A neonate with perianal cellulitis due to leukocyte adhesion deficiency - A case report

Muthu Kumaran Jagannathan[1], Swapna Lingaldinna[2], S Vivek[1], P Balasubramaniam[1]

From Departments of [1]Paediatric Surgery and [2]Neonatology, Institute of Child Health and Hospital for Children, Chennai, Tamil Nadu, India

Correspondence to: Swapna Lingaldinna, Department of Neonatology Surgery, Institute of Child Health and Hospital for Children, Chennai, Tamil Nadu, India. E-mail: drswapnalingaldinna@gmail.com

Received – 27 January 2017 Initial Review - 11 February 2017 Published Online – 15 April 2017

ABSTRACT

Leukocyte adhesion deficiency (LAD) is a rare autosomal recessive disorder characterized by absence or dysfunctional CD18 on the surface of leukocytes due to a mutation in ITGB2 gene. The hallmarks of LAD are defects in leukocyte adhesion and marked leukocytosis. It is characterized by recurrent bacterial infections of the skin and mucosal membrane. Here, we report clinical and flow cytometric immunophenotyping of a baby diagnosed with LAD Type 1.

Key words: *Perianal cellulitis, Leucocyte adhesion deficiency, Neonate*

Leukocyte adhesion deficiencies are a group of immunodeficiency disorders characterized by inability of leukocytes to migrate toward the site of infection [1]. Three types of leukocyte adhesion deficiency (LAD) have been described. Type 1, which is characterized by a mutation in the common chain (CD18) of β2 integrin family. Type 2 is characterized by absent fucosylated carbohydrate ligands in the neutrophils needed for binding to selections E and P in the activated endothelium and Type 3 which is characterized by a defect in the activation of integrins β1, β2, and β3. Here, we report a case of neonate diagnosed with LAD Type 1.

CASE REPORT

A 22-day-old female baby born to a primi mother at 39 weeks of gestation with a birth weight of 2.9 kg by forceps assisted vaginal delivery. She was admitted to us with a history of loose stools of around 25-30 episodes per day from the 7th day of life. Baby had a normal transition at birth and was on exclusive breastfeeding. Baby had normal urine output. Antenatal period was uneventful, and antenatal scans were normal. Parents were of third degree consanguineous. Baby also had pus discharge from umbilicus and perianal ulceration. For the above complaints, baby was being treated with oral and local antibiotics.

On examination, baby weighed about 2.780 kg and had erythema with induration around the umbilicus and severe perianal cellulitis and mild hepatosplenomegaly. Activity and suck were good. Perfusion and urine output was normal. On investigating, baby had a hemoglobin of 12.7 g%, with leukocytosis of 77,300 cells/mm^3 with polymorphs of 75% and normal platelet count. Peripheral smear showed hypersegmented polymorphs, toxic granules, moderate anisopoikilocytosis, and platelets in single and small clumps. Stool pH was 6 and stool reducing substance was negative. Septic work up showed positive C-reactive protein and blood culture has grown nonpathogenic organism. Stool electrolytes and stool examination were normal.

Baby was started initially with injection cloxacillin 50 mg/kg/dose TID and injection amikacin 15 mg/kg/OD and in view of no improvement, antibiotics were upgraded to injection meropenam 20 mg/kg/dose TID and injection vancomycin 15 mg/kg/dose TID and continued for 2 weeks. Periumbilical erythema and induration (Fig. 1) improved and the severity of perianal ulceration decreased (Fig. 2). Baby's umbilical cord fallen off on day 27 of life. In view of omphalitis, delayed fall of the umbilical cord and high leukocyte count, LAD was suspected and hence, flow cytometry was done. Flow cytometry showed 0% of the neutrophils are positive for CD18 and CD11a which confirmed the diagnosis of LAD (Fig. 3). Parents were counseled about the prognosis of the baby, and the mutational analysis has been sent for both the baby and the parents and the reports are awaited.

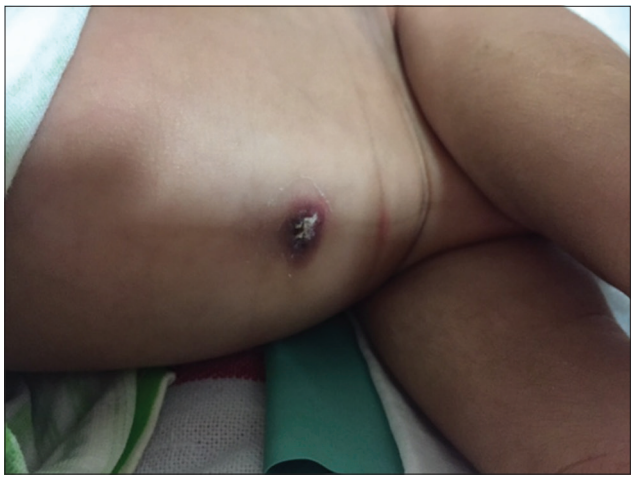

Figure 1: Healed omphalitis

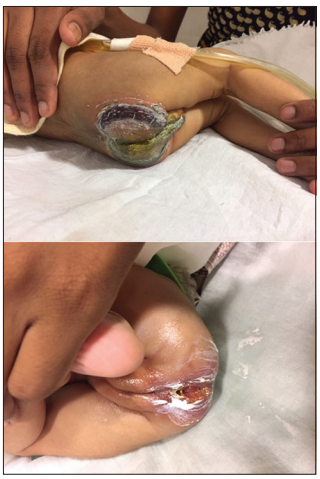

Figure 2: Perianal cellulitis

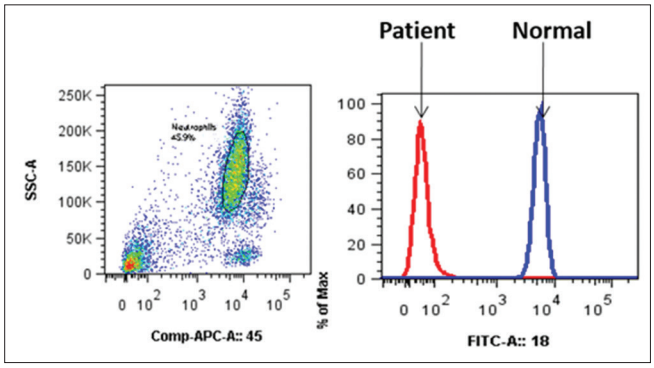

Figure 3: Flow cytometric analysis of neutrophil CD18 expression. Staining of CD18 from a normal baby is indicated in blue color and staining for CD18 from the baby with LAD is indicated in red color

DISCUSSION

LAD is a rare primary immunodeficiency disorder characterized by a lack of leukocyte recruitment to the site of infection [1]. The incidence of LAD is not known, but it is estimated to be one in one million. Till now, only 400 cases have been reported in literature. Males and females are affected equally. LAD is associated with failure to express CD18 on the surface of neutrophils. CD18 is the essential component of β2 integrin [1]. β2 integrins are glycoproteins that are expressed as transmembrane proteins which transmit signals from the extracellular surface to cytoskeletal proteins [1]. These integrins are primarily responsible for migration of leukocytes into the areas of inflammation.

The most common presentation of Type 1 is the delayed separation of umbilical cord [1]. Other features are omphalitis, oral ulcers, perirectal and labial cellulitis, otitis media, impaired wound healing, and periodontitis [2-4]. Life-threatening infections such as septicemia, bronchopneumonia, and aseptic meningitis can occur. Pus is usually not present [4]. The differential diagnosis includes conditions associated with leukocytosis such as infections, leukemia, leukemoid reactions, and lymphoproliferative disorders. The severity of the condition is related to the degree of CD18 deficiency. The mild to moderate type is characterized by 2-30% of the surface expression of CD18 while severe form is characterized by <2% surface expression of CD18 [5].

Diagnosis is based on flow cytometry detection of CD18 and the associated alpha subunits CD11a, CD11b, and CD11c on the surface of leukocytes [6]. The disorder is due to a mutation in gene (ITGB2) that codes for a subunit of β2 integrins mapped to chromosome arm 21q22.3 [7]. Management depends on the clinical severity. Mild to moderate disease usually responds to appropriate antibiotic therapy while severe disease requires bone marrow or hematopoietic cell transplantation [3]. Careful oral hygiene is important to control periodontitis and prevent oral infections. Babies with LAD can receive routine vaccinations including live virus vaccine. Patients with severe form of the disease often die in infancy unless hematopoietic cell transplantation is performed [8]. If transplant is accomplished before severe infections have occurred, the prognosis is very good [9]. Sequence analysis to define the molecular defect in β2 subunit is recommended to help in prenatal diagnosis. Leukocytes express CD18 at a surface level from 20 weeks of gestation; therefore, cordocentesis can contribute to the prenatal diagnosis. Prenatal diagnosis can be established using chorionic villus biopsy and mutational analysis [10].

CONCLUSION

This case to reiterates the importance of high index of suspicion to diagnose LAD, especially, in a case presenting with cellulitis and delayed fall of the umbilical cord.

REFERENCES

1. Madkaikar M, Currimbhoy Z, Gupta M, Desai M, Rao M. Clinical profile of leukocyte adhesion deficiency Type I. Indian Pediatr. 2012;49(1):43-5.
2. Wada T, Tone Y, Shibata F, Toma T, Yachie A. Delayed wound healing in leukocyte adhesion deficiency Type 1. J Pediatr. 2011;158(2):342.
3. Akbari H, Zadeh MM. Leukocyte adhesion deficiency. Indian J Pediatr. 2001;68(1):77-9.
4. Tipu HN, Tahir A, Ahmed TA, Hazir T, Waqar MA. Leukocyte adhesion defect. J Pak Med Assoc. 2008;58(11):643-5.
5. Fischer A, Lisowska-Grospierre B, Anderson DC, Springer TA. Leukocyte adhesion deficiency: Molecular basis and functional consequences. Immunodefic Rev. 1988;1(1):39-54.
6. Alizadeh P, Rahbarimanesh AA, Bahram MG, Salmasian H. Leukocyte adhesion deficiency Type 1 presenting as leukemoid reaction. Indian J Pediatr. 2007;74(12):1121-3.
7. Mathew EC, Shaw JM, Bonilla FA, Law SK, Wright DA. A novel point mutation in CD18 causing the expression of dysfunctional CD11/CD18 leucocyte integrins in a patient with leucocyte adhesion deficiency (LAD). Clin Exp Immunol. 2000;121(1):133-8.
8. Qasim W, Cavazzana-Calvo M, Davies EG, Davis J, Duval M, Eames G, et al. Allogeneic hematopoietic stem-cell transplantation for leukocyte adhesion deficiency. Pediatrics. 2009;123(3):836-40.
9. Hamidieh AA, Poupak Z, Behfar M, Faghihi-Kashani S, Fazlollahi MR, Hosseini AS, et al. Leucocyte adhesion deficiency Type 1: The outcome of reduced intensity conditioning hematopoietic stem cell transplantation. Biol Blood Marrow Transplant. 2015;21(2):S223.
10. Etzioni A. Defects in the leukocyte adhesion cascade. Clin Rev Allergy Immunol. 2010;38(1):54-60.

Funding: None; Conflict of Interest: None Stated.

How to cite this article: Jagannathan MK, Lingaldinna S, Vivek S, Balasubramaniam P. A neonate with perianal cellulitis due to leukocyte adhesion deficiency - A case report. Indian J Child Health. 2017; 4(2):277-278.