Chediak-Higashi Syndrome – A Case Report

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Chediak-Higashi syndrome (CHS) is an autosomal recessively inherited, rare disorder, characterized by oculo-cutaneous albinism, photophobia, nystagmus and an abnormal susceptibility to cutaneous and respiratory infections. Hematological and serious neurological abnormalities can also occur with progression of the disease. Many similar cases of the disease with additional features have been reported in foreign literature. We describe one case of this disorder along with review of literature.

Key words: Oculo-cutaneous, albinism, photophobia

Introduction

Chediak-Higashi syndrome is a rare lysosomal disorder which is characterized by incomplete oculo-cutaneous hypopigmentation, photophobia, nystagmus, large eosinophilic peroxidase-positive inclusion bodies in the myeloblasts and promyelocytes of the bone marrow, neutropenia and an abnormal susceptibility to cutaneous and respiratory infections.[1-4] Hepatosplenomegaly, lymphadenopathy, pancytopenia, jaundice and gingivitis with bleeding tendency are other common features[2]. The diagnosis can be confirmed by recognition of the characteristic large cytoplasmic inclusions in leukocytes by light microscopy of a bone marrow smear.[1,2] Morbidity results from patients succumbing to frequent bacterial infections or to an accelerated phase, consisting of a lymphoproliferative syndrome with hemophagocytosis and infiltration of most tissues.[2,4]

Chediak-Higashi gene product has been identified and mapped on chromosome 1q 43[4]. The defect is in the gene LYST (lysosome trafficking regulator), resulting in defective vesicular transport to and from the lysosome.[2,3]

Case report

A seven years old girl, resident of Thokar Niaz Baig, Lahore, presented at the Department of Dermatology Unit-I, King Edward Medical University/ Mayo Hospital, Lahore, Pakistan with complaints of multiple ulcers over various parts of body, asymptomatic small hypopigmented lesions on chest, abdomen and back and abdominal distension for the last 5 years. She was born at full term to a consanguineous couple after an uneventful pregnancy and labour. She was normal at birth and her symptoms began at the age of two years when she started having recurrent respiratory, gastrointestinal and cutaneous infections with fever off and on and abdominal distension. There was history of recurrent ulcers over the scalp and other body areas since the age of 2 years (Fig. 1). Multiple milky white lesions appeared on different parts of the body (Fig. 2). She also had a history of photophobia with gradual decrease in the vision, generalized weakness and weight loss for the last one year. One sibling succumbed at the age of 4 years during the accelerated phase of the similar disease. Another 3 years old, alive sibling has same illness and is living with chronic form of the disease.

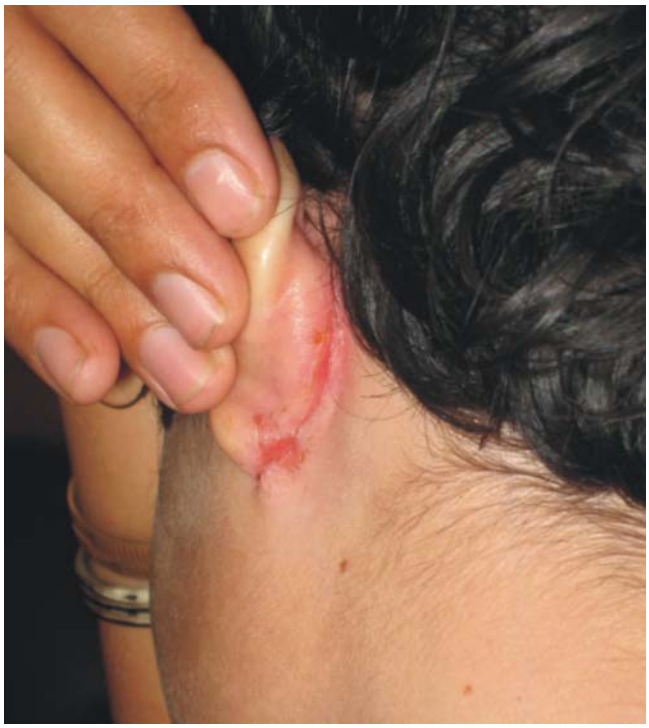

Fig. 1: *Ulcer on the retroauricular area.*

Physical examination (Table 1) revealed a female child of low IQ, looking pale and lethargic. A patch of cicatricial alopecia was noted on scalp and a scar of healed ulcer over the nape of neck (Fig. 3) while multiple scars of healed ul-

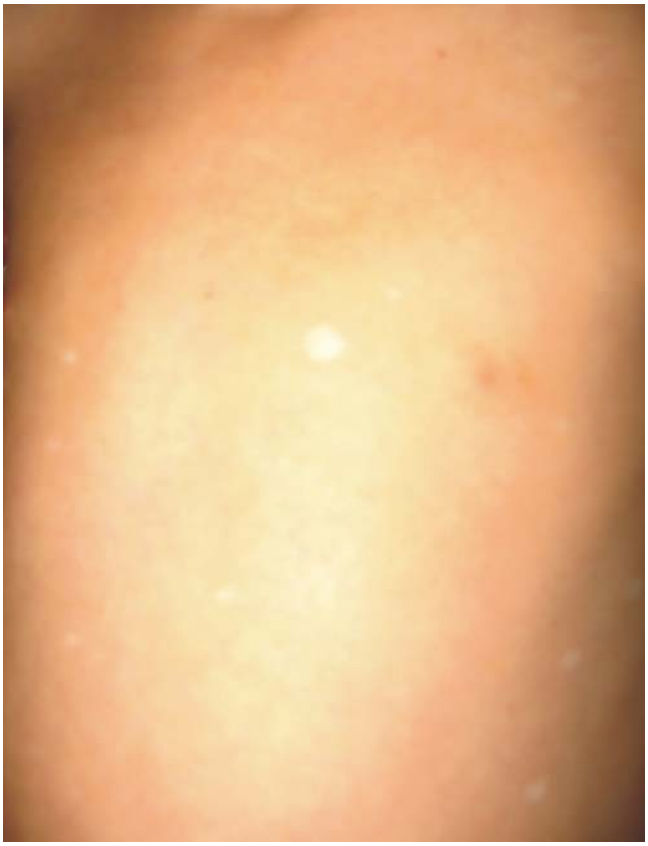

Fig. 2: *Hypopigmented macules.*

cers were present on legs and dorsum of feet. A fresh ulcer was found on the left retroauricular area. Cutaneous examination also showed multiple hypopigmented macules over chest, abdomen and back. Dorsa of both hands showed lesions of granuloma annulare, also confirmed on skin biopsy. Examination of oral cavity revealed ulcers and gingivitis with bleeding tendency (Fig. 4). Eye examination showed blepharitis (Fig. 4) and heterochromia while fundoscopy showed ocular albinisim. Systemic examination showed enlarged liver (total span 15 cm) with homogenous echotexture and smooth surface. Spleen was also enlarged (17 cm below the left costal margin).

Table 1: *General physical examination.*

Parameters	Values
Height	108 cm
Weight	18 kg
Blood Pressure	90/60 mmHg
Temperature	103°F
Pulse	140 / min
Respiratory rate	34 / min

Table 2: *Laboratory investigations.*

	Pt. Value	Normal Value
Complete Blood Count		
Haemoglobin	8.7	11.5 - 13.5 gm/ dl
Total Leucocyte Count	3.7 x 10^3	4.5 - 13.5 x 10^3/ cmm
Neutrophils	30%	53%
Lymphocytes	62%	39%
Monocytes	6%	4%
Eosinophils	2%	2%
Platelets Count	133 x 10^3	150 – 350 x 10^3/ cmm
Erythrocyte Sedimentation	110	10 – 20 mm
Rate		
Liver Function Tests		
Total Bilirubin	0.7	0.1 – 1.2 mg/dl
Alkaline Phosphatase	459	115 – 345 IU/ l
ALT	58	10 – 35 IU/ l
AST	57	15 – 40 IU/ l

Laboratory investigations (Table 2) revealed decreased haemoglobin, raised ESR, neutropenia and lymphocytosis. Blood culture showed a growth of staphylococcus aureus. On peripheral blood smear, giant granules were present in neutrophils, eosinophils and granulocytes. Bone marrow biopsy revealed myeloperoxidase positive inclusions in neutrophils and its precursors as well as in monocytes and lymphocytes. Hair microscopy revealed multiple small pigmented granules in the shaft. Molecular testing could not be performed due to unavailability and limited resources.

Patient was treated with appropriate antibiotics, ascorbic acid and blood transfusion. Currently the patient is under observation with continued symptomatic treatment.

Discussion

CHS affects multiple systems of the body[1-4] and has already been reported in Pakistani children.[5,6] Patients with CHS exhibit hypopigmentation of the skin, hair and eyes due to the presence of giant melanosomes which cause pigment dilution, possibly secondary to impaired melanin transport.[4,7,8] There are recurrent staphylococcal and streptococcal infections as a result of neutropenia and other complications such as anemia, thrombocytopenia and lymphoma can also occur in these patients.[1,2,4] In our case, there was incomplete oculo-cutaneous albinism, neutropenia, recurrent respiratory, gastrointestinal and cutaneous infections, distended abdomen and typical bone marrow smear report favourable to the diagnosis of this disease.

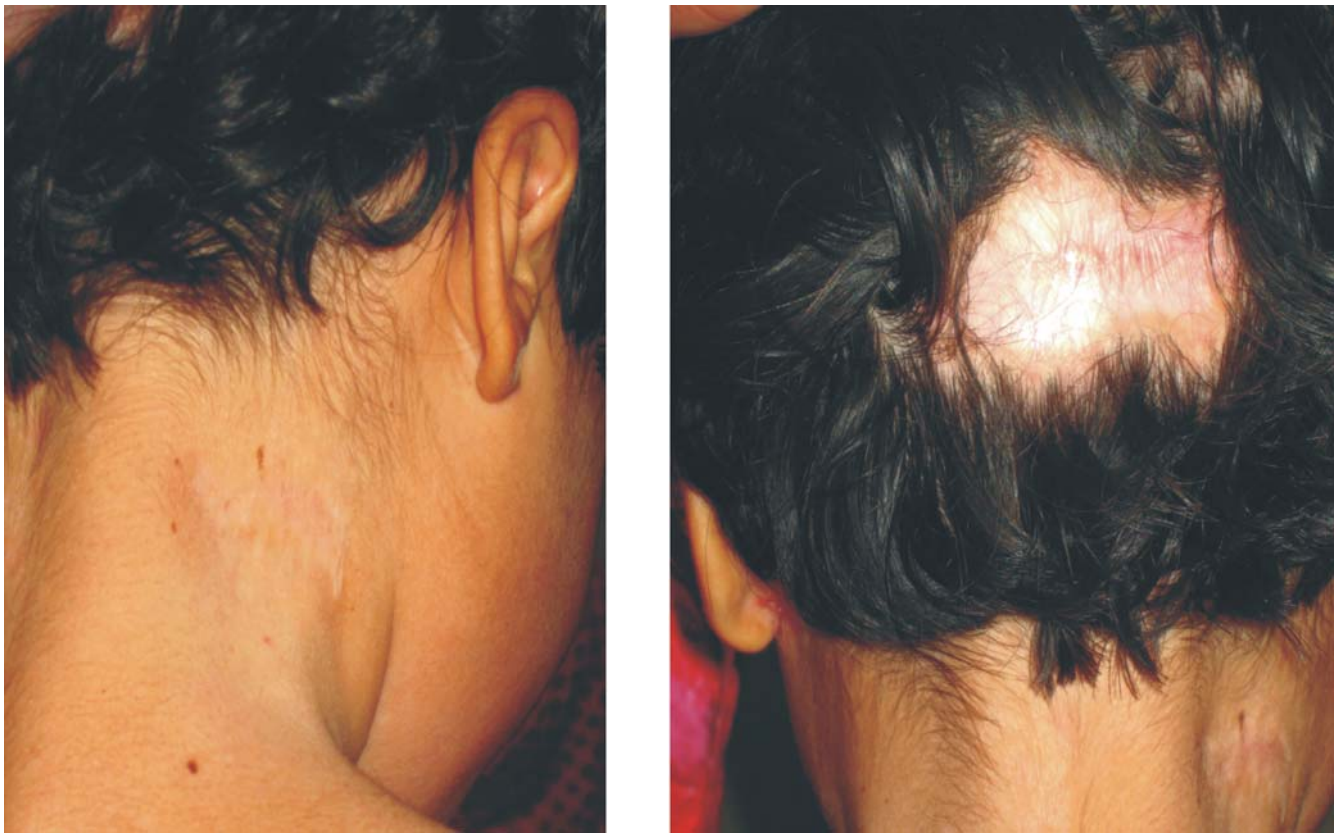

Fig. 3: *Scar on neck and Cicatricial alopecia.*

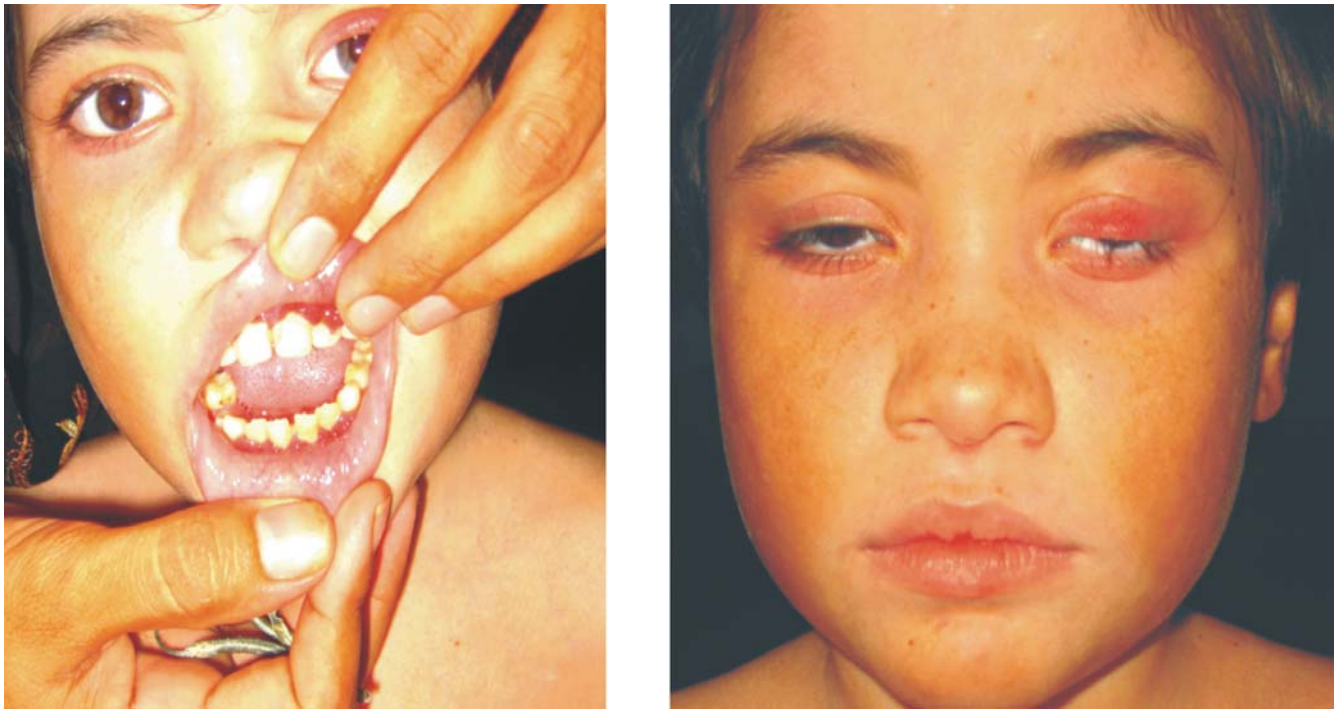

Fig. 4: *Gingivitis and Blephritis.*

Table 3: *Differential diagnosis.*

Griscelli syndrome
Hermansky-Pudlack syndrome
Prader-Willi's syndrome
Angelman's syndrome
Waardenburg syndrome
Lazy Leukocyte syndrome
Pyoderma Gangrenosum

The condition has to be differentiated from various clinical entities (Table 3). The clinical features of Griscelli syndrome are similar to Chediak-Higashi syndrome but the presence of photophobia and myeloperoxidase positive inclusions in the bone marrow helped to delineate the condition.[4,9] Hermansky-Pudlak syndrome is a platelet storage deficiency disorder manifesting as easy bruising and a bleeding tendency associated with oculo-cutaneous albinism and pulmonary fibrosis but there is no defect in circulating lymphocytes or neutrophils which differentiates this disease from the condition of our patient[8]. In patients of Prader Willi's syndrome and Angelman's syndrome, there is hypopigmentation but usually no typical ocular features of albinism[2]. In Prader Willi's syndrome, the characteristic features are neonatal hypotonia, hyperphagia, hypogonadism and mental retardation[2] while in Angelman's syndrome, there is severe mental retardation, microcephaly, neonatal hypotonia, ataxic movements and inappropriate laughter[2].

Waardenburg syndrome is a neural crest disorder. Piebaldism, with a white forelock hypopigmentation, congenital deafness, synophrys and dystopia canthorum (broad nasal root) are the distinct clinical features. Myeloblasts also fail to survive[4]. In lazy leukocyte syndrome, pus is absent in cutaneous lesions and neutrophilia is a constant finding[1]. Pyoderma gangrenosum was also considered in the differential diagnosis due to recurrent cutaneous ulcers but this condition was ruled out on the basis of typical clinical features and bone marrow report.[2,3,10]

The prognosis of CHS is generally not good.[2-4] Clinicians should be familiar with the severity of the disease because death often occurs in the first decade of life as a result of overwhelming infections, hemorrhage or development of the accelerated lymphoma-like phase.[2-4] Treatment is limited to allogeneic bone marrow transplantation,[1,11] although the accelerated phase may respond to etoposide plus systemic steroids and intrathecal methotrexate but the disease relapses invariably[4].

Conclusion

Chediak-Higashi syndrome is a well known clinical entity and there exists a strong possibility that the disease can lead to death without successful bone marrow transplantation.

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