INTRODUCTION

Leukocyte adhesion deficiency type I (LAD-I) is a rare autosomal recessive disorder with usual described incidence of 1 in 1 million. Overall about 300 cases have been reported until date with very few cases in newborn. LAD-I is characterized by delayed separation of the umbilical cord at birth, persistent leukocytosis and recurring bacterial and fungal infections involving skin, mucosa, impaired pus formation and wound healing. We present a case of unusual presentation of LAD-I in a neonate with normal separation of umbilical cord and absence of omphalitis.

CASE REPORT

The present case report is about a 23-day-old full term female infant, the first offspring of 3rd degree consanguineous marriage was admitted with a history of multiple bullous lesions starting from day 5 of life over right upper arm progressing to neck, upper limb and groin over subsequent 10 days, which did not respond to the local treatment. The baby was exclusively breast fed and was gaining adequate weight. There was history of cord separation on day 10 of life. There was no history of fever or decreased feeding. There had been no previous abortions, pregnancy and delivery was uneventful.

On examination, there were multiple necrotic ulcerative skin lesions [Figure 1] with erythematous base over neck, right elbow, groin and left thigh predominantly with evolving bullous and papular skin lesions over chest and trunk. There was no pus discharge from the aforementioned skin lesions. Investigations revealed hemoglobin 8.5 g/dl, total leucocyte count 85,800/mm³, absolute neutrophil count 66,066/mm³, band forms 11%, platelets 102,000 with peripheral smear showing anisopoikilocytosis and toxic granules.

Quantitative C reactive protein was 85 mg/L, cerebrospinal fluid values were within normal limits. Chest X-ray was suggestive of right paracardiac pneumonia. Ultrasonography showed no collection in subdiaphragmatic, pelvic or other sites. Blood culture revealed acinetobacter species and wound swab revealed proteus vulgaris. Infant was started on antibiotics as per sensitivity results. In view of high leucocyte counts in an apparently well grown child, the possibility of primary immunodeficiency was considered. Screening tests done for primary immunodeficiency were quantification of immunoglobulin levels (IgM, IgG, IgE and IgA), Flow cytometry, CH50 levels and nitroblue tetrazolium test. Apart from flow cytometry analysis results of above mentioned tests were normal. Flow cytometry analysis revealed that none of the neutrophils in the infant were positive for CD18, CD11a and CD11c with normal levels noted in both parents [Figure 2].

Diagnosis was confirmed as LAD-I severe form. Skin biopsy revealed epidermal necrosis with ulceration with inflammatory granular cell infiltrates composed largely of neutrophils and eosinophils. The case was managed by supportive care, increasing immunoglobulin levels and avoiding any stressful situations.

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by lymphocyte, plasma cell, histiocytes, macrophages and rarely eosinophils.

The baby responded to antibiotics clinically with resolution of pneumonia, healing of skin lesions and normalization of counts. Baby was discharged on oral antibiotics. On discharge the parents were advised to avoid Bacillus Calmette-Guérin, typhoid vaccines and were instructed to adhere to the national immunization schedule. In addition, advice regarding human leukocyte antigen typing and subsequent bone marrow transplantation was given but due to financial reasons the parents refrained from further diagnostic and therapeutic work-up.

**DISCUSSION**

LAD disorders are a group of rare diseases characterized by a lack of leukocyte cell surface expression of integrin molecules, which are essential for adhesion of leukocytes to the endothelial cells and chemotaxis.[1] Three types of this disorder are described to date; LAD-I caused by the lack of CD18 integrins on the neutrophils cell surface has the worst prognosis and most patients die within the 1st year of life.[3]

The severity of infections and complications is related to the severity of CD18 deficiency; cases with <1% expression are clinically severe, whereas those with 2.5-10% expression are...
moderate to mild. In LAD-II, the neutrophils are rich in CD11 and CD18 integrins, but lack the required surface membrane carbohydrate Sialyl-Lewis X which is essential for adherence to activated endothelial cells. A defect in activation of Rap1 protein has recently been described, which results in lack of integrin activation regulation and a set of similar manifestations which are diagnosed as LAD-III. LAD-III (also called LAD-I variant) is characterized by both severe bacterial infections and a severe bleeding disorder. LAD-I is caused by mutations in the ITGB2 gene (21q22.3), encoding the beta-2-integrin CD18. LAD-II results from mutations in the SLC35C1 gene (11p11.2), encoding the guanosine 5’-diphosphate-fucose transporter. LAD-III is caused by mutations in the FERMT3 gene (11q13.1), encoding kindlin-3 in hematopoietic cells.

LAD-I is clinically characterized by delayed shedding of the umbilical stump, recurrent bacterial infections mainly of the skin and mucosal membranes, leukocytosis, periodontitis, absence of pus and poor wound healing. The mean time of normal cord separation was reported between 5.8 and 10.9 days in different studies. Our patient presented with multiple skin lesions on day 23 with normal separation of cord on day 10 with absence of umbilical cord. The most commonly implicated microorganisms are *Staphylococcus aureus* and enteric gram negative bacilli. Severe form of LAD-I usually manifest in neonatal period but are diagnosed at a later age, require frequent hospital admissions for recurrent infection. Only 2 cases in literature have been diagnosed as LAD-I in neonatal period while others have been diagnosed in infancy.

Confirmation of the diagnosis requires demonstration of the absence of CD18 and the associated alpha subunit CD11a, CD11b and CD11c on the surface of the leucocytes, based on the flow cytometry using monoclonal antibodies CD11 and CD18. In LAD-III, platelet aggregation assays should be performed. In all cases, a genetic analysis confirms the diagnosis. Differential diagnoses include interleukin-1 receptor-associated kinase 4 deficiency, autosomal dominant hyper IgE syndrome, chronic granulomatous disease, neutrophil dysfunction and a leukemic reaction. The treatment of the disease depends on the severity of the clinical picture. In the case of patients with the severe disease phenotype, the only corrective treatment available to date is the transplantation of hematopoietic precursor cells. The absence of lymphocyte function-associated antigen 1 in these patients can constitute an advantage for transplantation, since graft rejection appears to depend in part on the CD18 complex. The largest series published to date describes 36 children in 14 centers subjected to transplantation between 1993 and 2007 and followed-up on for 5 years after transplantation. The reported survival rate was 75%. These patients die in childhood if transplantation is not carried out as soon as possible. If transplantation is performed before serious infections develop, the resulting prognosis is very good.

**CONCLUSION**

Based on the above case report it can be concluded that LAD-I is a rare form of congenital immune deficiency, it must be taken into account in neonates who present with this unusual clinical picture.

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