



SEVERE DILATED CARDIOMYOPATHY FOLLOWING ADALIMUMAB ADMINISTRATION IN SEVERE ULCERATIVE COLITIS

Gastroenterology

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ABSTRACT

Adalimumab (ADA) is a humanized monoclonal antibody against TNF- α which is indicated for moderate & severe disease Ulcerative Colitis (UC). Herein we report a severe adverse reaction to adalimumab in a 35 year old woman, after the first dose of Adalimumab (160 mg). Our patient developed fulminant cardiomyopathy causing severe cardiogenic shock requiring vasopressor support until recovery. Though this is a rare complication, it is prudent to evaluate cardiac function of IBD patients prior to Adalimumab administration.

KEYWORDS

Adalimumab, Ulcerative colitis, Cardiomyopathy, Heart failure, JVP, IBD.

INTRODUCTION

Biologic therapy is considered in moderate to severe UC. Selection of biologics depends on several factors. Prior exposure to the drug, availability, development of drug antibodies and clinicians expertise in biologics are crucial factors. With biologics, severe adverse reactions are uncommon, but in rare cases, life threatening adverse effects may occur like severe allergic reactions, cardiomyopathy, demyelinating disorders or activation of tuberculosis.

CASE REPORT

A 35 year old woman, a known case of Ulcerative colitis with a history of multiple flares requiring steroids and Infliximab had a relatively stable disease for the past 6 years. She now presented with multiple episodes of loose stools, rectal bleed, anemia and severe dehydration. She required prolonged hospitalization with administration of intra venous (IV) fluids, IV steroids and antibiotics.

Her stool frequency continued to remain high. Screening for C.difficile & CMV was negative. Stool culture was negative. CRP was high at admission and remained elevated. Starting biologics had been delayed, since she had earlier experienced TB reactivation with Infliximab 6 years ago which was treated as per standard guidelines. Presently, colectomy was advised but she was not in favor of surgery.

A decision was taken to administer Adalimumab and was given the first dose of 160mg. After 2 days, she complained of breathlessness and pedal edema. Lung auscultation revealed crepitations; 2D echo revealed dilated chambers with an ejection fraction of 28%. Baseline cardiac workup (including 2D echo) was normal at admission.

She was continued on IV steroids and decongestive therapy was initiated. Cardiac function improved in 2 weeks. She was stabilized and discharged later. As her evaluation did not show any previous heart ailment and complete reversal of cardiac dysfunction after stopping the drug (Ejection Fraction after 4 weeks-54%), it was concluded that the deterioration in cardiac function was due to Adalimumab in temporal correlation. No further adalimumab was given.

DISCUSSION

Adalimumab is a recombinant human monoclonal anti-TNF antibody administered subcutaneously and approved for use in Crohn's Disease (CD) & Ulcerative Colitis(UC)¹. ADA is administered by subcutaneous injection: 160mg at week 0 and 80mg at week 2 for induction followed by 40mg every fortnight for maintenance.

TNF- α has been implicated in the pathogenesis of heart failure (HF)

and cardiac cachexia. The occasional association between anti-TNF drugs and adverse cardiac events has no pathophysiological explanation. Studies have revealed negative inotropic and cardiac remodeling effects of TNF- α on the myocardium in various cardiac diseases²

Based on literature of other TNF- α inhibitors, new onset or worsening of HF is considered to be a rare side effect of Adalimumab treatment.

Initially assumed to have favorable effects on HF, randomized, and controlled clinical trials such as the 'Anti-TNF Therapy Against Congestive Heart failure' trial (ATTACH) had to be terminated prematurely due to lack of efficacy. Moreover, a dose-dependent increased risk of HF worsening after use of infliximab was seen in RA patients (3).

A recent updated analysis of global clinical trials involving use of Adalimumab in total 29967 patients for various indications showed that the most common adverse effects were related to skin & infections notably tuberculosis. In this analysis the incidence of heart failure was 0% in CD and <0.1% in UC, indicating a very low risk⁴.

A few case reports of adverse cardiac effects with Adalimumab have been published^{5,6,7} which included cardiomyopathy in Crohn's disease.

Based on the above available literature it can be considered that adalimumab use should be contraindicated in patients with moderate to severe heart failure & should be discontinued if a patient develops new or worsening heart failure. All patients should be subjected to complete cardiac evaluation and counselled for potential adverse reactions before starting Adalimumab.

CONCLUSION

Cardiomyopathy is a rare adverse effect of Adalimumab. Due to temporal association and lack of other predisposing factors this case highlights dilated cardiomyopathy as a possible severe adverse effect of Adalimumab treatment. It also signifies the importance of complete cardiac evaluation in patients with IBD receiving treatment with Adalimumab. Prompt identification and withdrawal of medication seems to be important in the management of this complication.

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