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Original Research Paper

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LEUKOCYTE ADHESION DEFECT: A CASE SERIES OF 3 CHILDREN

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ABSTRACT Leukocyte adhesion defect (LAD) is a rare, autosomal recessive primary immunodeficiency disorder of phagocytes, in which there is defective aggregation at the site of infection due to the absence of surface integrins. Diagnosis is based primarily on flowcytometric analysis of neutrophils for the surface expression of CD11, CD18 and CD15s. We describe here a case series of 3 children presented to us within a period of one year and diagnosed as LAD. Diagnosis was made on the basis of clinical features and simple laboratory investigations.

KEYWORDS : Leukocyte adhesion defect, Immunodeficiency disorder, Neutrophils

INTRODUCTION

Neutrophil responses to inflammation are initiated as circulating neutrophils flowing through the postcapillary venules detecting low levels of chemokines and other chemotactic substances released from a site of infection. The initial associations are low affinity, reversible and primarily mediated by cell-selectin-carbohydrate interactions. This leads to the phenomenon known as leukocyte rolling, which allows more intense exposure of neutrophils to activating factors TNF and IL-1, leading to induction of qualitative and quantitative changes in the family of 2 integrin adhesion receptors on the neutrophils (the CD11/CD18 group of surface molecules).[1]

Leucocyte adhesion deficiency is characterized by the inability of leucocytes, especially neutrophils, to emigrate from the blood stream towards sites of inflammation. First patient was described in 1980 by Crowley et al, they had elevated peripheral blood neutrophil count with few neutrophils at the inflammatory site and recurrent infections.[2] Only about 300 cases of LAD I have been reported worldwide.[3] Infectious foci characteristically are non-purulent and eventually become necrotic because of abnormal wound healing. Various molecular defects have been described: LAD 1 is due to mutation in ITGB2 gene on chromosome 21q22.3 that encodes the 2 subunit of integrin molecule.[2] In LAD 2 there is mutation in gene on chromosome 11 that encodes Golgi apparatus GDP-Lfucose transporter.[3-5] The genetic defect of LAD 3 is unknown but there is defect in integrin activation process.

More than 300 cases have been described for LAD 1 worldwide, while for LAD 2 and LAD 3; there are less than 10 cases each.[4] FACS (Fluorescence activated cell sorter) analysis of neutrophil surface CD18 and CD15s are diagnostic for LAD I and II respectively. Inability to express/up regulate CD18 on neutrophil surface following phorbol myristate acetate stimulation can be used as an alternative for diagnosing LAD1.[6]

Case 1

A one-month and 6 days girl presented with swelling and redness around umbilicus and palatal ulcer for 3 days (figure1a, 1b). She was born to a primigravida at term with normal birth weight. Cord shed at 3 weeks of life. She has no family history of early infant death and recurrent infections. On examination; erythema noticed around umbilicus; no discharge. Hemogram showed marked neutrophilic leukocytosis (table 1). Flow cytometry analysis showed deficiency of CD18 on neutrophils (figure 2).

Case 2

A one-month boy born to primigravida at term with birth weight 3 kg presented with history of vesicles around neck from one week of life followed by ulceration. Family history was not suggestive of recurrent infections and early deaths. On examination; necrotic ulcer was present on anterolateral aspect of neck (figure 1c) and periumbilical redness with normal systemic examination. Hemogram revealed neutrophilic leukocytosis (Table 1).

Case 3

A 3-month old, well thriving boy, born at term with normal weight presented with history of fever for 10 days. There was history of multiple vesicular lesions 15 days back, which healed spontaneously leaving behind black discoloration. Cord shed on day 22 of life. Family history was not significant. Examination revealed black coloured lesion on forehead (figure1d) and vesicles in groin, periumbilical redness with mucoid discharge. Hemogram revealed neutrophilic leukocytosis (Table 1).

DISCUSSION

Leukocyte adhesion defect, because of its rarity, presents a diagnostic dilemma. The first step in the accurate diagnosis is clinical suspicion (delayed separation of the cord, infection without pus formation) confirmation requires flowcytometric analysis of leukocytes for the presence of integrins. Although modern flowcytometry studies have facilitated the diagnosis, the practitioners must be aware of the clinical features that point towards this rare entity. The umbilical cord of the newborn usually sloughs by the end of 2nd postnatal week.[7] and mean time of separation of umbilical cord is 7.4 days.[8] However, it must be kept in mind that there could be other reasons for delayed separation of the umbilical cord such as urachal anomalies,[9] antibiotic administration, prematurity and low birth weight.[8]

Our patients presented with nonhealing, non-purulent and necrotic ulcer. There was also a history of delayed umbilical cord separation.

CONCLUSION

Awareness regarding primary immunodeficiency disorders is critical for their identification. A few important clinical clues and simple investigations help us diagnose these argely unrecognized conditions. Non purulent infections & neutrophilic leukocytosis are strongly suggestive of LAD.

Table 1: Laboratory investigations

	Case 1	Case 2	Case 3
Hb(g/dl)	12.1	10.6	8.2
TLC(/mm3)	127,950	161,000	44,300
DLC(%)	$P_{60}M_{15}L_{23}E_{2}$	$P_{91}M_{2}L_{7}E_{0}$	$P_{75}M_{0}L_{25}E_{0}$
ANC(/mm3)	**76,770**	**147,170**	**33,200**
Platelets(/mm3)	450,000	169,000	471,000

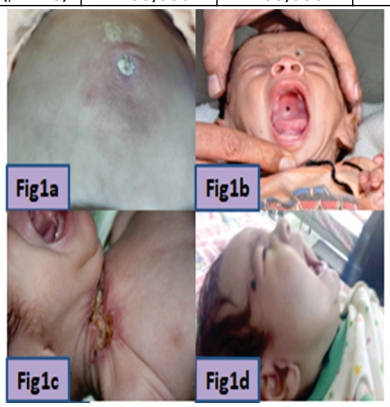

Figure 1: Clinical images

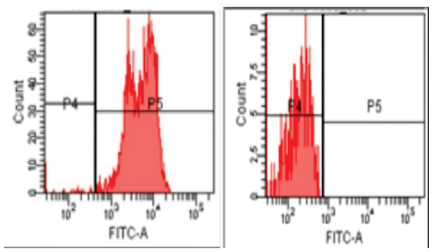

Figure 2: Flow cytometry (CD18 on neutrophils)

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