Unhealed Chin Wound in an Infant with Leukocyte Adhesion Deficiency Type-I

Department of Child Health, *Department of Pediatrics, College of Medicine, King Khalid University, Abha, Kingdom of Saudi Arabia

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ABSTRACT

Leukocyte adhesion deficiency type 1 (LAD-1) is a rare, autosomal recessive disorder in which phagocyte adhesion, chemotaxis and ingestion of C3 biopsonised microbes are impaired owing to mutations in the gene for CD18β sub unit of β2 integrin. We report a 38 day old male infant with LAD-1 and infected unhealed chin wound and history of delayed umbilical cord separation. It is highly recommended that patients who diagnosed with mild to moderate LAD-1 with recurrent skin infections and simultaneous weak responses to conventional therapy to undergo bone marrow transplantation (BMT) to prohibit subsequent life-threatening complications.

KEY WORDS: leukocyte adhesion deficiency type-1; primary immunodeficiency disorder; unhealed wound

CASE REPORT:

A 38-day old Saudi infant of unconsanguineous parents, product of full term pregnancy with normal delivery and birth weight of 2.8 kg, had received BCG and Hepatitis B vaccine at birth and he was discharged home in good condition. He was well till one week prior to admission; then he started to develop history of fever for one week followed by ulcerative lesion on his chin. Fever was on and off, high grade which reached 38.9.1°C, responding partially to antipyretics, not associated...
with chills or sweating. On the sixth day of fever, he developed ulcerative lesion on his chin about 0.5 cm below the lower lip which was single, rounded in shape and 1 cm in diameter, progressive with time in size and crusted. No history of mouth ulcers, oral thrush, skin rash or same lesion on other parts of the body. No history of poor feeding or lethargy. No history of cough, shortness of breath, ear discharge, abdominal distension, vomiting, diarrhea, change in color or odor of urine or joint swelling. No history of trauma, insect bites, traveling to endemic area or contact with sick patient. Systemic review was unremarkable apart from delayed umbilical cord separation; it was at age of 30 day old. He has three healthy siblings (one brother and two sisters). There was no history of same illness in the family.

On examination, patient was conscious, alert with normal body built. He was not on reparatory distress, not cyanosed, pale or jaundiced with no apparent dysmorphic features. BCG scar was present. Vital Signs: Temperature 38.6°C, BP: 91/62 mmHg, RR: 36 breath/min and pulse: 140 beat/min. Growth parameter: weight: 4.5 Kg, height: 53 cm and head circumference: 35cm (All growth parameters were on 50 percentiles for his age). There was well defined ulcerative lesion on the chin 0.5 cm below the lower lip which was single, rounded in shape about 1.0 to 1.0 cm in size, progressive with time in size and erythematic with central crustation (Figure 1). Systemic examination was unremarkable.

**LABORATORY WORKUP:**

Complete blood count: WBC: 98000, RBC: 4.60, HGB 12 g/dl, HCT 42, MCV 89, MCH 29, PLT 436, NEUT: 82.6%, LYMPH: 8.2%, MONO: 8.6%, ESO: 0.2%, BASO: 0.4%. Peripheral blood smear showed: Neutrophil count of 44,600, shift to left with normochromic normocytic anemia with leukocytosis and absolute neutrophilia. WBC 98,2 dropped down to 68000 after 2 days and then to 49000 in the 4th day of admission. ESR: 45 MM/hr, Renal and hepatic function tests were preserved. Blood culture: Staphlococcus Hominis. Urine and stool cultures were negative. Cerebrospinal fluid (CSF) was normal with negative culture. CD 18 and CD 11 were low.

The diagnosis of LAD-1 with leukocytosis and septicemia was made. Patient was admitted to pediatric medical ward and treated with antibiotics; repeated blood culture came negative and was referred to higher center for stem cell transplant. Patient underwent a successful allogeneic stem cell transplant from fully-matched mother at age of 4 month of age at King Faisal Specialist Hospital and Research Center in Riyadh. The lesion on the chin was improved. The patient had a follow up in the clinic in our hospital; he was fine with no chin wound and no complaint.

**DISCUSSION:**

Leukocyte adhesion deficiency type-1 (LAD-1) is a rare disease with only 200 cases reported in the medical literature. LAD-1 was first described as a separate entity among immunodeficiencies in 1979 by Hayward et al. LAD-1 is a rare, inherited immunodeficiency that affects one per million people yearly and usually presents with recurrent, indolent bacterial infections of the skin, mouth, and respiratory tract with impaired pus formation and wound healing. Patarroyo M, Makgoba M stated that Leucocyte adhesion deficiency is characterized by the inability of leucocytes, especially neutrophils, to emigrate from the blood stream towards sites of inflammation. Infectious foci are therefore non-purulent and eventually become necrotic because of abnormal wound healing. The genetic defect in LAD-1 has been mapped to mutations of the gene encoding for CD18 on chromosome 21q22.3. The clinical picture is characterized by delayed umbilical cord separation, recurrent life threatening bacterial infection of skin and mucous membrane, impaired pus formation, delayed wound healing and persistent neutrophilia. Early studies found that leukocytes from patients with LAD-1 were deficient in the expression of the three integrins containing beta 2 or CD18 (Mac-1, LFA 1, p150, 95). Paucity or absence of CD11/CD18 neutrophils by flow cytometry is diagnostic. If less than 1% of neutrophils have CD11/CD18 markers, the prognosis is poor; the
The average life span is 10 years. The only known therapy is bone marrow transplantation. Correct and early diagnosis of LAD-I is vital to the success of treatment and prevention of aggressive infections; early diagnostic suspicion and early treatment improve the prognosis.

Three different types of LADs are described in literature. LAD-I, in which the beta 2-integrin family is deficient or defective. LAD II, in which the fucosylated carbohydrate ligands for selections are absent. LAD III is due to defective activation of all beta integrins with tendency to bleed. Pathogenetically, 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. Leukocyte adhesion defect, because of its rarity, presents a diagnostic dilemma. In this report, we described the findings of a patient with clinical features of LAD-I disorders patient. Our patient did not have any clinical findings at birth and was discharged at the status of the health infant and in his family none of his brother or sister has suffered from the same illness. Clinical presentation includes delayed separation of the umbilical cord for less than 1 month, leukocytosis, periodontitis recurrent infections of the skin, fever. LAD was suspected. Movahedi et al. have described the clinical and laboratory findings of 15 patients with LAD I in Iran. The most commonly occurred manifestations were: recurrent infections (93.3%), poor wound healing (86%), oral ulcers (86%), and skin abscesses (80%) Patients with this disorder suffer from life-threatening bacterial infections, and in its severe form, death usually occurs in early childhood unless stem cell transplantation is performed. Bone marrow and other stem cell transplantation are the therapies of choice in leukocyte adhesion deficiency (LAD) and have a very high success rate. Thus, bone marrow or other stem cell reconstitution is a first-line treatment for severe leukocyte adhesion deficiency type I, in which less than 1% CD18 expression is detected. In addition, gene replacement therapy has shown good results in canine model of LAD I and may be beneficial also in human beings.

**KEY MESSAGES:**

The possibility of leucocyte adhesion deficiency (LAD) should be kept in mind in the event of severe and recurrent infections in a child.

It is highly recommended that patients who diagnosed with mild to moderate LAD-I with recurrent skin infections and simultaneous weak responses to conventional therapy to undergo BMT to prohibit subsequent life-threatening complications.

**CONCLUSION:**

Pediatricians should keep LAD-I in their mind; the rarity of this disease requires that physicians have a high index of suspicion in a child with history of delayed umbilical cord separation, repeated infections and marked leukocytosis with delayed unhealed lesions not improving well to medications even in the absence of infections.

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**REFERENCES:**


