LETTER



Infliximab induced endophthalmitis in a patient of fistulizing Crohn's disease

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Published online: 20 September 2011 © Indian Society of Gastroenterology 2011

We report a patient with fistulizing Crohn's disease who developed bacterial endophthalmitis following a single infusion of infliximab.

A 26-year-old lady presented with recurrent bloody diarrhea and perianal discharge since 2 years. She had undergone incision and drainage for a perianal abscess 9 months ago with no improvement. She had also received prednisolone and 5-aminosalicylic acid with no benefit. When she presented to us, she had episodes of bloody diarrhea and persistent perianal symptoms. Examination revealed multiple abscesses in perianal area with extensive cellulitis, and edematous left labia majora. She had leucocytosis and hypoproteinemia; liver function tests, renal function tests, chest skiagram and barium meal follow through were unremarkable. Pus culture grew Streptococcus hemolyticus. Colonoscopy showed multiple perianal sinuses, congested and edematous anal canal with aphthoid ulcers, areas of frank ulceration and mucosal bridging in sigmoid, descending and transverse colon. Histopathology from perianal area showed granulomatous inflammation consistent with Crohn's disease; colonic biopsies showed chronic inflammation. During drainage of perianal abscesses under spinal anesthesia, an underlying rectovaginal fistula was seen. She was treated with antibiotics, hydrocortisone and parenteral nutrition for 2 weeks. She was given a single

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V. Gupta Department of Ophthalmology, Postgraduate Institute of Medical Education and Research, Chandigarh 160 012, India infusion of 300 mg infliximab. As there was a marked decrease in vulval edema, erythema, induration and perianal discharge, she was not given further infliximab. She was discharged on prednisolone and azathioprine, and she continued to improve with healing of perianal sinuses over the next few weeks. Two months later she complained of progressive painless loss of vision. Evaluation revealed endogenous endophthalmitis in the left eye (Fig. 1a) which was treated with pars plana vitrectomy. Culture of vitreal fluid grew *Streptococcus pneumonia* which was treated with systemic and topical antibiotics (vancomycin and ceftadizime). Patient's vision and fundal findings improved on subsequent follow up (Fig. 1b). The patient remained in remission subsequently for 2 years.

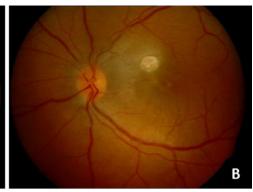
Infliximab is chimeric monoclonal antibody against TNF and is indicated in steroid dependent, refractory, fistulizing Crohn's disease and in systemic disorders like ankylosing spondylitis, sacroilietis, pyoderma gangrenosum etc. Infliximab in combination with azathioprine has a response rate as high as 56% in fistulizing Crohn's disease [1, 2]. However infliximab therapy has a number of side effects like infections, reactivation of tuberculosis, worsening of lymphoma and infusion reactions. In a large cohort study, infliximab related infections were found in 8.2% of 500 cases; 20 patients had severe infections [3]. Our patient developed endogenous endophthalmitis 8 weeks after infliximab infusion. In our patient, endophthalmitis following infliximab would classify as a probable adverse reaction, as per Naranzo's score for casuality analysis for drug-induced adverse effects [4].

Endophthalmitis can be classified as endogenous when it occurs as a result of hematogenous spread of infection from a distant source, and exogenous when it results from direct inoculation as a complication of ocular surgery or ocular trauma. Endophthalmitis has been reported rarely following



Fig. 1 a Fundus photograph of left eye at presentation showing fluffy, yellow-white exudates in the vitreous cavity in the posterior pole. b Fundus photograph 4 weeks later after pars vitrectomy, showing resolution of previous changes with a residual scar





infliximab therapy that too, only in patients with rheumatoid arthritis. Agarwal et al. described a patient with rheumatoid arthritis who developed endogenous endophthalmitis following treatment with infliximab; the patient was also receiving predinsolone and methotrexate [5]. Infliximab has also been incriminated in another report to cause exogenous ophthalmitis in 2 patients and in another patient endophlthalmitis occurred after treatment with another TNF- α antagonist adalimumab [6]. All these 3 patients had local risk factors for ocular infection like previous ocular surgery. Our patient did not have any risk factor for ocular infection. Immunosupressive drugs like prednisolone and methotrexate and TNF $-\alpha$ antagonists were thought to be responsible for endophthalmitis in the reported cases [5, 6]. Risk factors for endogenous endophthalmitis include chronic immunosuppresive illnesses and therapy, recent invasive surgery, long-term intravenous catheters and intravenous drug abuse [7].

Our case highlights the fact that endophthalmitis can occur after infliximab therapy. It is important to recognize this complication as it requires early surgical intervention in contrast to the autoimmune uveitis caused by Crohn's disease. Conflict of interest None

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