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Case Report

Pulmonary Alveolar Proteinosis in Association with Congenital Dyserythropoietic Anemia: A Case Report

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A two-year-old girl with congenital dyserythropoietic anemia (CDA) acutely developed fever, tachypnea, and increased oxygen requirement. Chest X-ray revealed bilateral interstitial infiltrates and mild cardiomegaly. Blood cultures grew no infectious agents, while pulmonary specimens grew cytomegalovirus (CMV). Treatment with intravenous ganciclovir was initiated but without response. Final cytologic preparations of bronchoalveolar lavage (BAL) fluid revealed eosinophilic amorphous material consistent with pulmonary alveolar proteinosis (PAP). CDA and PAP are extremely rare disorders in pediatrics. PAP should be considered in patients with hematological disorders who present with acute interstitial pneumonia, after infectious causes are ruled out.

1. Introduction

Congenital dyserythropoietic anemia type II (CDA II), also known as HEMPAS (hereditary erythroblastic multinuclearity with positive acid serum test), is a rare hematological autosomal recessive disorder whereby individuals have bone marrow biopsy findings indicating inappropriate red blood cell lineage progression [1]. Pulmonary alveolar proteinosis (PAP) is also a rare disorder in which lipoproteinaceous material congregates within alveolar spaces, leading to a host with impaired pulmonary immunity and susceptibility to opportunistic infection [2]. Although historically reported in patients with various hematological disorders [3–8], to our knowledge, this is the first case report of PAP associated with CDA.

2. Case Report

A 23-month-old girl presented to our facility with one week of worsening fevers, productive cough, and increased work of breathing. Over the previous 3 months, she was treated for presumed upper respiratory tract infections with inhaled beta-agonists, inhaled steroids, oral steroids, and several different oral antibiotics. Relevant medical history was significant for prematurity and severe anemia necessitating intrauterine blood transfusions, CDA diagnosed at 20 months by bone marrow biopsy and aspiration that was morphologically consistent with type II, and surgical placement of a Port-a-Cath for chronic blood transfusions.

Initial vital signs were temperature 37.9 degrees Celsius, heart rate 156 bpm, respiratory rate 50/min with oxygen saturation 83% on room air and 98% on 1 LPM oxygen by nasal cannula, and blood pressure 115/61 mm Hg. She appeared in mild distress with increased work of breathing. She had moderate frontal bossing with open anterior fontanelle. Heart examination was significant for a II/IV systolic ejection murmur. Lung exam revealed diffuse rales bilaterally but no wheezing. Abdomen was not distended. The liver was palpated 4 cm below the costal margin, and the spleen palpated to the level of the umbilicus. She had no clubbing, cyanosis, or peripheral edema.

Chest radiograph showed diffuse ground glass alveolar infiltrates which were chronic in nature when compared to a chest X-ray from one year prior (Figure 1). Blood, urine, and
Grocott’s methenamine silver (GMS) stain was negative for bronchoalveolar lavage (BAL) fluid was cloudy in appearance. Bronchoscopy was performed and was anatomically normal. The spike intermittent fevers and was still on oxygen treatment, influenza cultures of BAL fluid revealed no growth. Diacid-fast bacilli (AFB). Fungal, bacterial, AFB, RSV, and BAL fluid using Periodic acid-Schiff (PAS) stain was positive for abundant amorphous material within the pulmonary alveoli and results in a deficit of surfactant clearance by pulmonary macrophages [3]. There are 3 types: acquired, secondary, and congenital. Secondary PAP is associated with hematological malignancies and is well-established in the literature [14]. Complications that have been reported include splenomegaly, gallstones, jaundice, and pulmonary failure [13].

PAP is a rare disorder involving deposition of lipoproteinaceous material in alveoli and results in a deficit of surfactant clearance by pulmonary macrophages [3]. There are 3 types: acquired, secondary, and congenital. Secondary PAP is associated with hematological malignancies and is well-established in the literature [14]. Superimposed infection is known to complicate the course of secondary PAP, and reports of CMV and PAP have been reported [15].

To our knowledge, however, there are no published accounts of PAP associated with CDA and the incidence of these two rare disorders occurring simultaneously is remarkable and elucidating a possible mechanism is intriguing. While the acquired form of PAP is associated with an autoimmune process directed at the granulocyte-macrophage colony-stimulating factor (GM-CSF), resulting in suppression of proper alveolar function, the congenital type is associated with a rare mutation in the GM-CSF receptor [3, 16, 17]. Along those same lines, secondary PAP in association with hematological disorders such as CDA II could result from defective GM-CSF receptors on pulmonary macrophages and/or in a disrupted signal transduction pathway after GM-CSF and receptor interaction, which has been proposed elsewhere [8]. It is possible, as well, that our patient had a functional impairment of alveolar macrophages resulting from the environmental disruption of normal robust monocyte production caused by pathogenic erythrocyte production inherent to CDA II. Glycosylation defects of the monocytes themselves are less likely as it has been shown such errors are limited to erythroblasts [12].
The success of whole-lung lavage to relieve symptoms in secondary PAP has been documented thoroughly [2]. The sudden improvement of our patient after BAL supports this, and the lack of improvement after adequate antiviral therapy argues against CMV as the primary culprit. Experts feel CMV, and other infectious agents isolated in patients with secondary PAP and hematopoietic aberrancy are likely opportunistic infections superimposed on a preexistent PAP and compromised immune system [18]. The diagnosis of PAP alone, or in combination with superimposed CMV infection, should be entertained in any pediatric patient with a known hematological condition and new respiratory changes with a chest X-ray showing diffuse lung disease.

References


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