Case Report

Ophthalmic complications including corneal blindness in job's syndrome: Case report and review of literature

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Abstract

Job's syndrome or hyper-immunoglobulin E syndrome (HIES) is a rare multisystem disease in which the immune system, bone, teeth, lung, and skin are affected in association with characteristic elevated serum IgE levels. It has two different entities; autosomal-dominant HIES (AD-HIES), due to mutation in the signal transducer and the activator of the transcription 3 (STAT3) gene, causing a defective differentiation of Th17 cells, and autosomal-recessive HIES (AR-HIES) caused by mutation in dedicator of cytokinesis 8 (DOCK8) gene. Ocular involvement in Job's syndrome is rare, there are reports of staphylococcal chalazion with belepharitis, keratoconus, cataract, retinal detachment and Candida endophthalmitis by different authors. Diagnosis in young children can be challenging as symptoms accumulate over a period of time, but early diagnosis and treatment increase patient's life expectancy and also prevent blindness and improve visual prognosis. We present a case of 13-year-old female patient who admitted to our hospital with pustular lesions on the scalp, face, neck and upper chest; some of these were crusted with significantly impaired vision of perception of light in both eyes due to very severe ocular surface disorder leading to corneal blindness. The clinical manifestations and investigations have confirmed HIES.

Keywords: hyper-immunoglobulin E syndrome, Job's syndrome, ocular surface disorder, corneal blindness, recurrent pneumonia**,** cold skin abscess.

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Received Date: 17/09/2016 Revised Date: 06/10/2016 Accepted Date: 01/11/2016

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	DOI: 05 November 2016

INTRODUCTION

Job's syndrome or hyper-immunoglobulin E syndrome (HIES) is a rare multisystem disease in which the immune system, bone, teeth, lung and skin are affected. It first described by Davis *et al*. in 1966.[1,2,3] It has two different entities; autosomal-dominant HIES (AD-HIES), due to mutation in the signal transducer and the activator of the transcription 3 (STAT3) gene, causing a defective differentiation of T-helper 17 (Th17) cells[4], and autosomal-recessive HIES (AR-HIES) caused by mutation in dedicator of cytokinesis 8 (DOCK8) gene. Both males and females are affected, however, most cases of HIES are sporadic.[5,6,7] HIES syndrome characterized by recurrent sinopulmonary infections and cold skin abscesses in association with elevated serum IgE levels. Staphylococcal infection is common to all patients, but most have infections with other pyogenic organisms as well. Non-immunological features include impaired shedding of the primary teeth, recurrent bone fractures, hyper extensible joints and scoliosis. Prophylaxis with penicillinase resistant penicillins or cephalosporins is highly recommended to prevent staphylococcal infections. Pneumatoceles, a frequent complication of pneumonias, may require surgical excision.[8] Ocular involvement in Job's syndrome is rare; there are reports of staphylococcal chalazion with blepharitis[9],

How to site this article: Mohammad Mehdi Raji *et al.*, Ophthalmic complications including corneal blindness in job's syndrome: Case report and review of literature *MedPulse – International Medical Journal.* November 2016; 3(11): 915-917. http://www.medpulse.in (accessed 08 November 2016).

keratoconus[10], cataract, retinal detachment[11] and Candida endophthalmitis[12] by different authors. Diagnosis in young children can be challenging as symptoms accumulate over a period of time but, early diagnosis and treatment increase patient's life expectancy and also prevent blindness and improve visual prognosis.

CASE REPORT

A 13-year-old female child was admitted to our hospital with complains of recurrent pustular lesions on the scalp, face, neck and upper chest since 8 years with aggravation of lesions since 6 months and decreased vision in both eyes. At the age of 5 years, patient started developing itchy pustular lesions over face, neck and scalp, which used to increase in size and sometimes associated with serosanuinous discharge. Lesions used to heal with treatment or subside on their own in 2-3 months with recurrence within few days with intermittent fever. She was admitted several times and has been treated with oral and injectable antibiotics. Patient has had 3 episodes of herpetic gingivostomatitis and treated with oral antiviral drugs. She had a history of recurrent productive cough 4 years back till present and has received 6 months anti TB treatment (ATT) at that time.. Her unaided visual acuity was 20/30 in both eyes 3 years back, along with complaints of watering, itching and irritation of both eyes associated with pustular lesions over the face, around the eyes and lid margins. Diminished vision was gradually progressive since 2 years without any history of ocular trauma, but due to poor compliance of patient and her family, they have neglected these ocular symptoms. She also received dose of 5g/dl of intra venous immune globulin (IVIG) monthly injection for 3 continuous months 1 year back. Physical examination showed multiple pustular lesions over scalp, face, neck and upper trunk with itching and abscesses (Fig.1); few of these were crusted. Visual acuity of perception of light in both eyes with inaccurate projection of rays in right eye and accurate projection of rays in left eye. External ocular examination revealed bilateral grade III cicatricial ectropion, grade I symbelpharon, meibomitis and lagophthalmos. Also patient has very severe bilateral keratoconjunctival xerosis with early band keratopathy formataion and corneal deep vascularization. Direct and indirect pupillary reactions were intact. B-scan ultrasonography showed normal attached retina with normal shadow of both optic nerves. Blood investigation showed raised eosinophil levels (9.7% of WBCs). All the immunoglobulin (Ig) was within the normal range except IgE which was significantly elevated. Serum IgE was 6725 IU/ml (with normal range of 1.5-378 IU/ml), which exceeded the normal value by 18 times. The HIV test was negative. Rest of other biochemical blood tests were within the normal limits. Pus and exudates culture from skin lesions reported growth of beta hemolytic streptococci and staphylococcus aureus, sensitive to combination of amoxicillin-clavulanic acid, cefazolin, cefuroxime, chloramphenicol and oxacillin. Patient was treated with injection augmentin 600 mg IV every 8 hours for 14 days, tablet theophylline 300 mg once daily, tablet salbutamol 2mg once at night before sleep for 7 days. For skin lesions patient has been treated with betadine and ketoconazole bath, application of Neosporin ointment (combination of bacitraicin, neomycin and polymixin) along with fresh daily dressing and tablet cyproheptadiene 2mg twice daily. The skin lesions showed signs of healing and no new lesions were seen. Regarding ocular treatment patient has received ocular antibiotic ointment (ciprofloxacin) and methyl cellulose eye drop as a lubricating agent in both eyes. Patient and her parents were advised for keratoprosthesis implantation in both eyes after treating the corneal infection. Based on the systemic manifestations, ocular findings and significantly elevated serum IgE level the patient was diagnosed as a case of bilateral very severe ocular surface disorder leading to corneal blindness associated with features of HIES.

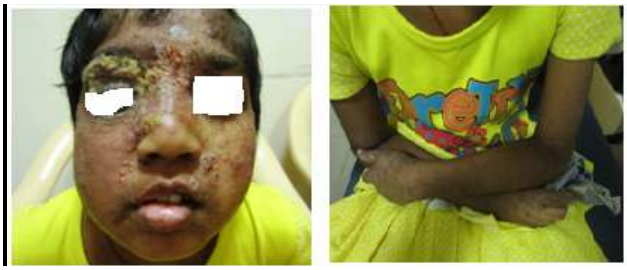

Figure 1: Multiple pustular lesions over scalp, face, neck and upper trunk of patient

DISCUSSION

The clinical manifestations of HIES (also known as Job's syndrome or Buckley syndrome) include: ezematous dermatitis, recurrent cold skin abscesses, staphylococcal infections and pneumatoceles in association with elevated serum IgE levels. It has two subtypes; one is AD-HIES, which develops due to STAT3 gene (17q21)[6] and the other one is AR-HIES, caused by DOCK8 gene (9p24) mutation. The AD-HIES is characterized by connective tissue and skeletal abnormaslitis, recurrent pulmonary infections and eczema. The AR-HIES presents with recurrent viral, staphylococcal skin infections and vasculitis. This form has higher mortality rate and lack of tendency to pneumatoceles formation.[3,13] STAT3 is a major signal transduction protein involved in various pathways including wound healing, angiogenesis, immune pathway. HIES patients have impaired differentiation of Th17 from mutations in STAT3 gene[4].

Frequent micro-organisms isolated in Job's syndrome are staphylococcus aureus, streptococcus pneumonia, haemophilus influenza and Candida albicans.[14] Frohn *et al*.[15] and Orhan *et al*.[16] have reported cases of corneal ulceration and perforation in patients with Job's syndrome presumably caused by Staphylococcus aureus despite aggressive systemic and topical antibiotic therapy. Haslet *et al*.[12] have reported a case of endogenous Candida albicans endophthalmitis in a 24-year-old female. Diagnosis of HIES is made based on: I) clinical features, II) blood test investigations include mild to moderate eosinophilia and significant elevated serum IgE levels (>10 times normal), III) genetic tests.[17] Treatment of HIES included prophylactic drugs (antibiotic and antifungal), management of infections, IVIG consumption and hematopoietic cell transplantation (HCT) is the last therapeutic method.[18] In case of HIES to prevent corneal blindness patient and family should have very good compliance, because periodic examination and review of patient is essential. An appropriate ocular treatment to reduce itching, management of dry eye and ocular surface disorder and prevent superimposed infections will improve the visual prognosis in long term management of these cases.

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Source of Support: None Declared
Conflict of Interest: None Declared