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CONTUMACIOUS LEG ULCER, AN UNCOMMON PRESENTATION IN NEWLY DIAGNOSED E/BETA THALASSEMIA

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Abstract-
Beta-thalassemia are a group of hereditary blood disorders characterized by anomalies in the synthesis of the beta chains of haemoglobin resulting in variable phenotypes ranging from severe anaemia to clinically asymptomatic individuals. Leg ulcers may develop in patients with sickle cell anaemia and other haemolytic disorders, as a result of red blood cell (RBC) deformability and endothelial changes. Following case report highlights undiagnosed E/beta thalassemia patient having being treated as a chronic non healing ulcer over the medial aspect of left leg above medial malleolus.

Keywords- leg ulcer, thalassemia.

Key message- Chronic non healing ulcers may be due to underlying haematological condition. Hence screening of patients for underlying hemoglobinopathy is important in a patient with anaemia and non-healing ulcer.

Introduction-

Chronic leg ulcers have varied aetiology. The main causes of chronic leg ulcers are chronic venous insufficiency and/or peripheral arterial occlusive disease in approximately 80% of all patients (3). However, disease such as vasculitis, livedo vasculopathy, pyoderma gangrenosum, necrobiosis lipoidica, Martorell hypertensive leg ulcer, calciphylaxis, infectious diseases, neoplasms, drugs, cutaneous artefacts and genetic defects have exemplary presentation (11). Another uncommon cause of chronic non healing ulcer is hemolytic anaemias like sickle cell anaemia, beta thalassemia. (4)
Beta-thalassemia (β-thalassemia) is characterized by reduced synthesis of the haemoglobin subunit beta (haemoglobin beta chain) (1) that results in microcytic hypochromic anaemia, an abnormal peripheral blood smear with nucleated red blood cells, and reduced amounts of haemoglobin A (HbA) on high performance liquid chromatography.
Three main forms have been described: thalassemia major, thalassemia intermedia and thalassemia minor. Individuals with thalassemia major usually present within the first two years of life with severe anaemia, requiring regular red blood cell (RBC) transfusions. Symptoms vary from growth retardation, pallor, jaundice, poor musculature, hepatosplenomegaly, leg ulcers to skeletal changes. Patients with thalassemia intermedia present later in life with moderate anaemia. Need for transfusion

may only be reserved for exceptional cases. Patient presents gallstones, painful leg ulcers and increased predisposition to thrombosis (9,10). Thalassemia minor is clinically asymptomatic in majority of patients.

A chronic non healing leg ulcer is a long-lasting (chronic) sore that takes more than four to six weeks to heal, not completely healed by 12 weeks (7). The aetiology of chronic ulcer varies from venous insufficiency, arterial occlusive disease, autoimmune diseases, diabetic foot ulcer to rare causes like haematological disorders, malignancies and vasculopathies. We hereby report a case of chronic ulcer treated by various clinicians including surgery and dermatology. Patient was finally diagnosed as a case of E/beta thalassemia and treated. Treatment mainly included blood transfusion every 21 days and ulcer size gradually decreased.

CASE HISTORY-

A 42 years old male admitted with chief complaints of chronic painful ulcer on left leg above the medial malleolus for 4 years along with easy fatiguability for 3 years. As stated by the patient the ulcer dates to 4 years when he met a car accident that led to a laceration. The injury was left unattended at that time and gradually got converted to an ulcer. The ulcer never healed completely during the span of 4 years for which the patient visited several doctors. Patient came to our surgery department for the painful chronic ulcer interrupting his daily activities. The size of ulcer was 2 cm*1.5 cm, well circumscribed, with surrounding erythema. After debridement and dressing of wound, patient was referred and admitted in medicine department in view of anaemia. CBC with peripheral smear, LFT, RFT included preliminary tests conducted. Detailed history and examination included exclusion of chronic illness like diabetes, hypertension, vasculitis disorders, autoimmune diseases, chronic medication and addiction history like smoking. Clinically relevant finding included pallor, massive splenomegaly which was confirmed by USG abdomen study. Decreased haemoglobin levels, microcytic picture, raised ferritin levels with massive splenomegaly raised the suspicion for hemolytic anaemia. Haemoglobin electrophoresis confirmed the diagnosis of E/Beta thalassemia. Patient was advised and given blood transfusion successively in view of chronic non healing ulcer and gradually ulcer size decreased. We hereby report a case of thalassemia who's only clinical presentation was a chronic ulcer.

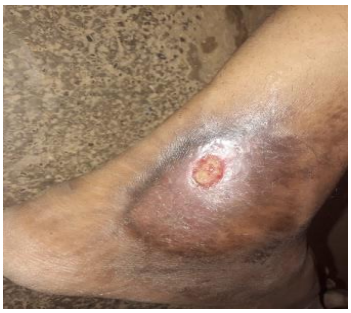

Fig a)

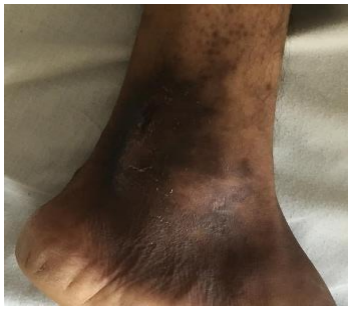

Fig b)

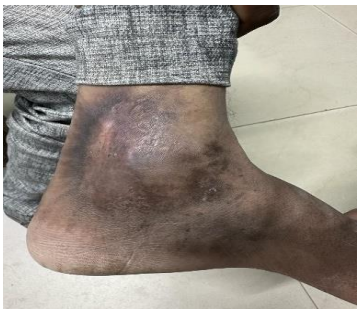

Fig c)

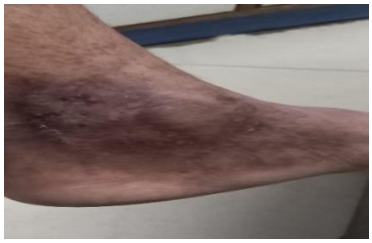

Fig d)

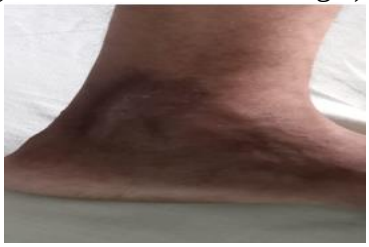

Fig e)

Fig a) chronic non healing ulcer at the time of presentation.
Fig b) ulcer site after 3 months with successive blood transfusion at the interval of 21 days
Fig c) ulcer site at follow up visit 3 months after healing of wound with successive transfusion.
Fig d) ulcer site healthy after 6 months of transfusion.
Fig e) ulcer site at 1 year of follow up.

LAB REPORTS OF THE PATIENT

INVESTIGATION	LAB VALUE
hemoglobin	6.4
MCV	55.9
TLC	5000
PC	179000
RETICULOCYTE COUNT	3%
B.Urea	25
Creatnine	0.43
T.bilirubin	3.54
In. bilirubin	3.33
SGOT	23
SGPT	14
S.Vit B12	153
STOOL FOR OCCULT BLOOD	negative
S. FERRITN	451
RBG	84

HEMOGLOBIN ELECTROPHORESIS REPORT OF THE PATIENT

Hb VARIANT	VALUE
Hb A	15.7
Hb A2	9
Hb F	25
Hb S	0
Hb D	0
Hb E	50.3
OTHER PEAKS	0

The development of trophic changes and subsequent leg ulcers is supposed to be multifactorial. The occurrence of leg ulcers is not related to the severity of the anaemia or to the patient's transfusion requirements, but may be related to high foetal haemoglobin concentration as per the hypothesis (5). The ulcers are slow to heal and tend to recur. Since tissue hypoxia may be the underlying pathophysiology, the use of topical hyperbaric oxygen chamber therapy may be beneficial in the treatment of thalassaemic leg ulcers (6). Other treatment modalities include chelation therapy and blood transfusions which have shown to be beneficial in the treatment in selective patients. Multiple skin-grafting operations may be attempted if satisfactory results are not obtained with conservative means.

Discussion-

Legs ulcers in association with hemoglobinopathies are a rare but global issue. The diagnosis of thalassemia should be considered in patients who have unexplained chronic leg ulcers with coexisting anaemia. Development of ulcers in non-transfusion dependant thalassemia is the outcome of interaction of multiple pathophysiological factors: ineffective erythropoiesis, iron overload (IOL), and hypercoagulability. Ineffective erythropoiesis and haemolysis are associated with chronic hypoxia and a hypercoagulable state.

The pathophysiology and treatment of this condition have not been well-elucidated. This is mainly because of the rarity of the disease and the lack of well-structured studies. The goal of documenting the case report is to bring focus on hemoglobinopathy as being the cause for non-healing ulcer and blood transfusion being the necessity in otherwise healthy individual. Nonetheless, some studies have attempted the treatment with Hydroxyurea, granulocyte macrophage colony-stimulating factor (GM-CSF) and topical antibiotics. More sample size studies regarding the possibility, whether foetal haemoglobin is directly related to the development of these ulcers need to be conducted.

Conclusion-

Treating the cause and correcting anaemia is the main part of management. The approach to these ulcers follows the same principal of wound bed preparation, moisture balance, control of infection, and debridement. Pain management is a detriment in the management of these patients. Also, more studies need to be conducted as to confirm the relation between levels of foetal haemoglobin and development of chronic ulcers (7). The case report therefore serves the purpose to look such causes as thalassemia in individuals having non healing ulcers.

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