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Leucocyte Adhesion Deficiency-1 Presenting asLeukocytosis and Pyoderma Gangrenosum

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ABSTRACT

Leukocyte Adhesion Disorder is a rare autosomal recessive disorder characterized by immunodeficiency caused by compromised neutrophil adhesion and transmigration activity to inflammation sites resulting in recurrent infections, of which type 1 is the most common. We are herewith reporting an interesting case of a 17-year-old female patient who presented with skin lesions over the lower limb for 15-30 days which on further investigating found out to be Pyoderma Gangrenosum in a case of LAD type 1. Patient was managed with antibiotics, steroids, hydration, and supportive care. The lesion responded to steroids and completely vanished with some residual scarring in 3-4months time. Early diagnosis and appropriate line of treatment with oral as well as injectable steroids and antibiotics helped us in combating this rare disease.

Keywords: Leukocyte Adhesion Disorder, LAD Type 1, Pyoderma Gangrenosum, CD18, CD34

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INTRODUCTION

Leukocyte adhesion deficiency (LAD) is a rare primary immunodeficiency disorder characterized by impairment of leukocyte migration and neutrophilic adhesion during an inflammatory response resulting in recurrent neutrophilic wounds like pyoderma gangrenosum (PG), predominantly of the skin and mucosal surfaces.[1] LAD-1 affects about 1 per 10 million individuals and is characterized by recurrent bacterial and fungal infections and depressed inflammatory responses despite striking blood neutrophilia.[2] The diagnosis of LAD1 should be considered in all patients with unexplained skin ulcers, even in the absence of serious infections.[3] Clinicians should be careful in making a diagnosis of idiopathic PG and consider LAD1 in the differential diagnosis.

CASE REPORT

A 17-year-old female patient presented with complaints of hyperpigmented lesions over the right lower limb for 1 month and over the left calf for 20 days associated with burning pain. She had a history of multiple hospital admissions in the past since the age of 3months. Moreover, has had H/O pneumonia at the age of 4 years. Had similar lesions 4 months prior, which resolved on its own with time. This skin lesion started from a pea sized bleb which went on increasing in size and had attained the current size of 8X10cm [Figure.1] & 20X15cm [Figure 2.] with hyperpigmented hyperkeratotic plaques with erythematous base. No H/O fever, cough, cold, or any comorbidities or any significant family history. On further enquiry, Mother gave H/O delayed separation of the umbilical cord. Patient was then investigated and evaluated further, CBC reports suggestive of Hb - 8.8; WBCs - 35,160 ; PLTs - 2.63 with PBS showing microcytic, hypochromic

RBCS and neutrophilic leukocytosis. Rest of the biochemical parameters were within normal limits. In view of significant history of recurrent infections, neutrophilia and lack of pus formation, possibility of primary immune disorder like Leucocyte adhesion defect was kept. We did her basic PID work up. LAD1 analysis report came out to be positive S/O significant CD18 deficiency.

The expression of CD 18 this patient was just 11% (normal range being 95-100%). Pus culture grew pseudomonas aeruginosa. Skin biopsy was suggestive of Pyoderma Gangrenosum. With treatment of antibiotics, injectable and oral steroids along with supportive care, the patient started improving and the lesion slowly started decreasing in size. [Figure 3] She was even initiated on steroid sparing agents like cyclosporine after which steroids were tapered off gradually and stopped after 3 months of treatment. The lesion now has faded away with residual scarring and hypertrophy. [Figure 4 and 5]

Figure 1: Right thigh lesion at the time of admission

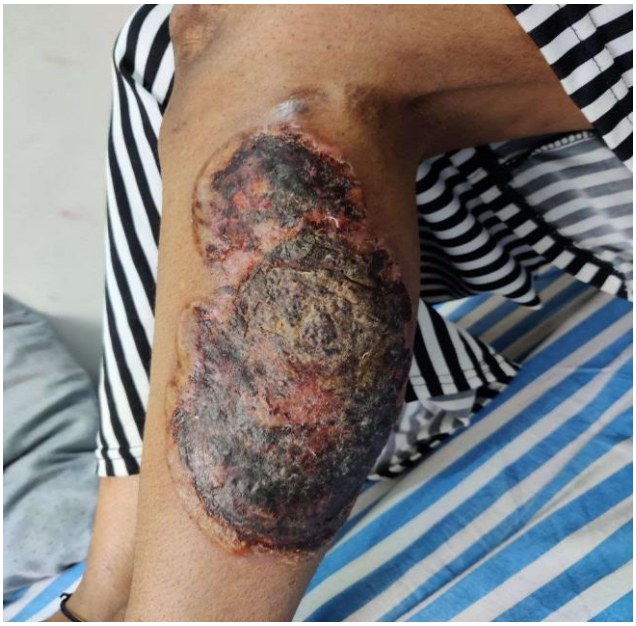

Figure 2: Left calf lesion on the day of admission day 1

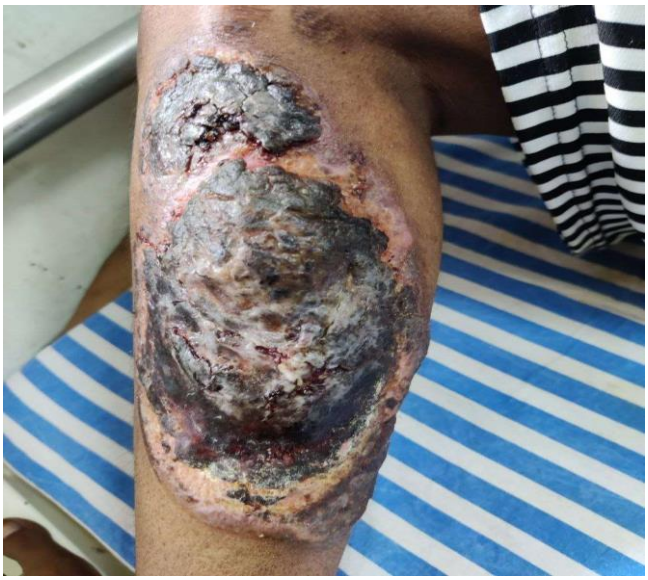

Figure 3: Left Calf Lesion

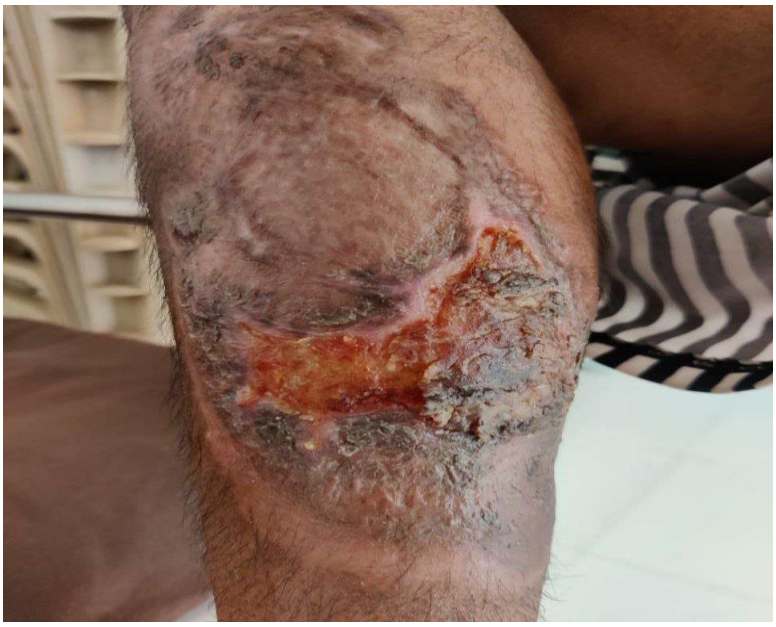

Figure 4: Left calf lesion on discharge

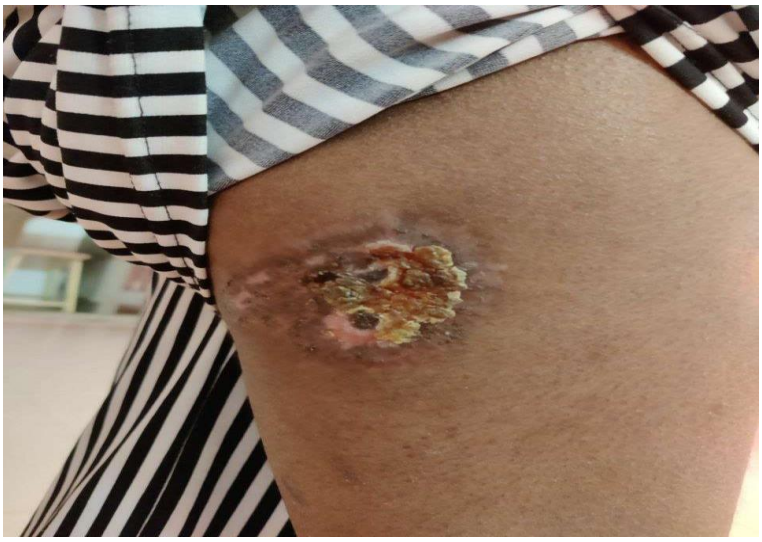

Figure 5: Right thigh lesion on discharge

DISCUSSION

Leukocyte adhesion deficiency type-1 (LAD-1) is a rare autosomal recessive primary immunodeficiency caused by mutations in the *ITGB2* gene, which encodes the CD18 subunit of the β2 integrin, leading to compromised neutrophil adhesion and transmigration to infection or inflammation site.[4]

Recurrent, severe, and difficult-to-treat bacterial infections are the predominant clinical manifestation of these patients, sometimes presenting as life-threatening infections, such as septicemia, bronchopneumonia, and aseptic meningitis. Skin and mucosal surface infections may present as indolent and necrotic lesions that can enlarge and recur, commonly leading to systemic spread of infections[5]. Our patient presented with necrotic skin lesion and leucocytosis. Skin lesion was classically looking like a pyoderma gangrenosum. Skin biopsy was suggestive of pyoderma gangrenosum[PG]. As patient had underlying PID, it was a

difficult to treat condition. We have started her on steroids under the cover of antibiotics and anti PCP cover.

She was showing the signs of improvement; we could taper the steroids with addition of Cyclosporine. Gradually cyclosporine also tapered and stopped.

Infections usually appear first in the neonatal period as omphalitis and delayed umbilical detachment,[6] similar history was given by our patient.

Our patient also had one episode of dental infection which was difficult to heal. Gingivitis, periodontitis, and impaired wound healing are characteristic of LAD. Absence of pus formation is significant due to the impaired migration of leukocytes and a defect in extravascular accumulation of polymorphonuclears and monocytes.

Severe LAD-1 is associated with significant mortality (reported as 75% by the age of 2 years), persistent neutrophilia in the absence of infections and dramatically increased myeloid leukocyte counts in the presence of infection are characteristic.[7]

The severity of the clinical manifestations is directly related to the degree of CD18 deficiency, with the mild-to-moderate types characterized by 2–30% CD18-expressing neutrophils and severe LAD-1 classified as <2% CD18-expressing neutrophils.[8] As our patients initial analysis suggested mild type of LAD-1, it could explain the survival till the age of 17 years.

However, most of the patients are diagnosed based on their typical clinical manifestations and in vitro diagnostic tests, including CBC and blood flow cytometry. Patients suffering from severe LAD often have high mortality rates because of sepsis, so they require prompt hematopoietic stem cell transplantation.[9]

CONCLUSION

LAD type 1 is a type of primary immunodeficiency disorder (PID), which is characterized by *ITGB2* gene mutations that lead to the production of a β2 subunit that cannot bind with other subunits to form β2 integrins. To conclude, the findings indicate that LAD-1 remains a life-threatening condition with omphalitis, pneumonia, oral, skin, and ear infections as the most common complications. Mild to moderate cases can be managed conservatively as seen in our case. Thus, early identification of these patients is essential in ensuring a definitive diagnosis and early implementation of hematopoieticstem cell transplantation.

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