

Sever ulcerative colitis associated with coombs positive autoimmune haemolytic anemia (AIHA) response to infliximab

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CASE STUDY

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ABSTRACT

Autoimmune Haemolytic Anemia is rarely associated with Ulcerative Colitis, and counts for just 0.2-0.7per cent of adult patient. It is a complication that is present by having a positive coombs test which account for only 1.82per cent in a patient with ulcerative colitis without any haemolytic evidence.

Hence there is only one case report has published the effective response to infliximab by both rare combined conditions.

Here we report the second case of sever ulcerative colitis associated with coombs positive autoimmune Haemolytic Anaemia (AIHA) response to infliximab.

Key Words

Autoimmune Haemolytic Anaemia (AIHA), ulcerative colitis, infliximab

Implications for Practice:

1. What is known about this subject?

Autoimmune Haemolytic Anaemia is rarely associated with Ulcerative Colitis, and counts for just 0.2-0.7per cent of adult patient in which both are treated differently.

2. What new information is offered in this case study?

A new medical approach by using infliximab for treating both a combined condition Ulcerative colitis and

Autoimmune haemolytic Anaemia.

3. What are the implications for research, policy, or practice?

A trial of using the biological agent infliximab for threating both Ulcerative colitis and Autoimmune Haemolytic Anaemia before the surgical approach.

Background

Autoimmune Haemolytic Anaemia is rarely associated with ulcerative colitis, and if they come together, this would count for only 0.2-0.7per cent of adult patient. Hence, it is a rare complication that is presented by having a positive Coombs test which account for only 1.82per cent in-patient with ulcerative colitis without any haemolytic evidence.

The reason and the aetiology are not yet really understood or completed. However, it seems that there are different factors, which play a role in such event. Starting with the production of anti-erythrocytes antibodies by the colon, which explains the therapeutic effect of haemolysis after colectomy in Ulcerative Colitis patient¹.

Where both conditions are usually have different approaches of medical treatment.

Monoclonal antibodies like infliximab has potent of anti-inflammatory activity, which helps as a therapeutic agent for Rheumatoid arthritis, inflammatory bowel disease, and many other autoimmune diseases².

Hence there is only one case report has published the effective response to infliximab by both rare combined conditions.

Here we report the second case of sever ulcerative colitis associated with coombs positive autoimmune Haemolytic Anaemia (AIHA) response to infliximab.

Case details

This is a 35 years old Saudi male study in Australia, Known case of SCT. He was diagnosed as a case of UC in 2011 by colonoscopy, were it showed a mild to moderate left side colitis and he is on mesalazine enema foam since then. One week after the patient presented with signs and symptoms of anaemia and haemolysis (Hb 5g/dl) (Jaundice - high

Indirect bilirubin - high LDH- high reticulosis - Reduced Haptoglobin), after further investigation Coombs test was positive, which suggested autoimmune hemolytic anemia, with exclusion of other aetiologies. And Prednisolone 60mg, Azathioprine 150mg was prescribed.

Patient's health showed deterioration after tapering down and discontinuation of steroid so his medications were kept on: (Steroid 7.5mg - Azathioprine 150mg - Mesalazine granules - Calcium, Vitamin D, Folic acid).

On 11/2013 the patient presented back to the hospital with Symptom of anaemia fatigability, tiredness, and palpitation, Symptom of myopathy, muscle pain weakness, unable to stand, walking with difficulty, Bowel movement 2-3 time with occasional blood in stool, He was on his maintain drugs.

On Exam: patient looks sick, cachectic, and pale, not jaundice. Vital signs were stable. Chest, CVS and abdomen were normal; Patient had proximal upper and lower limb weakness. Normal reflexes and sensation

Investigations: wbc: $3.6 \times 1000/\text{mm}^3$, Hb: 8.3 g/dl, platelet: $660 \times 1000/\text{mm}^3$, MCV: 79 fl, MCH: 33pg, RFT, LFT and electrolytes : normal, Total Protein 44mg, Albumen: 14 g/liter, Ca: 1.96mg/dl, ESR: 120 mm/hr, CRP:8.3 mg/dl, Coombs test direct; +++++

B12, Folate, are normal

Patient's medications were adjusted again to be (Prednisolone 50 mg -Azathioprine 100mg - Mesalazine granules 1 gm PO daily -Calcium -Vitamin D-Folic acid-Human albumin)

*Colonoscopy was done and revealed the following: [pic-1]

Up to T colon 70 cm only, it was vary sever diffuse inflammation with multiple variable size of Pseudo polyps with narrow lumen at 70 cm, scoop cannot pass it. So accordingly Multiple Biopsies were taken. Histopathology: Chronic Active Colitis

*Ct Abdomen report:

Diffuse thickened wall of recto sigmoid as well as transverse and descending colon, with increased pericolic vascularity (Comb sign), multiple polyp like structures seen at rectosigmoid region mostly represent pseudopolyp, it is seen associated with cast like intracolonic structure along descending colon, with target like appearance on axial images and contrast seen interposed between it and colonic wall, mostly represent sloughed thickened mucosa, for clinical correlation and further evaluation.

The final diagnosis was made to be Sever Ulcerative colitis associated with Autoimmune Haemolytic Anaemia. In regard the therapeutic, we were in front of two approaches after the failure of steroid and immunosuppressant agent in the therapy of both Ulcerative colitis and AIHA. Hence,

based on a literature review of a case report with similar issues, that reported the biological drugs like infliximab is a good option to start a therapy with before going for surgical options (splenectomy / colectomy)(1) we decided to institute a biological agent therapy instead of colectomy, as Second case.

So patient is currently on: Infliximab infusion every 8 weeks. Mesalazine granules 1 gm. Po daily, and he showed an improvement in general condition clinically and laboratory investigations. In the form of ulcerative colitis and in the Autoimmune Haemolytic Anaemia as it can be represented in the table. 2018 [Table-1] moreover the patient shows no more endoscopic activates regarding his colitis. [Figure 1, Figure 2].

Discussion

[Infliximab is biological drugs, which function by blocking the action of tumour necrosis factor- α , to decrease or slow the body immunity as a it is used do treat autoimmune diseases.

Monoclonal antibodies like infliximab has potent of anti-inflammatory activity, which helps as a therapeutic agent for Rheumatoid arthritis, inflammatory bowel disease, and many other autoimmune diseases².

There are many side-effects associated with the infliximab in general and in infusion particularly which is called the infusion reaction, and can be manifested by swelling or pain on the site of injection. or general reaction like flushing, shortness of breath, risk of infections, pancytopenia and haematological malignancies²⁻³.

Ulcerative colitis (UC) is an inflammatory bowel disease that affects the colon mainly, while autoimmune haemolytic anaemia is a rare complication of such a disease and it represents only minority of patient.

UC Mainly response to steroid agent as a first line management, and shows a remission in 21per cent-50per cent of cases¹⁻⁹. But unfortunately this line of management did not work with our patient; going back to the aetiology of having a Coombs positive autoimmune haemolytic anaemia associated with ulcerative colitis is not fully understood. There are multi theories that may explain some points. The first one is stated by the provocation of the immune system by chronic IBD, or induced by anti-erythrocytes antibody the second one was explained by the cross- reaction antibodies between both RBCs and the colon⁴.

In cases where patients does not show any improvement with the immunosuppressant agent or systemic steroid, most of them were treated with surgical approach. While a one literature review reported was suggesting the use of biological agent (infliximab) for the treatment of

Autoimmune Haemolytic Anaemia Associated with Ulcerative Colitis⁵.

Many cases of AIHA, which are treated with rituximab (anti CD-20)⁶⁻⁸, has been reported in different literature reviews, but only one that suggest the use of infliximab for treatment of both AIHA and Ulcerative colitis. Based on this, we decided to use the anti TNF as an inducer and a maintenance therapy on our case as a second case. The good response of ulcerative colitis may be explained by the previously suggested above-mentioned theories⁴⁻⁷.

In which the healing of the mucosal layer, will suppress the expression of antigens that may cross-react with antigen of RBCs.

Conclusion

Here we concluded that the usage of biological agent like infliximab can be used in the treatment of not only the UC but also the Autoimmune Haemolytic anaemia and more over it may shows a great response for both conditions if they came together. therefore, such case can opens a huge opportunities for more researches about using infliximab as a new therapeutic agent for both ulcerative colitis and AIHA especially after failure of controlling the UC with the immunosuppressant agents. Or even for AIHA with any other disease other than inflammatory bowel diseases.

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PEER REVIEW

Not commissioned. Externally peer reviewed.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

PATIENT CONSENT

The authors, Busbaih, Albatool; Busbaih, Jawad, declare that:

1. They have obtained written, informed consent for the publication of the details relating to the patient(s) in this report.
2. All possible steps have been taken to safeguard the identity of the patient(s).
3. This submission is compliant with the requirements of local research ethics committees.

Table 1: Timetable of investigation before and after receiving infliximab infusion

Date of infliximab infusion	First infusion 5/10/2013	Second infusion 29/11/2013	Third infusion 25/12/2013	Forth infusion 7/2/2018
WBC × 1000/mm ³	3	1.6	7	5
HB g/dl	7.7		11	15
Platelets × 1000/mm ³	660		300	210
Total Protein mg	44		58	75
Albumin g/litre	14		44	45
ESR mm/hr	120		46	13
CRP mg/dl	8.3		2.7	0.5
Weight	52 kg			77 kg

Figure 1: endoscopy result before starting infliximab

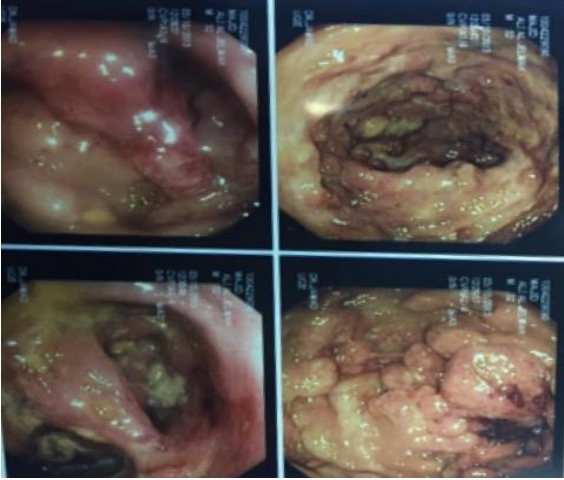


Figure 2: endoscopy result after 4th dose of infliximab infusion

