CASE REPORT

Ophthalmic Complications of Jobs Syndrome: Case Report

Shekhar Akarkar[1], Ugam Usgaonkar[1]*

[1]Department of Ophthalmology, Goa Medical College, Bambolim-403202 (Goa) India

Abstract:

Job's syndrome or Hyperimmunoglobulinemia E is characterized by increased levels of IgE, recurrent cutaneous and systemic pyogenic infections, atopic dermatitis, and peripheral eosinophilia. Ocular associations which have been reported in the literature include keratoconus, chalazia with blepharitis, candida endophthalmitis and retinal detachment. We present the case report of a young patient with bilateral eczematous lid involvement with molluscum contagiosum infection and bilateral corneal vascularisation. Patient also had cutaneous, pulmonary involvement and showed general improvement with systemic antibiotics and immunoglobulin therapy. Diagnosis was based on clinical findings and raised serum IgE levels and eosinophilia. Even though rare, Job's syndrome can present with ophthalmic features.

Keywords: Job's syndrome, Corneal Vascularization, Molluscum Contagiosum, Keratinization

Introduction

Hyperimmunoglobulinemia E (HIE) or Job's syndrome is an immunodeficiency condition that was first described by Davis et *al.* [1]. It affects both males and females with symptoms usually beginning in childhood. The most common features are eczema, increased susceptibility to infections and markedly raised levels of IgE which occurs due to a defective T suppressor cell function. Ocular involvement in Job's syndrome is rare. Cases are reported having keratoconus, *Staphylococcal chalazia* with blepharitis, Candida endophthalmitis and retinal detachment. Herein we report a case with characteristic manifestations along with the additional finding of corneal vascularization and molluscum contagiosum infection.

Case Report:

A young patient was presented to the outpatient department with swelling of both the eyes with skin lesions with discharging pus of 8 days duration and loss of vision in both eyes. There were multiple skin lesions over the body and face. There was history of itching and fever with cough was present. No history of drug intake or positive family history of any skin diseases was present. On examination visual acuity both eyes was perception of light with inaccurate projection of rays. External ocular examination revealed severe bilateral cicatricial ectropion with infective ulcerative blepharitis. Multiple umbilicated skin lesions were present over the lids. Anterior segment examination of right eye was not possible due to extensive involvement of lids. Left eye corneal vascularization was present (Fig.1). Patient had similar lesions in oral mucosa with secondary candidial infection.

Blood investigations showed total counts of 10,800 cmm (Neutrophils-60%, Lymphocytes-24%, Eosinophils-16%) and increased serum IgE levels of 2500 IU (Normal range- <200 IU). Conjunctival swab of right eye showed growth of *Staphylococcus aureus* and that of left eye was sterile. Indirect salt split study of skin was done which showed the linear staining of basement

membrane zone with IgG in 1:100 titre of patient's serum and the presence of band on epidermal side in the form of roof pattern, suggestive of subepidermal disease including mucous membrane pemphigoid. Tzanck smear showed multinucleated giant cells.

Histopathologically, lesions over eyelid were positive for molluscum contagiosum which showed large hyaline acidophilic molluscum bodies. HRCT thorax revealed areas of cystic bronchiectasis with segmental collapse of right middle lobe (Fig. 2). MRI of Brain and Orbit revealed preseptal extraconal soft tissue thickening involving right orbit. Skin swab culture showed the growth of *Staphylococcus aureus*. Blood culture/sputum culture was sterile. Other tests like sputum of AFB, HIV-ELISA, and PPD were negative. On the basis of ocular findings, systemic manifestations and raised serum IgE levels, the patient was diagnosed as a case of Job's syndrome with bilateral eczematous lid involvement with molluscum contagiosum infection. Patient was treated with intravenous antibiotics, IV Linezolid 10mg/kg/dose for 14 days and IV metronidazole for 10 days for staphylococcal infection. Tab fluconazole 6mg/kg on day 1 followed by 3mg/kg for 2 weeks was given for oral candidiasis. Three cycles of IV Immunoglobulins (IVIG) were given weekly to boost immunity. Oral corticosteroids 10mg/kg were started for pemphigoid lesions under cover of antibiotics and continued for 4 months. Locally twice daily cleaning of both eyes with saline/distilled water tds was done. Topically tobramycin eye ointment qid and lubricant eye ointment 2 hourly were used. For the molluscum contagiosum lesions, imiquimod once a day was started three times a week on alternate days for a period of 10 weeks. Patient responded to therapy in terms of infection control. Right eye showed thickened lid margins, trichiasis, ectropion with conjunctivalization and severe keratinization of cornea. Fibrotic nodule in conjunctiva was present at medial canthus. Left eye showed the presence of healing molluscum contagiosum lesions over the lid with total vascularization of cornea with minimal conjunctivalization from 6-12 o'clock position (Fig. 3A, 3B & 3C). Both eyes vision was perception of light present with accurate projection. Ultrasonography B scan showed normal posterior segment. Patient is referred to higher centre for consideration of keratoprosthesis.

Fig. 1: Presentation of Patient with Infective Ulcerative Blepharitis and Severe Ectropion

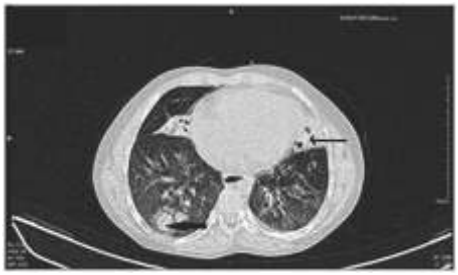

Fig. 2: HRCT Thorax of Patient showed Subsegmental Collapse with Bronchiectasis in Right Middle Lobe (Thin Arrow) and Pneumatocele (Thick Arrow)

Fig. 3A, 3B & 3C: Patient after 3 Months of Treatment- Right Eye (Fig. 3B) showed Thickened Lid Margins, with Conjunctivalization and Severe Keratinisation of Cornea. Fibrotic Nodule seen at Medial Canthus. Left Eye (Fig. 3C) showed the Presence of Healing Molluscum Contagiosum Lesions over the Lid with Total Vascularization of Cornea with Minimal Conjunctivalization from 6-12 O'clock Position

Discussion:

Jobs syndrome is an autosomal dominant disease with variable expressivity. The responsible gene has been mapped to chromosome 4q [2]. Cell mediated immunity is abnormal. Patient presents with chronic and intense pruritus and chronic eczema. Pruritis is attributed to intradermal mast cell histamine release triggered by elevation of IgE [3]. Staphylococcal skin infection is common and manifests in the form of impetigo, furunculosis, paronychia or cellulitis. The characteristic feature of staphylococcal infection in Job's syndrome is abscess formation without anticipated degree of erythema and warmth. Peripheral eosinophilia may be marked. Other ophthalmic manifestations reported are eczema of eyelids, dry eye, extensive xanthelasmas, giant chalazias, undefined eyelid nodules, strabismus and retinal detachment and complicated cataracts. Destafeno *et al*. [4] reported a case with recurrent chalazia associated with *Staphylococcus aureus* along with other manifestations of this syndrome. Frohn *et al*. [5] and Orhan *et al*. [6] 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. Haslett *et al*. [7] reported a case of endogenous *Candida albicans* endophthalmitis.

In this case, patient has got severe lid involvement due to mucous membrane pemphigoid with secondary staphylococcus infection leading to severe cicatricial ectropion. Due to altered immune response patient also developed molluscum contagiosum infection. Corneal neovascularization has occurred secondary to inflammatory disease leading to conjunctival scarring, conjunctivalization of cornea and keratinization.

Cicatricial ectropion occurs when there is a shortening of the anterior lamella due to cutaneous or subcutaneous scarring. A typical molluscum lesion begins as a small, round, firm, non-inflamed papule. The virus replicates in the epithelial cells as the lesion grows to 3-5mm in diameter. Ultimately, cellular destruction occurs resulting in central umbilication of the lesion. The lesion then typically appears pearly white, with caseous material in a centrally depressed area.

Diagnosis of Job's syndrome is by presence of eczema, increased rates of infections especially lung infections and raised IgE levels. Often the IgE levels are > 2000 IU (normal range < 200 IU). Recent advances in genetics now allow for testing for a mutation of a gene called STAT3. Bacterial pneumonia and emphysema are the most frequent systemic infections and may result in

pneumatoceles. The most common infecting organisms are *Staphylococcus aureus* and *Hemophilus influenzae*. Job's syndrome has also been associated with scoliosis in 76% of adult patients and hyperextensibility of joints in 68% of patients [2].

Peripheral blood eosinophilia may be marked, reaching levels of 50–60%. Serum IgE levels are consistently high (more than 10 times the upper limit of normal), even in infancy.

Management in our case was systemically high dose IV antibiotics for 14 days for the treatment of infections followed by prophylactic antibiotics at low dose. Some patients while having high levels of IgE have low levels of some or all of the other immunoglobulins (IgM, IgA, IgG). They are important in helping the immune system to fight off infections. These patients may be given immunoglobulin replacement therapy (IVIg) usually every 3weeks. Three doses of IVIg were given to our patient every 3 weeks. Corticosteroids are given for anti-inflammatory effect. For molluscum contangiosum patient was started on tab imiquimod thrice a week for 10 weeks.

Conclusion:

Ocular involvement in Job's syndrome is rare. Cases are reported having keratoconus, staphylococcal chalazia with blepharitis, *Candida endophthalmitis* and retinal detachment. We presented the case of Job's syndrome with bilateral eczematous lid involvement with molluscum contagiosum infection and bilateral corneal vascularization.

References

1. Davis SD, Schaller J, Wedgewood RJ. Job's syndrome. Recurrent, "cold", staphylococcal abscesses. *Lancet* 1966; 1(7445):1013-5.
2. Paller AS. Genetic immunodeficiency diseases. In: Eisen AZ, Wolff K, Frank Austen K, Goldsmith LA, Katz SI, editors. Fitz Patrick's Dermatology in general medicine.6th ed. New York: McGraw-Hill; 2003: 1125-6.
3. Patterson R, Oh SH, Roberts M, Hsu CC. Massive polyclonal hyperimmunoglobulinemia E, eosinophilia and increased IgE – bearing lymphocytes. *Am J Med* 1975; 58(4): 553-8.
4. Destafeno JJ, Kodsi Sr, Primack JD. Recurrent *Staphylococcus aureus* chalazia in Hyperimmuno-globulinemia E (Job's) syndrome. *Am J Ophthalmol* 2004; 138:1057-8.
5. Frohn A, Weidle EG, Seelhorst A, Steuhl KP, Thiel HJ. Eye involvement in hyperimmunoglobulinemia E syndrome. *Klin Monatsbl Augenheilkd* 1990; 197:432-5.
6. Orhan M, Ozkan Y, Irkec M. Eye involvement in hyperimmunoglobulinemia E (Job's) syndrome. *J Pediatric Ophthalmol Strabismus* 2001; 38:313-4.
7. Haslett RS, Moriarty AP, Vijayadurai P, Mc Galliard JN, Chandna A. Candida endophthalmitis in Job's syndrome. *Arch Ophthalmol* 1996; 114: 617–8.

Author for Correspondence: Dr Shekhar Akarkar, Department of Ophthalmology, Goa Medical College, Bambolim-403202 Goa India Email: shekharakarkar@gmail.com, Cell: +919765664117