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COMBINED IMMUNODEFICIENCY WITH HLA-DR DEFICIENCY COMPLICATED BY A PARTICULAR FORM OF TUBERCULOSIS: A CASE REPORT

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Abstract

Membrane expression of major histocompatibility complex class II (MHC-II) molecules plays a crucial role in the presentation of antigens to CD4+ T lymphocytes and in triggering the immune response. Defects in the expression of these molecules are responsible for a combined immune deficiency and the occurrence of severe infections. We report the case of a 13-month-old infant from a second-degree consanguineous couple with a history of two early deaths in the siblings in an infectious setting. He presented with recurrent bacterial bronchopneumopathies since birth, for which immunological investigation revealed an HLA-DR deficiency. The patient was admitted at the age of 13 months with ascites and an intraperitoneal mass, the aetiological investigation of which was difficult. Tuberculosis was strongly suspected and confirmed by culture of the ascites fluid. The diagnosis of pseudotumour peritoneal tuberculosis was accepted and treatment was initiated. After an initial improvement, his tuberculosis had progressed. Despite treatment, the outcome was fatal at the age of 23 months. Our patient illustrates the difficulty of diagnosing and managing peritoneal tuberculosis in a primary immune deficiency.

Index Terms: Immune Deficiency, HLA-DR, Pseudotumors Tuberculosis, Bone Marrow Transplantation.

I. INTRODUCTION

Primary combined immunodeficiency related to a defect in antigen presentation caused by a deficiency in the expression of HLA class II major histocompatibility complex molecules is a rare inherited disorder with autosomal recessive inheritance [1]. It is a common disease in the Mediterranean basin. In Algeria, where consanguinity is common,

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the prevalence is unknown but not exceptional. In a series of 30 patients reported by Klein et al [2], 22 were of North African origin due to the high rate of consanguinity.

It is a severe disease, leading to increased susceptibility to infections that are often serious and recurrent, such as tuberculosis, a serious infectious disease caused by a bacteria called Mycobacterium tuberculosis. All organs can be affected in the course of abdominal tuberculosis. The clinical and radiological aspects are non-specific, making diagnosis difficult, particularly in the case of pseudotumour tuberculosis, a form that is essentially common in immunosuppressed patients. We report the case of a 13-month-old infant who illustrates the difficulty of diagnosis and management of peritoneal tuberculosis in primary immunodeficiency.

II. DESCRIPTION OF THE CASE

A 13-month-old boy from a consanguineous marriage, with a family history of early death among siblings (sister and brother died at the ages of four and five months successively) following a severe pulmonary infection hospitalized at the age of 40 days then at 3 months for bilateral bronchopneumonia. Given this family and personal history, an HLA DR combined immunodeficiency was quickly diagnosed and the patient benefited from cure of immunoglobulins associated with antipneumocystis antibiotic prophylaxis (trimethoprim-sulfamethoxazole).

At the age of 13 months, he was hospitalized for severe malnutrition, significant abdominal distension and moderate ascites. The ascites puncture revealed an exudative fluid at 1200 elements/ml predominantly lymphocytic and a non-contributory direct bacteriological investigation. Abdominal ultrasound revealed an abdominal mass with ascites confirmed by an abdominopelvic CT scan that revealed the presence of a solid, hypodense, intraperitoneal mass protruding on the left flank, slightly enhanced after injection of contrast 54/53/ 80 mm in diameter, pushing back the intestinal loops, and multiple confluent primary celiac-mesenteric and iliac lymphadenopathy. (Image 1).

A scan-guided biopsy of the mass was performed, the pathological study of which was in favor of an inflammatory myofibroblastic tumor without major nuclear abnormality. In fact, it was difficult to determine the nature of the tumor. The germline tumor markers alpha-fetoprotein (AFP) and human chorionic gonadotropin (β-hCG) were negative, thereby reducing the risk of malignancy. Infectious causes were considered and serologies for aspergillosis, brucellosis and toxoplasmosis were negative. The Widal and Felix serologies were also negative, excluding typhoid fever.

Peritoneal tuberculosis was strongly suspected based on anamnestic criteria (endemic country, specific patient condition) and clinical criteria (appearance and cytology of ascitic fluid).

Anti-tuberculosis treatment was initiated, which contributed to the reduction of ascites but did not radically eliminate it. The ascites culture on the 28th day looking for mycobacteria was positive, confirming the tuberculous origin of this pseudotumoral peritoneal mass.

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After eight months of treatment, the patient was hospitalized again due to the resumption of ascites. A follow-up abdominal CT scan confirmed the disappearance of the mass, but it showed abundant ascites with an appearance of L1-L2 spondylodiscitis. Maintenance treatment was extended and reinforced with pyrazinamide. The progression of the disease was marked by a recurrence of pulmonary infections and superinfections of ascitic fluid, with severe cachexia despite adequate nutritional and dietary treatment. The short and medium term prognosis was complicated by serious complications with the appearance of portal hypertension (PH) and rapid deterioration leading to death.

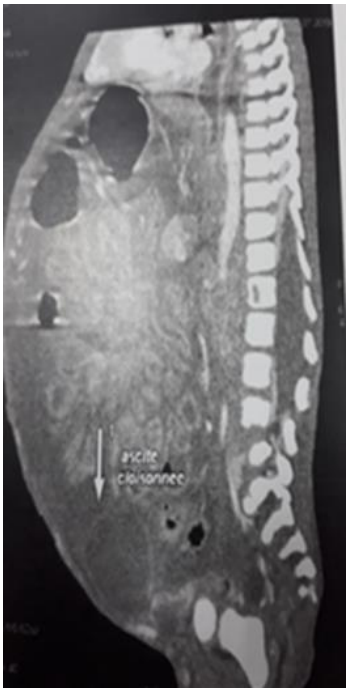

Figure 1: Abdominopelvic CT scan: Partitioned Ascites and a Hypodense Intraperitoneal Mass Projecting from the left Flank, Poorly Enhanced after Injection of Contrast Medium With Unclear Boundaries 54*53*80 mm in Diameter with the Presence of Multiple Confluent Primary Coelio-Mesenteric and Iliac Adenopathies

III. DISCUSSION

Membrane expression of major histocompatibility complex class II deficiency (DR, DQ, and DP) is a rare form of primary combined immunodeficiency syndrome. It is a disease linked to mutations in four genes: CIITA, RFXANK, RFX5 and RFXAP that encode four gene regulatory proteins of the MHC-II complex leading to defective expression of HLA class II molecules on all derived immunocompetent cells bone marrow [3].

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It therefore, leads to a severely impaired cellular and humoral immune response to foreign antigens, in this case severe CD4+ T lymphopenia and hypogammaglobulinemia associated with serious infections.

Clinically, the disease is manifested by the early onset of severe and recurrent infections during the first year of life, mainly of the respiratory and gastrointestinal tracts, and persistent diarrhoea accompanied by delayed growth in height and weight, often leading to death in infancy. The diagnosis must be strongly suspected in the event of recurrent infections, especially if there is a history of death among siblings in infancy.

Extrapulmonary tuberculosis accounts for 15-20% of tuberculosis cases, of which abdominal tuberculosis accounts for 12%, ranking sixth after lymph node, pleural, genitourinary, osteoarticular and neuromeningeal tuberculosis [4].

In abdominal tuberculosis, all organs may be affected; in order of frequency, abdominal sites include intra-abdominal lymph nodes, the peritoneum, the digestive tract and solid intra-abdominal organs [4, 5, 6].

The clinical and radiological aspects are not specific making diagnosis difficult, particularly in the case of pseudotumor tuberculosis, which is reported in only 5% of cases and is more frequent in immunocompromised patients explained by central caseous necrosis and the peripheral inflammatory reaction. Computed tomography is decisive, with the characteristic but not pathognomonic appearance of a hypodense formation that enhances in the periphery after injection of the contrast medium [7, 8].

Our patient illustrates the seriousness of this immune deficiency, which predisposes to the occurrence of tuberculosis infection, characterised by diagnostic difficulty given the frequent anergy to tuberculin associated with CD4 lymphopenia and the difficulty of obtaining sterilisation despite the chemosensitivity of mycobacterium tuberculosis on antibiotic susceptibility testing, linked above all to lymphopenia and malnutrition [9].

Bone marrow transplantation remains the only curative treatment, but has a lower success rate than other immunodeficiencies, and death usually occurs in early childhood in the absence of a bone marrow transplant.

IV. CONCLUSION

MHC-II molecule deficiency is a serious disease with increased susceptibility to infections. As with other primary immune deficiencies, it must be considered in the presence of recurrent and/or persistent infections, especially if there is a history of similar cases or early death in a serious infectious situation among siblings.

Marrow transplantation is currently the only curative treatment and while waiting for it to be carried out, the aim of management is to reduce the risk of infectious carriage as much as possible. Our patient's prognosis was poor because of an invasive infection that was difficult to diagnose and sterilise.

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Declaration of Competing Interest

The authors of this manuscript declared that there is no conflict of interest.

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