



ADALIMUMAB INDUCTION AND MAINTAINING REMISSION FOR CROHN'S DISEASE IN PATIENT WHO LOST RESPONSE TO INFLIXIMAB. Case report

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ABSTRACT:

This is a report of 30 years old woman suffering from Crohn's disease who had a good clinical response to Infliximab (Remicade) at first, but during the treatment after 5 months she lost response. After receiving Adalimumab (Humira) clinical remission was reached on the day 20. The case demonstrates rapid response to adalimumab in incidence of losing efficacy to another tumor necrotic factor - alpha (TNF- alpha) antagonist.

Keywords: Crohn's disease, TNF- alpha inhibitors, adalimumab, infliximab

INTRODUCTION:

Crohn's disease (CD) is an idiopathic, chronic granulomatous disorder characterized by the presence of inflammatory ulcerative lesions in the gastrointestinal tract. [1] Tumor necrotic factor- alpha (TNF- alpha) antagonists have advanced the management of patients with moderate-to-severe CD [2] leading to improvement of patient's quality of life with reduction of the number of surgeries and hospitalizations. [3] Despite these advances, 20-40% of patients do not respond to the induction therapy (primary non-response — PNR) [4] and 23-46% lose response during the treatment (secondary loss of response—LOR). [5] Secondary LOR, also referred to as secondary non-response, describes patients who respond to the therapy after an induction regimen, but subsequently lose response during maintenance treatment. [6] Immunogenicity is the most common cause of lost response during the treatment, as formation of antibodies can neutralize the drug or hasten its clearance. [7] There's no unified opinion concerning the question whether to continue the same therapy, and the strategy is dose intensification, to include immunomodulator - azathioprine or to switch to another anti-TNF alpha agent. [8]

CASE PRESENTATION:

It concerns a patient with Crohn's disease verified endoscopically and histologically in September 2015 abroad, where she was treated initially with corticosteroids

and Imuran with unsatisfactory effect. In January 2016 therapy with Infliximab (Remicade) under a scheme was started which in the first five months had a good effect. It was discontinued from April 2016 on the occasion of frequent defecations up to 10 for 24 hours, abdominal pain and febrilit. The patient had good clinical response to IFX initially, but during the treatment after 5 months she lost response. She came in Bulgaria and a therapy was started with Mesalazine (Salofalk) 4g, Azathioprin (Imuran) 100 mg and Prednisone (Dehydrocortison) 40 mg daily. She tells about reduction of weight with 5-6 kg. Fecal Calprotectin was examined ambulatory – 270 mg/ml (normal 0 – 50) and CRP - 20. In May 2016 and active Crohn's disease with pancolitis was confirmed by colonoscopy and biopsies showed noncaseating granulomas. Colonoscopy showed "skip" areas, spontaneous bleeding, submucosal edema, aphthous ulcers (fig.1).

Fig. 1. Colonoscopy before treatment with adalimumab



From September 2016 a therapy was started with Adalimumab (Humira) fl. 40 mg. At start of treatment CDAI was 310, severe Crohn's disease and A1, L2, B1 type according to Montreal classification. [9] The patient was 48 kg, good general condition, non smoker, no family defects, and no concomitant diseases. Induction dose of

adalimumab was 160/80/40 mg at weeks 0, 2 and 4, followed by maintenance therapy - 40 mg at weeks 2 and at week 4. The therapy with Imuran was stopped. The dose of Dehydrocortison was reduced with 10 mg every week until reaching dose of 20 mg/daily and after that with 5 mg to finally stopping the medicine. The therapy with Salofalk continued with a dose of 3 mg daily. The patient's complaints subsided quickly – she had no pain on the 20th day and normal defecation, CRP dropped from 20 to 4,69. No adverse drug reactions were registered. The patient had good clinical response and maintenance the remission with adalimumab. The period of follow-up on adalimumab was 3 months. Control endoscopy showed reduction of submucosal edema, aphthous ulcers (fig.2), a CDAI dropped to 140.

Fig. 2. The improved endoscopic finding at endoscopy after 3 months treatment with adalimumab



DISCUSSION:

Infliximab (IFX) is the first drug directed against TNF-alpha. [10] Our case report describes the loss of response to IFX in patient with CD. The reason may be immunogenicity because IFX is murine chimeric monoclonal antibody. Adalimumab is a subcutaneously (SC) self-administered recombinant fully-human monoclonal immunoglobulin (IgG1) antibody. It binds with a high affinity and specificity to soluble TNF- alpha and neutralizes its biological function by blocking its interaction with TNF- alpha receptors. [2] Our case report indicates that Adalimumab induces remissions in adult patients with CD who have symptoms despite receiving infliximab therapy. Data from literature support the effect of adalimumab therapy after failure of infliximab. [12]

CONCLUSIONS:

Adalimumab, a fully human, monoclonal antibody can be self-administered and has demonstrated efficacy and safety for induction of remission in patients with CD, who lost response from the therapy with Infliximab. Adalimumab every other week additionally maintains remission. The ease of administration, sustainability, and convenience of adalimumab make this an attractive therapeutic agent for treatment of patients with CD.

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