

Clinical study on efficacy of infliximab on severity and occurrence of acute anterior uveitis in HLA-B27

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Abstract

Aim: To study the efficacy of Infliximab on the severity and occurrence of Acute Anterior Uveitis in HLA B27 positive patients. **Materials and Methods:** This is a prospective observational study done on 30 patients with acute anterior uveitis who were HLA B27 positive presenting to Uvea and Retina Services at Regional Institute of Ophthalmology Government Ophthalmic Hospital, Chennai between April 2013 to May 2015. Of which 16 patients were on Infliximab therapy (3-5mg/kg) for Ankylosing Spondylitis, 6 patients were on Tablet Sulfasalazine for the articular symptoms of Ankylosing Spondylitis and 8 patients were not on any medication and were retrospectively diagnosed as HLA-B27 positive. A detailed history, systemic examination, ocular examination using Slit lamp, 90D biomicroscopy, blood investigations for HLA B27 and MRI Sacroiliac joint was done. Patients were started on topical corticosteroids and cycloplegics, the response noted and followed up for 3 months. **Results:** Severity of uveitis did not show any variation between groups that were on infliximab and sulfasalazine and those who were not on any treatment. Patients in the three groups responded dramatically well to topical corticosteroids and cycloplegics. **Conclusion:** Infliximab (3-5mg/kg) regime used for the control of symptoms of Ankylosing Spondylitis neither prevents the occurrence nor decreases the severity of Acute Anterior Uveitis in HLA-B27 patients. Further studies are needed to establish the safe and effective dosage of Infliximab to prevent the occurrences of Acute Anterior Uveitis in HLA B27 patients.

Keywords: Acute anterior uveitis, Ankylosing Spondylitis, HLA B27, Infliximab.

Introduction

Acute Anterior uveitis (AAU) is the commonest form of uveitis which is characterized by the breakdown of blood-aqueous barrier [1]. Immunopathologically, cell adhesion molecules are upregulated in the uveal vasculature and there is aqueous humor expression of cytokines such as tumor necrosis factor alpha, interferon gamma, and chemokines that recruit and activate inflammatory cells such as neutrophils, monocytes and lymphocytes into uvea and anterior chamber [2]. The breakdown in blood-aqueous barrier causes leakage of serum proteins from uveal vasculature resulting in aqueous cells and fibrin extravasation. About 50% Acute Anterior Uveitis are associated with

HLA B27, a class I major histocompatibility complex (MHC) [3]. HLA-B27 associated uveitis is a distinct clinical entity associated with severe intraocular inflammation and systemic inflammatory disease like seronegative spondyloarthropathies such as Ankylosing Spondylitis (AS) and Reiter's disease. AS has the strongest association for HLA-B27 around 90% and about a third of these patients develop AAU [4]. HLA-B27 is the strongest known genetic risk factor for AAU while the pathogenesis still remains an enigma [5]. There are multiple subtypes of HLA-B27 based on the variation of one or several amino acids. This supports the arthritogenic and uveitogenic peptide hypothesis for AS or HLA-B27 associated AAU and the pathogenesis where the T lymphocytes are activated against a specific peptide found only in the joint or uvea. Clinical

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presentation of HLA-B27 associated AAU is that of a sudden onset, unilateral often alternating, non-granulomatous AAU, characterized by acute onset red, painful, photophobic eye with significant aqueous cells, flare and fibrinous extravasation and having a high tendency to recur. Though HLA-B27 associated uveitis responds well to treatment, recurrent episodes of severe AAU can lead to posterior synechiae, cataract, secondary glaucoma and cystoid macular edema with a potential for visual impairment [6]. Severity and

Materials and Methods

Study Design: A prospective observational study done at Uvea and Retina Services Department of Regional Institute of Ophthalmology, Government Ophthalmic Hospital.

Patient Selection: The study included 30 patients with Acute Anterior Uveitis who were HLA-B27 positive presenting to Uvea and Retina Services Department of Regional Institute of Ophthalmology Government Ophthalmic Hospital. Of the 30 patients, 16 patients were on Infliximab therapy (3-5mg/kg) for Ankylosing Spondylitis, 6 patients were on Tablet Sulfasalazine for the articular symptoms of Ankylosing Spondylitis and 8 patients were not on any medication and were retrospectively diagnosed as HLA-B27 positive.

Inclusion criteria

1. Patients aged between 15 – 45 years.
2. Patients with HLA-B27 positive AAU.

Exclusion criteria

1. Patients with chronic anterior uveitis.
2. Patients with posterior segment inflammation.
3. Patients with infectious cause of uveitis.

Procedure- A detailed history regarding the ocular symptoms, age at the time of diagnosis of Ankylosing Spondylitis, family history, HLA-B27 status and treatment history were taken. Visual acuity test, tonometry using Goldmann Applanation tonometer, slit lamp examination; biomicroscopy using 90D and systemic examination were performed. Blood investigation for HLA-B27 status and MRI of sacro-iliac joint were done. Uveitis was graded according to Standardized International Grading system using Standardization of Uveitis Nomenclature [7].



Figure-1: Acute Anterior Uveitis in HLA-B27 positive patient.



Figure-2: Resolved Anterior Uveitis with broken synechiae

Of the 30 patients, 16(53%) were on Infliximab therapy (3-5mg/kg) for AS, 6(20%) were on tablet Sulfasalazine for the articular symptoms of AS and 8(27%) presented with AAU and were retrospectively diagnosed as HLA-B27 positive. Severity of AAU did not show any variation among the three groups [figure1]. All patients were started on intensive topical steroids along with cycloplegics, 1% prednisolone acetate eye drops hourly and 2% homatropine eye drops twice a day. The response to treatment was noted by decrease in the symptoms, anterior chamber cells and improvement in visual acuity. All patients responded dramatically well [figure2]. Steroids were tapered over 6-8 weeks with constant monitoring of intraocular pressure.

Results

Severity of uveitis did not show any variation between groups that were on infliximab and sulfasalazine and those who were not on any treatment. Patients in the three groups responded dramatically well to intensive topical corticosteroids and cycloplegics.

Discussion

HLA-B27 AAU accounts for 50% of Acute anterior uveitis and presents in severe form with plasmoid aqueous, fibrinous reaction and sterile hypopyon in anterior chamber. It can occur as ocular involvement or as part of seronegative spondyloarthropathies such as Ankylosing Spondylitis, reactive arthritis (Reiter's syndrome), psoriatic arthritis or inflammatory bowel syndrome. It commonly affects the middle aged, males more than females and has high recurrence rate. It usually presents unilateral and frequently alternates between eyes during the recurrent episodes. HLA B27 AAU responds dramatically well to topical corticosteroids. A minority of cases involve the posterior segment secondarily leading to cystoid macular edema, vitritis, pars planitis and papillitis. In cases of delayed or recurrent or inadequate treatment complications such as seclusio pupillae, secondary glaucoma and complicated cataract can occur. HLA B27 consists of 24 subtypes, encoded by 26 different alleles [8].

These subtype varies with ethnic origin and some more risk for AAU. HLA B*2705 and B*2702 are associated more with AAU than HLA B*2706 and B*2709. Apart from genetic the pathophysiology is also linked to environment. There is extensive evidence implicating bacterial infections as trigger for HLA B27 AAU. The organisms implicated include Chlamydia trachomatis, Klebsiella, Yersinia, Shigella and Salmonella species and Campylobacter jejuni [9]. HLA B27 responds well to topical corticosteroids and cycloplegics. The development of newer drugs is aimed at decreasing the recurrence rate and severity. Drugs such as Sulfasalazine and Methotrexate are used in association

with Inflammatory Bowel Disease and Ankylosing Spondylitis and there are evidence that they may reduce the severity and recurrence [10]. Newer biologics such as Infliximab, a chimeric human-murine immunoglobulin G1 monoclonal antibody directed against soluble form as well as membrane bound form of tumor necrosis factor -alpha(TNF-a) are being tried in cases of recurrent and refractory HLA B27 AAU [11]. TNF-a is a pro-inflammatory cytokine elevated in the aqueous of patients with AAU. It attracts the inflammatory cells to the uveal vasculature causing the blood-aqueous barrier breakdown. The acute or recurrence rate of AAU in HLA B27 patients is 75% [12].

This study evaluates the effective dosage of Infliximab in decreasing the severity and occurrence of AAU in HLA-B27 positive patients. The current dosage used in Ankylosing Spondylitis varies from 3-5 mg/kg and gives a good control of articular symptoms. And this study shows that the severity and occurrence of AAU remains the same in patients who were on Infliximab using the current dosage for Ankylosing Spondylitis but responding extremely well for topical corticosteroids and cycloplegics. El-Shabrawi Y et al in 2002 conducted the study of Infliximab infusion at a dosage of 10mg/kg as an effective alternative in the treatment of HLA-B27 associated uveitis [13]. This shows the need for further studies regarding the adequate safe dosage of Infliximab for its effective use in AAU in HLA B 27 positive patients.

Conclusion

Infliximab (3-5mg/kg) regime used for the control of symptoms of Ankylosing Spondylitis neither prevents the occurrence nor decreases the severity of Acute Anterior Uveitis in HLA-B27 patients. Further studies are needed to establish the safe and adequate dosage of Infliximab to prevent the occurrences of Acute Anterior Uveitis in HLA B27 patients.

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