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Leukocyte adhesion deficiency and cardiac arrhythmia

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Abstract

Leukocyte adhesion deficiency (LAD) is a rare inherited primary immunodeficiency disorder characterized by the presence of a defect of phagocytic function resulting from a lack of leukocyte cell surface expression of β_2 integrin molecules (CD11 and CD18) that are essential for leukocyte adhesion to endothelial cells and chemotaxis. It is characterized by delayed separation of the umbilical cord, recurrent bacterial and fungal infections, defective wound healing, blood neutrophilia and a high mortality rate at an early age. Here, we report a case of LAD in a 38-day-old male with recurrent hospitalizations because of severe pneumonia and positive bacterial cultures. His medical history included neonatal sepsis and delayed umbilical cord detachment. Laboratory studies showed marked leukocytosis with predominance of neutrophils and decreased CD11b and CD18.

Keywords: Immunologic deficiency, Leukocyte-adhesion deficiency syndrome, CD11/CD18

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Introduction

Leukocyte adhesion deficiency (LAD) is a rare inherited primary immunodeficiency disorder characterized by the presence of a defect of phagocytic function resulting from a lack of leukocyte cell surface expression of β_2 integrin molecules (CD11 and CD18) that are essential for leukocyte adhesion to endothelial cells and chemotaxis. It is characterized by delayed separation of the umbilical cord, recurrent bacterial and fungal infections, defective wound healing, blood neutrophilia and a high mortality rate at an early age (1).

LAD type 1 (LAD-I) is the most common. It results from a mutation in the integrin β 2 (ITGB2) gene that codes the ITGB subunit (CD18 antigen).

Severe LAD-I (predominantly classified as <2% of CD18-expressing neutrophils) is characterized by recurrent, life-threatening infections that have high mortality in patients who do not receive allogeneic hematopoietic stem cell transplant (HSCT) (2).

We report a case of an infant with LAD type 1 who was diagnosed at the Ali Asghar Pediatric Hospital in Iran.

Case Report

A 38-day-old male infant, who was the only child of consanguineous parents, was admitted to the intensive care unit of our hospital with diagnoses of PSVT and sepsis.

Three days prior to admission, he had developed fever that partially responded to acetaminophen. The physical examination revealed tachycardia, weak peripheral perfusion, and PSVT evidence in ECG. He had also induration the scar of BCG and a necrotic wound (Figures 1-2). Adenosine rapidly

infused for him but PSVT does not improve, so defibrillator shock used to treatment. Five episodes of PSVT repeated and each time he treated with defibrillation device. His blood pressure recovered soon after admission, through rapid infusion of intravenous fluids. Flecainide and Propranolol and Intravenous Meropenem, Vancomycin and Ampisulbactame were started. Echocardiography was normal. The laboratory tests at the time of admission revealed leukocytosis with neutrophil predominance (31x $10^3/mm^3$). The chest radiography showed mild, bilateral, symmetrical interstitial infiltrates. Urine and cerebrospinal fluid (CSF) cytochemistry were normal. Blood, urine and CSF cultures were sterile. The antibiotic treatment was maintained for 14 days, with a good clinical response.

The patient's past medical history consisted of uncomplicated fetal development with full-term NVD and weight of 3,400 grams. He had respiratory depression and sepsis of unknown origin at birth and was treated empirically with broad-spectrum antibiotics. His umbilical cord detached late, at 22 days of age. On the basis of the recurrent infections and physical findings, a diagnosis of primary immunodeficiency was suggested. An ELISA test for human immunodeficiency virus and tests for complement components and quantitative immunoglobulin isotypes A, G, M and E were done. In addition, determinations of CD4, CD8 and the CD4/CD8 ratio were all normal. Flowcytometry analysis for CD18 and CD11 were requested, and also bone images.

The diagnosis of leukocyte adhesion deficiency (LAD) type 1 was suspected because of the persistent leukocytosis and the history of a delay in umbilical cord detachment. Because of this suspicion, the patient was started on prophylactic oral therapy with amoxicillin/clavulanate and nystatin, and Bone marrow transplant were done and he was discharged.

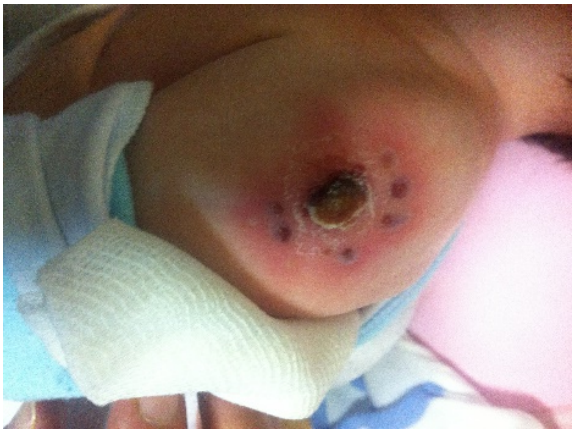

Fig. 1. *Scar of BCG (taken with permission of the patient's proxy).*

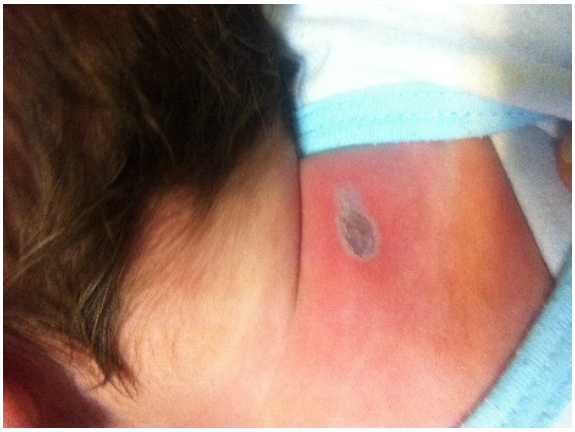

Fig 2. *Wound in back of neck (taken with permission of the patient's proxy).*

Discussion

Congenital immunodeficiency is generally suspected during early infancy (3). Pathogenically, LAD is characterized by loss of the leukocytes' ability to adhere to the endothelium during the inflammatory cascade, thus preventing their migration to the infected tissues. In a normal person, leukocytes first adhere to and roll along the wall of blood vessels through using selectins and glycoconjugate ligands. They then adhere firmly and transmigrate using integrins and endothelial ligands. Total or partial absence of these molecules leads to LAD (4). Adhesion molecule deficiencies have been classified into two types: LAD-1 and LAD-2, depending on the molecule that is defective, i.e. integrins in LAD-1 and selectins in LAD-2. Both forms of LAD have an autosomal recessive transmission pattern (5). Patients with LAD-1 typically present recurrent bacterial and fungal infections of the skin and mucosa, delayed detachment of the umbilical cord, rapidly progressive periodontitis, osteomyelitis and less commonly, hepatosplenomegaly (6-7). Bone marrow or stem cell transplant has been shown to improve the survival of LAD-1 patients. The prognosis for patients with the severe form of LAD-1, like the patient presented here, is poor. Most of them will die before reaching 10 years of age if a transplant cannot be performed (8).

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