symptoms (4,7). Patients usually have a history of weight loss or loss of weight gain (in children). They have fatigue, due to undiagnosed and intermittent diarrhea, suggestive of malabsorption due to undiagnosed CD. Pallor and exertional dyspnea are possibly related to iron deficiency anemia caused by both IPH and CD (4).

While hemoptysis can be a frightening symptom, it can also be considered valuable in its guidance of the diagnosis. In patients without hemoptysis, attention may be directed to areas such as the GI, urinary system and metabolism, which may be related to iron deficiency anemia and malabsorption, resulting in a delay in diagnosis. In such cases, detecting abnormalities suggestive of DAH on lung imaging may lead clinicians to perform BAL to identify hemosiderin-laden macrophages.

While several possible mechanisms have been suggested to clarify the common pathogenesis, such as the circulating immune complex deposition containing food allergens on the basement membrane of alveolar capillaries, the interaction between antireticular antibodies and alveolar basement membrane antigens, and the potential influence of adenovirus 12, the precise underlying cause remains elusive (8).

The primary treatment for LHS is a GFD, which leads to the regression of both IPH and CD-related symptoms in most cases (4,9). While some patients may be prescribed steroids or other immunosuppressive drugs to control hemoptysis, GFD can lead to the discontinuation of these drugs in most patients.

In summary, LHS is a co-occurrence of two diseases, among which, IPH suggests the diagnosis, and CD guides the treatment. It is important to keep LHS in mind in every patient diagnosed with IPH, and to test for accompanying CD. A gluten-free diet continues to be the most common and efficient treatment, although the etiology connecting the two disorders is yet to be fully described.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - E.A.A., O.K., O.U.; Planning and Design - E.A.A., O.K., O.U.; Supervision - E.A.A., O.K., O.U.; Funding - E.A.A.; Materials - O.K.; Data Collection and/or Processing - O.K.; Analysis and/or Interpretation - E.A.A., O.U.; Literature Review - E.A.A., O.K.; Writing - E.A.A., O.K., O.U.; Critical Review - O.U.

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