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Poverty in the Midst of Plenty – A Case of Leukocyte Adhesion Defect

Dr. Saraladevi Manimaran[1], Dr. Hariharasudhan Thiyagarajan[2*], Dr. Sundari Subramanian[3]

[1]Junior Resident, Department of paediatrics, Sree Balaji Medical College and Hospital, Chennai.
[2]Senior Resident, Department of paediatrics, Sree Balaji Medical College and Hospital, Chennai.
[3]Professor And Head of Department, Department of paediatrics, Sree Balaji Medical College and Hospital, Chennai.

Corresponding Author: Dr. Hariharasudhan Thiyagarajan[2*]
Senior Resident, Department of paediatrics, Sree Balaji Medical College And Hospital, Chennai.
Email id: msaraladevi24@gmail.com

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ABSTRACT:
An autosomal recessive inheritance pattern characterizes LAD I, a genetic condition. It is characterized by a CD18 expression deficiency, which leads to major deficits in the ability of white blood cells to migrate and respond to chemical signals. From a clinical perspective, this condition is characterised by repeatedinfections by bacteriaaffecting the mucosa and skin. Absence of pus formation results in impeded wound healing. This condition often begins with omphalitis, an infection of the umbilical cord. Timely identification and hematopoietic cell transplantation (HCT) before serious infections occur are critical for a positive prognosis. Although LAD-1 cases present with hallmark feature of delayed separation of umbilical cord, We present a 35-day-old baby who had separation of umbilical cord at correct time but presented with a perinasal hypopigmented lesion and omphalitis, exhibiting delayed healing (POVERTY) despite a high WBC count (PLENTY).

Keywords: LAD, AR, Omphalitis, Leukocytosis, HSCT.

1. Introduction

Changes in the ITGB2 gene, encoding the CD18 subunit of the β2 integrins, lead to leukocyte adhesion deficiency type-1. This is a autosomal recessive condition with primary immunodeficiency that makes it hard for neutrophils to stick to and move to an infection or inflammatory site. The severity of LAD-1 correlates with the degree of deficiency of CD18. A group of integrin molecules on the surfaces of leukocyte cells control leukocyte trafficking. This is a key response to integrins and an important dynamic immune surveillance activity.LAD-1 disorders may arise as a result of genetic changes in leukocyte integrin numbers or activation. The β2 integrins is very important for theadhesion-dependent activities of neutrophils and monocytes because they help integrin dimerization happen correctly.
The LAD-1 syndrome is brought on by low levels of any one of four β2 integrin subfamilies: αXβ2, αMβ2, αLβ2, or αDβ2. Certain lymphocyte subsets and macrophages are immunological effector cells that also express the β2 integrins. αMβ2 and αLβ2 function as the C3b receptor in myeloid and lymphoid cells, but αDβ2 is exclusive to human and mouse macrophage subsets. The ITGB2 gene, presentin the chromosome 21q22.3 (long arm) , encodes the β2-integrin component CD18. This gene has reported over 80 mutations to date. The level of CD18 deficiency strongly correlates with how bad the symptoms are; mild to moderate types are defined by neutrophils that express 2 to 30% CD18, while severe LAD-1 is defined by neutrophils that express less than 2% CD18.

When they are newborns, people with LAD-1 often have recurrent slow-growing necrotic infections of the mucosa and skin, along with omphalitis and a delay in separating the umbilical cord. Furthermore, severe malnourishment, an inability to flourish, and delayed wound healing are prevalent, whereas colitis is rare. Due to a lack of awareness among doctors regarding LAD-1, a large number of individuals may have infections prior to receiving the diagnosis. Although LAD-1 cases present with hallmark feature of delayed separation of umbilical cord, We present a 35-day-old baby who had separation of umbilical cord at correct time but presented with a perinasal hypopigmented lesion and omphalitis, exhibiting delayed healing (POVERTY) despite a high WBC count (PLENTY). (Figure 1 describing the title)

Case Presentation
We admitted a35-day-oldterm infantwith complaints of a perinasal pyoderma-like lesion (figure 2 showing skin lesion), which slowly healed with hypopigmentation and abdominal distension. The infant was first born to consanguineous marriage, of a 28-year-old mother delivered by normal labour, and she had aApgar within normal limit and AGA at birth. She was sick and febrile (39 oC) when she was admitted. Despite the separation of the umbilical cord at correct time, this child presents with redness around umbilicus and poor healing of skin lesion. Examination revealed erythema and serous discharge around umbilicus, suggests omphalitis (figure 3 showing omphalitis), and hepatosplenomegaly. Lab test shows significant leukocytosis (a WBC count of 98000 mm3 with 66% polymorphonuclear cells). Flow cytometry analysis performed immunophenotyping, revealing gated neutrophils without surface expression of CD18 and CD11, consistent with LAD Type 1(Table 1 showing laboratory investigations). Hematopoietic stem cell transplantation (HSCT) was done with HLA matched mother.

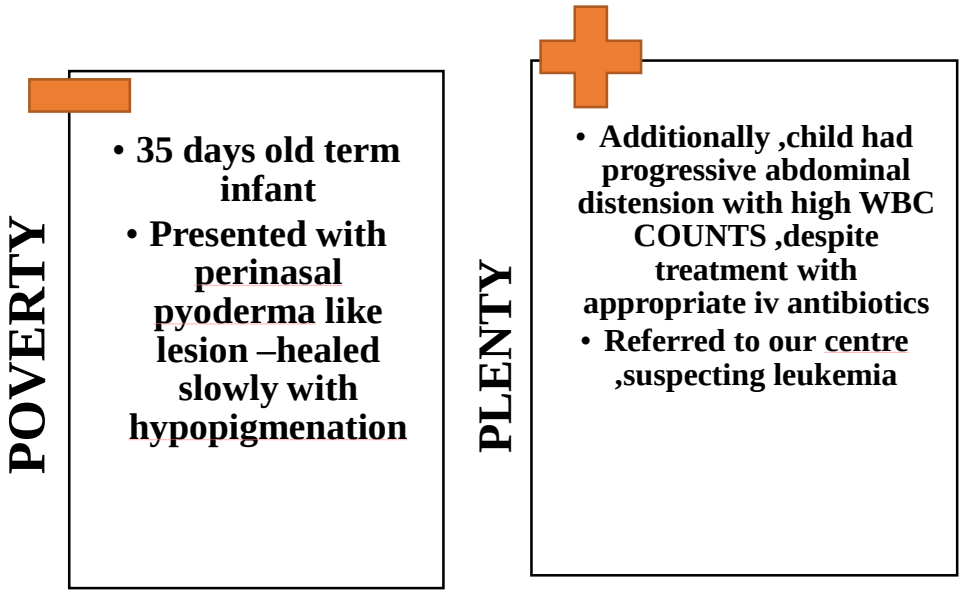

Figure 1

Table-1: Hematological and Immunological Parameters in a Patient with LAD I

Parameters	**value**
Hemoglobin	8.4 g/dl
RBC count	$4.3*10^{12}$/L
WBC count	98000/mm^3
Differential count	N – 66% L – 33%
Platelets	61000/mm^3
QCRP	64
Blood culture	sterile
Flow cytometry	Gated neutrophils with no surface expression for CD18 and CD11

Figure 2

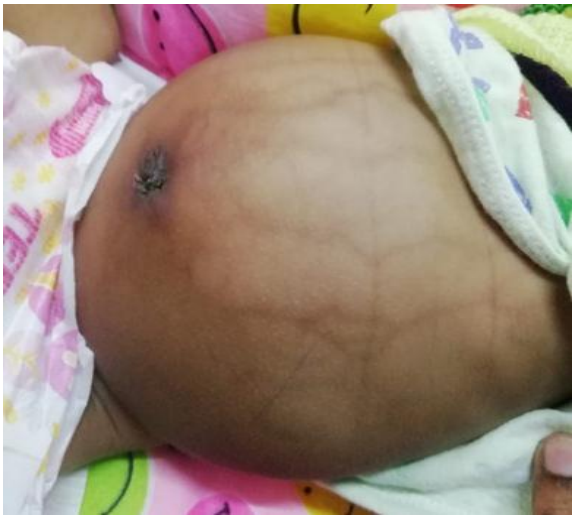

Figure 3

2. Discussion

Thus far, we have described three types of leucocyte adhesion deficiency (LAD). Changes in the subunit of the β2 integrin cause leukocyte adhesion deficit type I (LAD I). Individuals with LAD I experience severe, recurrent infections of their mucous membranes and skin. Without hematopoietic precursor cell transplantation, those with severe presentations often face premature mortality. The LAD IIis shown by neutrophils that don't have the fucosylated ligand they need to stick to selectin E and selectin P in the active endothelium. Clinically, individuals with LAD II exhibit fewer severe infections but have delayed psychomotor development, weight gain, and height growth. Leucocyte adhesion deficit type III (LAD III) is when integrins β1, β2, and β3 don't work right, which can lead to serious infections. Infection triggers an innate immune response. Peripheral circulation recruits neutrophils and monocytes to the infection site, where they adhere to endothelial cells by adhesion molecules and respond to chemotactic factors generated by the infection.

The principal abnormality in LAD I is associated with the β2 subunit, which is essential for the surface expression of α subunits. Patients' peripheral blood leucocytes show a complete lack of CD18 expression, compromising the expression of the three β2 integrins. We have observed significant abnormalities in adhesion, migration across the endothelium cell layer, and chemotaxis in vitro. LAD I is caused by changes in the β2 integrin (ITGB2) gene, which codes for the CD18 part and is found on the chromosome 21q22.23 (long arm).

CD18 deficits are caused by a different of molecular abnormalities, including mutations that result in quantitatively normal but functionally abnormal CD18, point mutations that cause single amino acid substitutions, and splicing errors that produce unstable proteins. These changes usually happen near where β2 integrins bind to their ICAM . This causes less CD18 mRNA expression and protein precursors or mRNA that are the wrong size. Late falling of the umbilical stump, leucocytosis, periodontitis, recurrentinfections by bacteria in mucosa and skin, a lack of pus, and slow wound healing are all signs of LAD I. The degree of CD18 loss correlates with the severity of the infectious consequences. LAD I is categorised into severe (≤2% of normal CD18 expression) and moderate to mild (2–30% of normal CD18 expression) phenotypes.

Severe cases often result in early childhood mortality without proper care, as well as frequent and severe infections. Moderate to mild cases experience fewer significant infections, with most patients surviving into adulthood. These patients do not have an increased risk to viral infections but struggle with bacterial and fungal protection. Infections, starting from birth, affect the gut, skin, respiratory system, and perirectal region, often progressing rapidly towards systemic infection. Omphalitis characterised by delayed umbilical stump shedding, is a hallmark infectious manifestation. Surviving infants commonly suffer from severe gingivitis and periodontitis. Enteric gram-negative bacilli and Staphylococcus aureus are the most common pathogens.

But in our case child had normal separation of umbilical cord. In addition, the child had an initial presentation of pyoderma like lesion in perinasal region which showed delayed healing.

LAD I is characterised by the absence of pus at infection sites due to restricted extravascular leucocyte mobilization. Inflammatory site biopsies show inflammation without neutrophils. Because of LFA-1's critical role in lymphocyte function, fewer lymphocytes are present in lymphoid tissue. Late umbilical stump shedding and dystrophic scar tissue formation are indicators of poor wound healing. Laboratory tests show significant neutrophilia, even without infection. During infection, we observe leucocytosis with neutrophilia (five to twenty times normal, up to 100,000 cells/mm3). For a diagnosis to be final, the patient must have low levels of CD18 in neutrophils (less than 5% of normal) and either a β2 integrin gene mutation or no β2 integrin mRNA in leucocytes. Low levels of CD18 in neutrophils (less than 5% of normal), recurring bacterial or fungal infections, leucocytosis (more than 25,000 cells/mm3), and delayed umbilical stump shedding or wound healing problems are all signs of a likely diagnosis. Leucocytosis >25,000 cells/mm3 with recurrent bacterial infections, deep-seated and severe infections, or the lack of pus at infection sites are all possible diagnoses.

Monoclonal antibodies for CD11 and CD18, used in flow cytometry, show that leucocytes do not have CD18 or related alpha subunits (CD11a, CD11b, and CD11c). This confirms the diagnosis. Sequence analysis is recommended to identify the β2 subunit's molecular fault. After week 20 of intrauterine development, cordocentesis can establish a prenatal diagnosis by detecting CD18 surface expression in leucocytes. Early prenatal diagnosis in families with known molecular abnormalities is possible using chorionic biopsies and mutation analysis. Recently, researchers have developed pre-implantation diagnostic methods. The diagnosis is usually determined by clinical signs and laboratory tests. Differential diagnosis is needed for conditions that have a lot of white blood cells, like leukaemia, leukaemoid reactions, infections, and other processes that cause lymphocytes to multiply.

3. Conclusion

An autosomal recessive inheritance pattern characterizes LAD I, a genetic condition. It is characterized by a CD18 expression deficiency, which leads to major deficits in the ability of white blood cells to migrate and respond to chemical signals. From a clinical perspective, this condition is characterised by repeatedinfections by bacteria that mainly affect the mucosa and skin. Absence of pus formation results in impeded wound healing. This condition often begins with omphalitis, an infection of the umbilical cord. Timely identification and hematopoietic cell transplantation (HCT) before serious infections occur are critical for a positive prognosis.

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4. Reference

1. Al-Herz W, Bousfiha A, Casanova JL et al.. Primary immunodeficiency diseases: an update on the classification from the international union of immunological societies expert committee for primary immunodeficiency. Front Immunol 2014;5:162 10.3389/fimmu.2014.00162
2. Smith CW. Adhesion molecules and receptors. J Allergy ClinImmunol 2008;121:S375–9. 10.1016/j.jaci.2007.07.030
3. Hanna S, Etzioni A. Leukocyte adhesion deficiencies. Ann N Y Acad Sci 2012;1250:50–5. 10.1111/j.1749-6632.2011.06389.
4. Harris ES, Weyrich AS, Zimmerman GA. Lessons from rare maladies: leukocyte adhesion deficiency syndromes. Curr Opin Hematol 2013;20:16–25. 10.1097/MOH.0b013e32835a0091
5. van de Vijver E, Maddalena A, Sanal O et al.. Hematologically important mutations: leukocyte adhesion deficiency (first update). Blood Cells Mol Dis 2012;48:53–61. 10.1016/j.bcmd.2011.10.004
6. van de Vijver E, Van den Berg T, Kuijpers T. Leukocyte adhesion deficiencies. Hematol Oncol Clin North Am 2013;27:101–16. 10.1016/j.hoc.2012.10.001