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A 16-Year-Old Moroccan Child's Diffuse Bronchiectasis Exacerbation Revealed Deficient Expression of HLA Class II Molecules

Chaanoun Khadija[1*], Haouassia Fatima Zahra[1], Zaghba Nahid[1], Hanane Benjelloun[1], Yassine Najiba[1]

[1]Department of Respiratory Diseases, Universite Hassan II de Casablanca, Casablanca, Morocco

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***Corresponding author:** Chaanoun Khadija
Department of Respiratory Diseases, Universite Hassan II de Casablanca, Casablanca, Morocco

Abstract **Case Report**

Deficiency in HLA class II expression is an uncommon autosomal recessive immune deficiency associated with mutations in genes that regulate major histocompatibility complex class II (MHC II) expression. Despite being diagnosed during adolescence, our case is distinguished by a delayed diagnosis and a weak clinical presentation. We describe the medical history of a 16-year-old child who has been treated intermittently for constipation and meningitis since early childhood. The child also experienced alternating episodes of diarrhea and constipation. As a result of a bacterial exacerbation of diffuse bronchiectasis, the patient was hospitalized. Deficient expression of HLA class II molecules was confirmed by immune assessments. Favorable clinical development was achieved by starting antibiotic medication in conjunction with nutritional control. Bone marrow transplantation is the sole curative treatment available for this real-life Maghrebian illness.

Keywords: Deficient expression of HLA class II molecules; bronchiectasis; immunodeficiency; combined immunodeficiency.

INTRODUCTION

Deficient expression of HLA class II molecules is a rare, severe autosomal recessive disorder. This immune deficiency is prevalent in the Maghreb region. The sole curative treatment is bone marrow transplantation. We report the case of a 16-year-old patient whose infectious symptomatology reveals the disease.

CASE DESCRIPTION

A 16-year-old male patient was admitted to the respiratory diseases department at CHU Ibn Rochd, Casablanca, for exacerbation of diffuse bilateral bronchiectasis. Born to third-degree consanguineous parents, he is the youngest of four siblings, all healthy. However, a paternal cousin died at 9 months in a severe infectious context. He had an unmonitored pregnancy, delivered vaginally, without neonatal distress. Exclusive breastfeeding until 4 months, followed by the introduction of first-stage artificial milk at 5 months. Yet, he developed cow's milk intolerance, manifested by liquid diarrhea and abdominal pain, managed by an exclusion diet of dairy products. Adequately vaccinated per national guidelines. Recurrent respiratory infections since age 3 were treated on an outpatient basis. At 13, he experienced meningitis, likely of pulmonary origin, necessitating a 3-week hospitalization with a positive outcome.

Twenty days before admission, he presented thick purulent bronchial symptoms, exertional dyspnea without hemoptysis or thoracic pain, alongside mild febrile sensations and slight decline in general condition, prompting consultations with various private practitioners. He received intravenous amoxicillin-clavulanic acid. Due to persistent bronchial symptoms and worsened dyspnea, he was referred to CHU Ibn Rochd, a level III hospital, for further management.

Upon admission, the patient appeared tachypneic, dehydrated, weighing 29 kg, height 147 cm, BMI 13.42, indicating stunted growth without notable facial dysmorphia. Manifest digital clubbing, sunken chest (pectus excavatum), and coarse breath sounds on left lung auscultation were noted. Recurrent respiratory infections, stunted growth, cow's milk intolerance, meningitis with probable pulmonary origin, and unexplained early familial death led to two possible diagnoses: immune deficiency or cystic fibrosis.

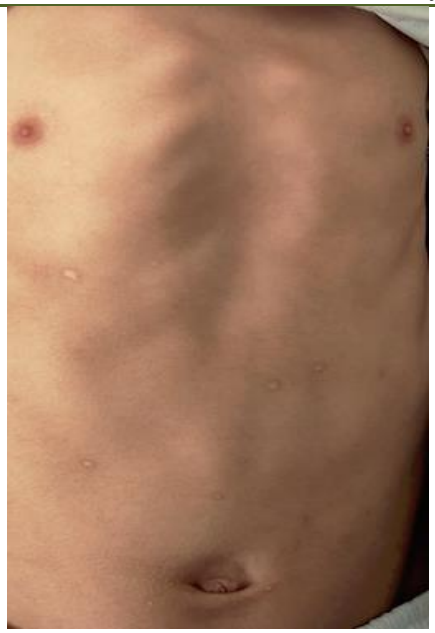

Figure 1: Image taken during examination; showing sunken chest (pectus excavatum)

Laboratory tests showed hemoglobin levels at 11.4 g/dL, MCV 76.4 µ3, MCHC 21%, WBC count 19050/mm3, neutrophil count 12490/mm3, lymphocyte count 1630/mm3, and platelet count 230000/mm3. CRP level was 51.4 g/L, normal kidney and liver function. Infectious screening showed negative X-pert gene in sputum, cytobacteriological examination of sputum revealed elevated white blood cells (>25 elements per field), no red blood cells, 6 epithelial cells per field, and sterile culture. Radiologically, bilateral cylindrical bronchiectasis predominated on the left with mucus impactions and small mediastinal lymph nodes.

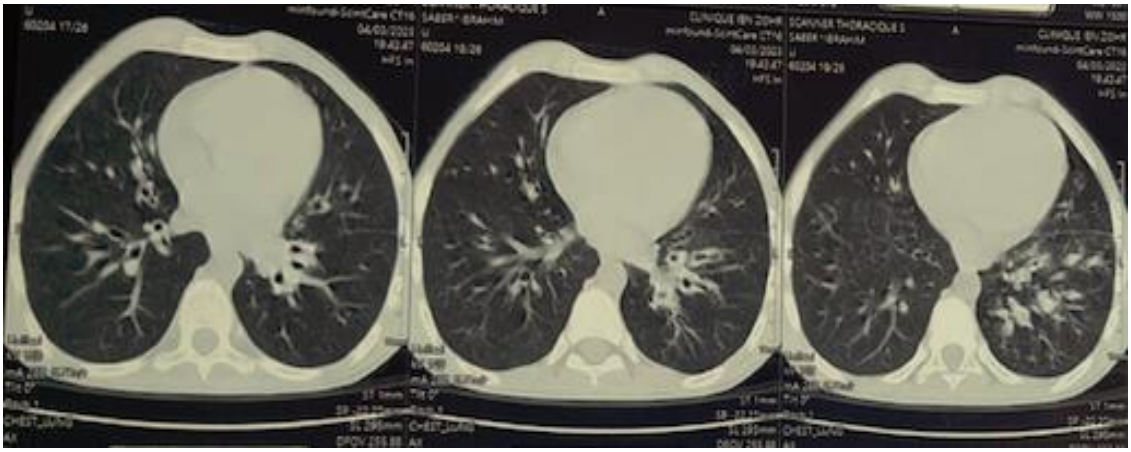

Figure 2: Axial CT scan slice showing diffuse bronchiectasis with mucus impactions

Sweat test results ruled out cystic fibrosis. Viral serologies (HIV, HCV/HBV/Syphilis) were negative. Immunoglobulin weight assay indicated hypogammaglobulinemia below 13.2 IU/mL. Lymphocyte subset analysis revealed HLA class II expression deficiency with T CD4 lymphopenia (Total IgE <13.2 IU/mL).

Therapeutically, the patient was diagnosed with primary combined immune deficiency due to deficient expression of HLA class II molecules. Initially treated with ceftriaxone for 10 days, daily respiratory physiotherapy, rehydration, and nutritional support. Additionally, the patient underwent hospitalization for intravenous immunoglobulin administration and discussions regarding a possible allograft.

DISCUSSION

Deficient expression of HLA class II molecules is a rare autosomal recessive disorder first described in 1980. The major histocompatibility complex (MHC) genes are located on chromosome 6. HLA class II molecules participate in antigen recognition phenomena. Their deficiency results from mutations in genes encoding the RFX protein complex or the CIITA gene [1].

Immunologically, T and B lymphocytes are present in normal quantities but functionally abnormal, exhibiting disrupted cellular and humoral responses to antigens. Absence of delayed hypersensitivity reactions correlates with impaired lymphoblast proliferation in the presence of various antigens. However, these patients retain the ability to proliferate lymphoblasts in the presence of mitogens or allogeneic cells. Serum immunoglobulin levels vary between patients, but antibody production post-vaccination is severely impaired, suggesting normal cellular activation mechanisms, yet B lymphocytes' capability to produce immunoglobulins is compromised in the absence of HLA class II molecules [2].

According to a study by Klein *et al*., 22 out of 30 patients were of Maghrebian origin due to high parental consanguinity. Onset of clinical signs varies from the first week of life to 8 months. Diagnosis is considered upon observation of similar cases or early deaths in the family due to severe infections, chronic resistant diarrhea, and recurrent bronchopneumopathies leading to growth arrest. Unusual infections such as severe septicemia from Gram-negative bacilli, skin, ENT, or urinary infections are reported. Susceptibility to viral infections, often leading to early death, has been noted. Additionally, liver involvement in the form of biliary dilation, cholangitis, or hepatitis has been described in several articles [3, 4].

Bone marrow transplantation remains the only curative treatment. Without transplantation, death typically occurs between 5 and 18 years. Success rates are higher with an HLA-identical intra-familial donor [5]. Chronic pre-existing viral infections and rejection are the two primary causes of graft failure [1, 4, 5]. To enhance success rates, transplantation should ideally occur before 2 years of age, reducing the risk of chronic viral carriage and infection-related sequelae. However, compared to other immune deficiencies, success rates are lower. Apart from bone marrow transplantation, patient management includes adequate nutritional support, curative infection treatment, pneumocystis prophylaxis (trimethoprim-sulfamethoxazole 25mg/kg, 3 times per week), and monthly intravenous or subcutaneous immunoglobulin infusions (0.4 g/kg over 3 weeks) [2, 7]. Live vaccines are strictly contraindicated. Gene therapy holds promise in three scenarios [6]: as an alternative to bone marrow transplantation, pre-transplantation to reduce infection rates, and post-transplantation in cases of failure [1, 8].

CONCLUSION

Deficient expression of HLA class II is a rare and severe autosomal recessive immune deficiency. It should be considered in cases of recurrent and/or unusual infections. Our case is unique due to the mild clinical presentation despite the patient being in adolescence, resulting in a delayed diagnosis, contrary to what is typically observed in cell-mediated deficiencies. Significant efforts are needed in Morocco to improve the infrastructure for diagnosis and management of primary immune deficiencies, particularly the development of bone marrow transplantation. Special attention should be given to HLA-II deficiency, a genuine Maghrebian condition.

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