

Clinical Article**Leukocyte Adhesion Deficiency in a Case Presenting as Septic Arthritis**

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Abstract

Reported is the first description of septic arthritis in a patient with leukocyte adhesion deficiency (LAD-1). A three-month-old boy was referred due to an antibiotic resistant sepsis and a history of delayed umbilical cord separation. Leukocyte adhesion deficiency (LAD) is an autosomal recessive genetic disease involving deficient expression of three related leukocyte adhesion glycoproteins: LFA-1, the C3b receptor (CR3, mac-1) and p150, 95. All three glycoproteins are expressed on monocytes and granulocytes, while LFA-1 is expressed on lymphocytes. These molecules are essential for many leukocyte adhesion related functions, including chemotaxis, aggregation, phagocytosis, and antibody directed cellular cytotoxicity. The diagnosis of LAD-1 relies on both clinical and in-vitro observation. *Int Pediatr.* 2002;17(2):96-97.

Key words: adhesion molecules, arthritis, leukocytes

Introduction

Leukocyte adhesion deficiency (LAD) refers to two disorders of blood cell adhesion (LAD-1 and LAD-2) leading to life-threatening recurrent infections. LAD-1 affects about 1 in 10⁶ individuals and is characterized by delayed separation of the umbilical cord, recurrent episodes of septicemia, skin and wound infection as well as severe gingival and periodontal disease.^{1,2} Fujita et al reported a sister and a brother with leukocyte adhesion deficiency developed systemic-onset juvenile rheumatoid arthritis.³ But septic arthritis has not been reported in LAD patients so far. In this report, we provide the first description of septic arthritis in a patient with LAD-1.

Case Presentation

A three-month-old boy was referred due to antibiotic resistant sepsis and a history of delayed umbilical cord separation. There was no parental consanguinity. Previously, before being accepted to our clinic, he had been followed with the diagnosis of omphalitis, sepsis and meningitis at another hospital while he was 10 days. His umbilical cord detached when he was 30 days of age. The physical ex-

amination revealed oral moniliasis, wide spread rales on both lung and splenomegaly.

Laboratory data showed high leukocyte counts (67.000/mm³) associated with neutrophilia. The flow cytometric analysis of peripheral blood neutrophils revealed a complete absence of CD18, CD11a integrin proteins. The count of T, B lymphocytes and serum immunoglobulins were normal.

Having been diagnosed LAD type-1, he was treated with cefuroxime, clindamycin combination and fluconazole. His chest x-ray showed a consolidation of the right upper lobe. *E. Coli* 10⁵ CFU/ml was isolated from tracheal aspirate culture.

On the 10th day of admission, the patient became febrile (39°C) and he was not able to move his left knee. The knee became progressively swollen and he had difficulty leaning on the left leg. The physical examination revealed that the left knee was considerably swollen with a large effusion. The joint was tender and warm, but there was erythema and limitation of motion. The circumference of left knee was 20 cm at the middle of the patella; the right was measured 17 cm. Arthrocentesis of the left knee yielded 5 ml of hemorrhagic fluid, containing 18 200 white blood cells/mm³ with 70% polymorphonuclear cells and 30% mononuclear cells. Gram stain of the synovial fluid did not reveal any organism. Culture of fluid both aerobic and anaerobic bacteria showed no growth. Synovial fluid glucose was 22 mg/dl, protein was 1.7 g/dl. He had leucocytosis (80 000/mm³), neutrophilia and increased erythrocyte sedimentation rate and serum CRP. Vancomycin, imipenem and granulocyte transfusions (1-2x10⁹/kg/daily, three times in a week) were administered. He recovered successfully after 6 weeks of the therapy and bone marrow transplantation was planned.

Discussion

Congenital CD11/CD18 deficiency was initially described in 1974 by Boxer et al,⁴ and in 1980, Crowley et al⁵ first proposed its molecular basis. The diagnosis of LAD-1 relies on both clinical and in-vitro observation. LAD is characterized by the inability of leukocytes, in particular neutrophilic granulocytes, to emigrate from the blood stream towards sites of inflammation. In-vitro studies show strongly reduced neutrophil adhesion and migration, deficient CD11/CD18 integrin expression on leukocytes, and

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a genetic defect of the β_2 integrin subunit.⁶ We have identified a patient whose clinical presentation is compatible with the diagnosis of LAD syndrome, in the presence of leukocytosis and deficient expression of CD11/CD18.

LAD type-1 is characterized by recurrent severe bacterial infections, impaired pus formation and wound healing. During neonatal period, septicemia may occur as a complication of omphalitis and detachment of the umbilical cord may be delayed for 21 days or longer.¹ Our patient had an antibiotic resistant sepsis and delayed umbilical cord detachment. Patients with LAD have recurrent necrotic and indolent infections of soft tissues, primarily skin, mucous membranes and intestinal tracts. Gingivitis and periodontitis are a constant feature, leading to gingival proliferation and loss of teeth and alveolar bone. Recurrent otitis, sinusitis, pneumonia, perirectal abscess and cellulitis are common. Ileocolitis, appendicitis, intestinal ulceration, tracheitis and esophagitis have also been reported.^{7,8}

Septic arthritis can result from hematogenous dissemination of bacteria, contiguous spread of an osteomyelitis, or direct inoculation of microorganisms into the joint cavity as a result of penetrating trauma. Haemophilus influenzae type b has been the most pathogen between 2 months and 5 years of age, but S aureus, E. coli or Candida albicans are often observed in immunocompromised patients.⁹ However, the yield of bacterial growth for synovial fluid is disappointingly small.

Bacteria are deposited in the subsynovial capillary vessel network, with migration of bacteria and blood products into the joint space. If the host's immune system does not contain the infection, bacterial multiplication occurs and the inflammatory cascade is triggered, resulting in joint damage. In congenital LAD, neutrophils and monocytes are deficient in three membrane proteins, leading to high susceptibility to bacterial infections. Patients with LAD require early and aggressive treatment of infections with appropriate antibiotics.⁷ Granulocyte transfusions have been used successfully for some patients with acute bacterial infections. HLA matched as well as haploidentical allogeneic bone marrow transplantation has been per-

formed in several patients with some success.¹⁰ We determined E coli in our patient's tracheal aspirate culture, but there was no sign of any growth of the synovial fluid. His symptoms resolved completely within 3 weeks after starting of the broad-spectrum antibiotics and granulocyte transfusions.

To our knowledge, we report the first case with LAD who developed septic arthritis treated with antibiotics and granulocyte transfusions.

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