CASE REPORT

Infliximab induced remission in a case of severe Crohns enteropathic arthropathy with pyoderma gangrenosum

Ghetia TA[1], Ghetia HA[2], Kenawy SA[3]

[1]Rheumatology Department, Faculty of Medicine, Cairo University
[2]Pharmacology Department, Atomic Energy Authorization, Cairo, Egypt
[3]Pharmacology and Toxicology Department, Faculty of Pharmacy, Cairo University

Corresponding author:
Prof. TA Ghetia
Rheumatology Department, Faculty of Medicine, Cairo University. Email: gheitamer@hotmail.com

Abstract

Background: The indications for anti-TNFα therapy for inflammatory bowel diseases (IBD) have increased to include demonstrable mucosal healing, improvement in quality of life, and treatment of extraintestinal manifestations including arthritis, sacroiliitis and pyoderma gangrenosum (PG).

Case report: A male smoker, 27 years old, with enteropathic arthropathy on top of Crohns disease (CD) had a disease duration of 2.25 years. He had severe Crohns disease activity index (CDAI = 473) and a poor health status as assessed by the IBD questionnaire (IBDQ) of 39. He had oligoarthritis and bilateral sacroiliitis. There was limited chest expansion and lumbar spine mobility. The patient had PG on the dorsum of the right foot and mild bilateral uveitis. He was receiving sulphasalazine 2000 mg/day and low dose corticosteroids 10 mg/day and was then given cyclosporine for a month and the steroid dose elevated (60 mg/day) but with partial improvement. Cyclosporine was stopped and the patient remarkably improved after receiving, in addition to the corticosteroids, IV induction regimen of infliximab 5mg/kg at 0,2 and 6 weeks. A remission occurred (CDAI 98.5) with fading of arthritis, notable decrease in the size and severity of the PG lesion and a significant disappearance of the back stiffness with an increase in the chest expansion and lumbar spine mobility. The IBDQ significantly improved to be 159.

Conclusion: Anti-TNFα such as infliximab could be considered as a promising option for treatment of severe CD patients and for those with PG.

Keywords: Crohns disease, Infliximab, Pyoderma gangrenosum

Introduction

Inflammatory bowel diseases (IBD) are intestinal inflammatory conditions of unknown etiology, characterized by remissions and exacerbations, with Crohn's disease (CD) as one of the main phenotypes[1]. The pathogenesis of CD is not totally understood, but bowel damage is induced by uncontrolled immune activation and inappropriate response to luminal antigens resulting in an imbalance between pro and anti-inflammatory cytokines which maintains chronic tissue damage[2]. Arthritis is the most common extraintestinal manifestation of IBD having an impact on morbidity and quality of life, yet the mechanisms surrounding its development remain unclear [3,4].

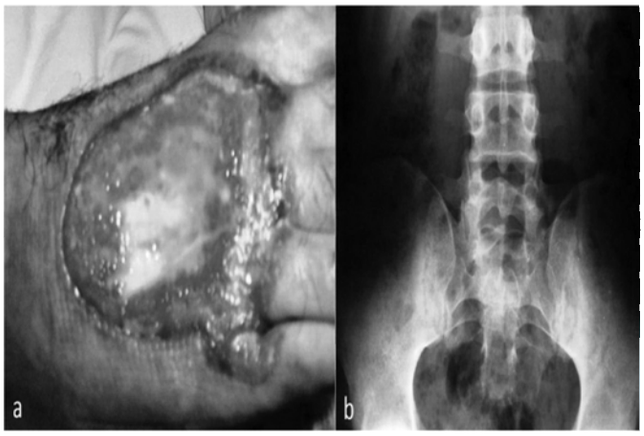
Major advances have been achieved over the last decade both in the clinical and scientific understanding of the spondyloarthritides (SpA). The proven high efficacy of TNF blocker treatment has meant a breakthrough for SpA patients, who until recently had only quite limited treatment options[5].

Case report

A male smoker, 27 years old, with enteropathic arthropathy on top of Crohns disease (CD) fulfilled the European spondyloarthropathies study group (ESSG) spondyloarthropathy classification criteria[6]. The disease duration was 2.25 years. The Crohns Disease Activity Index (CDAI) was assessed[7] as well as the Inflammatory Bowel Disease Questionnaire (IBDQ)[8]. Thorough rheumatologic examination was performed for any joint or axial involvement. Plain X-ray of the affected and sacroiliac joints was performed. The New York scoring method for the sacroiliac joints (SIJ) was followed[9]. The study was approved by the local ethics committee and a written consent was obtained according to the Declaration of Helsinki.

The patient had severe CD (CDAI = 473) and IBDQ of 39. He had oligoarthritis involving the left knee and ankle. There was severe tenderness of the ankle and moderate in the knee with moderate effusion in both. There was associated bilateral clinical sacroiliitis with moderate tenderness. The plain X-ray of the SIJ showed grade II-III while the X-ray of the knee and ankle were free. The patient had enthesitis of the tendoachillis of the left side and chostochondritis. There was back stiffness for 40 minutes and limited lumbar spine mobility as measured by the Schöber test (which increased from 15 cm to 16.7 cm). The chest expansion was limited (2 cm). The patient had an associated skin lesion diagnosed as pyoderma gangrenosum (PG) on the dorsum of the right foot (8.5 x 6 cm). The histopathology revealed infilterate of inflammatory cells with predominance of lymphocytes and polymorphonuclear leukocytes and few histiocytes. The patient had mild bilateral uveitis.

Figure 1: A male patient with enteropathic arthritis with underlying Crohns disease. (a) dorsum of the foot showing Pyoderma gangrenosum. (b) Plain X-ray showing bilateral sacroiliitis.



The laboratory investigations of the patient were unremarkable; rheumatoid factor was negative, hemoglobin level (9.8 g/dl), white blood cell (WBC) count (4.85 x10^3/mm^3), platelets (152.97 x10^3/mm^3), and erythrocyte sedimentation rate (ESR) (46.12 mm /1st hr). The HLA-B27 was negative. The patient received azathioprine 100 mg/day for 5 months after the disease onset with different doses and variable periods of oral steroids and sulphasalazine. On presentation, the patient was receiving sulphasalazine 2000 mg/day and low dose corticosteroids 10 mg/day.

The patient was given cyclosporine for a month and the steroid dose elevated (60 mg/day) but with partial improvement. The cyclosporine was stopped and the patient remarkably improved after receiving, in addition to the corticosteroids (60mg/day), IV induction regimen of infliximab 5mg/kg at 0,2 and 6 weeks. A remission occurred (CDAI 98.5) with fading of arthritis, notable decrease in the size and severity of the PG lesion and a significant disappearance of the back stiffness with an increase in the lumbar spine mobility (from 15 cm to 18.6 cm). The chest expansion increased to be 3.5 cm. The uveitis resolved in one eye and remained mild in the other. The IBDQ significantly improved to be 159. The patient was then maintained on infliximab 5mg/kg every 8 weeks and 20 mg prednisolone. Figure 1 shows the skin lesion and sacroiliitis in this patient at his initial presentation.

Discussion

In the present case with an IBD (Crohns disease), arthritis and sacroiliitis was present. It has been reported in other studies that seronegative spondyloarthropathy (SpA) symptoms are present in up to 50% of IBD patients[10] with articular involvement being the most common extraintestinal manifestation occurring in 16% to 33% of the cases[3].

The present case also had an associated rare skin lesion, pyoderma gangrenosum (PG) which improved more after the administration of infliximab. The advent of biological therapies for IBD began in 1998 with the approval of infliximab for the treatment of refractory (to conventional agents) Crohn's disease. Since then, the indications for anti-TNFα therapy for IBD have increased to include demonstrable mucosal healing, improvement in quality of life, reduction in surgeries and hospitalizations, and the treatment of extraintestinal manifestations including arthritis, sacroiliitis and PG[11]. Pyoderma gangrenosum is an uncommon and challenging inflammatory, neutrophilic ulcerative dermatosis, highly associated with co morbidities, but poorly characterized from a therapeutic perspective[12,13].

In this case, HLA typing was negative. This is supported by the findings that the association with HLA-B27 is less strong in IBD-associated SpA than in ankylosing spondylitis (AS). The adaptive immune response in IBD is thought to be strictly differentiated through Th1 in CD. Recent findings, suggested that novel effector pathways could drive tissue damage, the most important pathway now emerging is the IL-23/IL-17 axis. A common inflammatory pathogenic pathway has been suggested in gut and joint inflammation in IBD. Treatment of SpA associated with IBD has gained important progress with the introduction of anti-TNF-α therapy[14].

This patient remarkably improved regarding the peripheral and axial arthritis with a notable decrease in the PG size after a combination of high dose corticosteroids and infliximab therapy. In another study, PG was 34% associated with IBD and 19% with seronegative arthritis. Similarly, it was most commonly located on the lower leg; contrarily, was found to be more frequent in females and unfortunately had a high mortality rate (16%)[15]. Pyoderma gangrenosum is associated with a variety of systemic diseases including IBD as CD and arthritis. The pathogenesis of PG remains unknown. Some patients with PG have abnormalities in cell and humoral immunity, with an increase in interleukin expression, particularly

TNF-a [11]. It has been reported that treatment of IBD is not always sufficient for control of arthritis and treatment with biologic agents is promising[4].

Over recent years, the management of IBD has dramatically changed. In particular, advances in understanding the pathogenesis and the natural course of the disease have substantially changed the therapeutic algorithms with the introduction of new biological drugs. Among these the anti-TNF-a monoclonal antibodies infliximab is currently approved for the management of CD, in particular for patients with moderately and severely active luminal disease who are nonresponders to conventional therapy[2]. These newly developed treatment modalities are proving to be valuable additions to the current therapeutic armamentarium and add to our knowledge so that IBD patients could be treated with the right drug at the right time.

In conclusion, anti-TNFa such as infliximab could be considered as a promising option for treatment of severe CD patients and for those with PG. To confirm our results we propose that more cases of CD and/or PG are studied and for longer periods of follow up.

Conflicts of interest: none.

References

1. Baumgart DC, Carding SR. Inflammatory bowel disease: cause and immunobiology. *Lancet.* 2007; **369**:1627-1640.
2. Guidi L, Pugliese D, Armuzzi A. Update on the management of inflammatory bowel disease: specific role of adalimumab. *Clin Exp Gastroenterol.* 2011; **4**:163-172.
3. Brakenhoff LK, van der Heijde DM, Hommes DW, Huizinga TW, Fidder HH. The joint-gut axis in inflammatory bowel diseases. *J Crohns Colitis.* 2010; **4(3)**:257-268.
4. Arvikar SL, Fisher MC. Inflammatory bowel disease associated arthropathy. *Curr Rev Musculoskelet Med.* 2011; **4(3)**:123-131.
5. Sieper J. Developments in the scientific and clinical understanding of the spondyloarthritides. *Arthritis Res Ther.* 2009; **11(1)**:208.
6. Dougados M, van der Linden S, Juhlin R. *et al.* The European Spondylarthropathy Study Group preliminary criteria for the classification of spondyloarthropathy. *Arthritis Rheum.* 1991; **34**:1218-1227.
7. Best WR, Becktel JM, Singleton JW, Kern F Jr. Development of a Crohn's disease activity index. National Cooperative Crohn's Disease Study. *Gastroenterology.* 1976; **70:** 439-444.
8. Guyatt G, Mitchell A, Irvine EJ. *et al.* A new measure of health status for clinical trials in inflammatory bowel disease. *Gastroenterology.* 1989; **96:** 804-810.
9. van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. *Arthritis Rheum.* 1984; **27**:361-368.
10. Zochling J, Smith EU. Seronegative spondylarthritis. *BestPract Res Clin Rheumatol.* 2010; **24**(6):747-756.
11. Yanai H, Hanauer SB. Assessing response and loss of response to biological therapies in IBD. *Am J Gastroenterol.* 2011; **106**(4):685-698.
12. Binus AM, Qureshi AA, Li VW, Winterfield LS. Pyoderma gangrenosum: a retrospective review of patient characteristics, comorbidities, and therapy in 103 patients. *Br J Dermatol.* 2011; **165** (6): 1244-1250.
13. Santos M, Talhari C, Rabelo RF, Schettini AP, Chirano CA, Talhari S. Pyoderma gangrenosum: a clinical manifestation of difficult diagnosis. *An Bras Dermatol.* 2011; **86**(1): 153-156.
14. Faustini F, Zoli A, Ferraccioli GF. Immunologic and genetic links between spondylarthropathies and inflammatory bowel diseases. *Eur Rev Med Pharmacol Sci.* 2009; **13** (Suppl 1):1-9.
15. Asarch A, Barak O, Loo DS, Gottlieb AB. Th17 cells: a new therapeutic target in inflammatory dermatoses. *J Dermatol Treat.* 2008; **19**(6):318-326.