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Severe Crohn's Disease in Combination with Undifferentiated Autoimmune Liver Disease - A Case Report

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Abstract: Crohn's disease is a chronic autoimmune pathology of intestinal mucosa in the form of segmentary lesions of various parts with the development of transmural granulomatous inflammation and the formation of strictures, stenosis, fistulas, as well as damage to other organs. The disease tends to be developed mainly in young people. Over recent years anti-TNF mAb has been widely used in the treatment of Crohn's disease. Case Report: from the age of 13 Patient A suffered from Crohn's disease, weight deficit, muscular atrophy. At the age of 19, autoimmune hepatitis with developing cirrhosis joined. At the age of 22 there was another disease exacerbation. The efficiency of treatment with steroids, aminosalicylates and cytostatics was low. After replacing cytostatics with anti-TNF mAb, the patient's condition became even worse: body weight, total protein, albumin, hemoglobin and coagulation indices decreased critically. A treatment in intensive care and multiple blood transfusions were required for the period of 1 year. Changes in the treatment strategy in the form of maintaining the therapy with steroids and aminosalicylates, withdrawing anti-TNF mAb and adding the plasma exchange and injection of native DNA (sodium deoxyribonucleate) led to an increase in body weight, total protein and hemoglobin to normal values, as well as improved bowel function and performance status. Under condition of sever Crohn's disease with autoimmune hepatitis, the catabolic effects of the anti-TNF mAb can be extremely dangerous. In such a case, it is preferable to use steroids and aminosalicylates in combination with plasma exchange and reparation activators (e.g., native DNA).

Keywords: Crohn's Disease, Monoclonal Antibodies, TNF-α, Anemia, DNA, Sodium Deoxyribonucleate, Plasma Exchange

1. Introduction

Crohn's disease is a rare chronic pathology that mainly affects young people and manifests itself in the form of recurrent disease of the gastrointestinal tract of autoimmune origin with segmentary lesions of mucous membrane of various parts of the intestine, the development of transmural granulomatous inflammation and the formation of strictures, stenosis, fistulas, as well as damage to other organs.

The need to use surgical methods in the treatment of Crohn's disease arises in cases with development of complications. Within 20 years from the onset of Crohn's disease, up to 80% of patients undergo surgical treatment [1-3]. The associated liver lesions in case of Crohn's disease are rare (less than 3%). Among them, the following are noted most often (up to half of all cases): fatty liver infiltration and periangiocholitis. Chronic active (autoimmune) hepatitis develops in very rare cases (1-3% out of all cases) [2, 4, 5].

2. Case Presentation

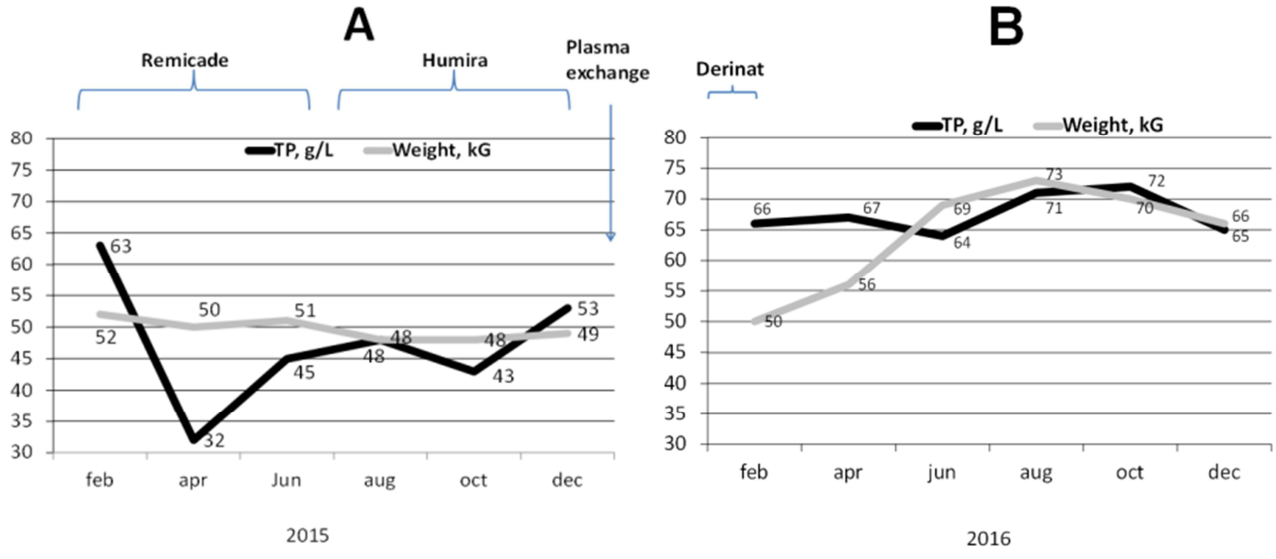
We present the experience of observation and 2-year treatment of a patient with a severe form of Crohn's disease on the background of severe autoimmune hepatitis.

The Patient A at the age of 13 was diagnosed with Crohn's disease. The main manifestations of the disease included frequent loose stools, lancinating abdominal pains, sometimes vomiting. There were noted a lack of weight, muscular atrophy, delaying in physical growth and development.

At the age of 19, after a period of improvement the lower limb edema and then ascites joined the existing enteral disorders. He was diagnosed with autoimmune hepatitis with developing cirrhosis. The conducted hepatotropic and anti-inflammatory treatment, and soon afterwards long-term therapy with aminosalicylate Mesacol® ((Sun Pharmaceutical Industries Ltd. [India]), as well as prebiotics and probiotics, enzyme preparations contributed to the improvement of the patient's condition, weight increase from 38 kg to 55 kg (with a height of 188 cm), bowel movement normalization.

After 3 years of relative well-being, there was an exacerbation of Crohn's disease (abdominal pain, frequent loose stools). Steroids were added to the permanent treatment regimen (Prednisolonum 60 mg/day with gradual decreasing to 40 mg/day). The improvement turned out to be short-term. Pain, nausea, diarrhea, vomiting began growing. The use of cytostatic (azathioprine) and special enteral nutrition did not improve the situation. When performing endoscopic examination of the large intestine it was revealed a swollen and hyperemic mucous membrane in the form of «cobblestone appearance» with multiple pseudopolyps, cicatricial tissues and ulcerous defect of slit-like form. The laboratory examination revealed signs of increased inflammatory and cytolytic activity of the blood (an increase in C-reactive protein, alanine-aminotransferase, aspartate-aminitransferase, gamma-glutamyl transpeptidase) in combination with hypoproteinemia and anemia. The homeostatis corrective intensive therapy under conditions of intensive care unit involving the application of intravenous parenteral nutrition, infusions of albumin and others contributed to the stabilization of the general condition with a background of normalization of total blood protein level. Further, to the pathogenetic treatment regimen there was added the therapy mAb targeted against TNF-α (mixt murine (25%) and human (75%) Infliximab (Remicade®, Centocor [CA, USA]) by 0,3 in 0-2-6 weeks) in combination with aminosalicylate Budenofalk® (Doctor Falk Pharma GmbH, [Germany]) or Salofalk® and steroids (Prednisolonum). After each administration Remicade® the patient's condition was getting worse. The body weight, total protein and red blood cell count decreased. As a result, with a critical decrease in the level of hemoglobin and total protein, it was required to perform transfusions of erythromass and fresh frozen plasma. Subsequently, Remicade® was replaced with a fully human anti-TNF mAb Adalimumab (Humira®, Abbott Labs [IL, USA]) 0,04 time every 2 months), however, it did not change the general trend to the condition worsening. And still the body weight continued to decrease. The values of blood hemoglobin, total protein and albumin improved after blood transfusion also decreased. The signs of impaired coagulation were detected in the blood. Again, inpatient treatment was required with the performance of transfusions of donor blood components (erythromass and fresh frozen plasma) to maintain vital activities. Analysis of the humoral immunity condition revealed a moderate increase in the levels of immunoglobulins G, A and especially high level of secretory immunoglobulin A (sIgA) which is 7 times higher than the normal range, which is typical for sever local inflammation of the intestinal mucosa.

The change of pathogenetic treatment carried out in 2016 consisted in the rejection of administration of medication with monoclonal antibodies to TNF-alpha, maintaining aminosalicylate and steroid therapy in combination with the correction of dysbiosis and the addition of extracorporeal hemocorrection procedures (plasma exchange) aimed to remove autoimmune antibodies, in combination with administration of repair-activating native fragments of deoxyribonucleic acid. All listed above resulted in a favorable change in the course of the disease.



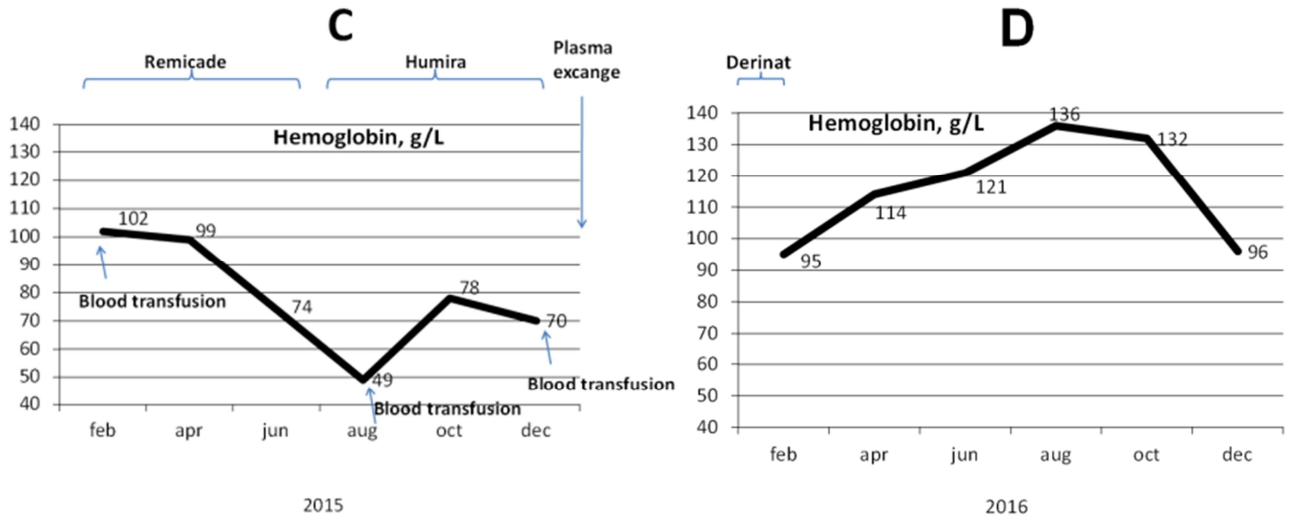


Figure 1. *Dynamics of patient homeostasis indicators.*

A (2015 year) and B (2016 year) – total protein of serum, g/L and body weight, kG;
C (2015 year) and D (2016 year) – blood hemoglobin, g/L

On the background of the continued therapy with steroids (Prednisolonum 60 mg/day for the first 2 weeks, followed by a subsequent decrease in dosage to 40 mg/day) and aminosalicylate Salofalk® (Doctor Falk Pharma GmbH [Germany]) 3 g/day plus Pentasa® (Ferring Int. Cent. S. A., [Switzerland]) the patient underwent 1 plasma exchange with removal of 80% of volume of the circulating plasma and its replacement with fresh frozen plasma. To activate the reparation the sodium deoxyribonucleate consisting of native DNA (Derinat®, OOO "FZ Immunolex", [Moscow, Russia]) was injected intramuscularly 10 times by 75 mg at a frequency of 3 times a week [6].

The dynamics of the patient's condition in 2015, preceding this treatment, is presented in diagrams A and C in Figure 1.

3. Discussion

Without going into details of short-term (under administration) immune-mediated (including infectious) [7, 8] and long-term (possible oncogenicity) [9] undesirable consequences of use of the monoclonal antibodies to TNF-alpha, it should be highlighted that their administration in case of Crohn's disease can in rare cases provoke hematopoietic disorders [10, 11] and liver functioning [12, 13]. In our case with severe Crohn's disease and, especially, against background of autoimmune liver damage, the administration of antibodies to TNF-alpha led to a catastrophic increase in catabolism. Moreover, the cancellation of treatment with medications of this group, transfusion of blood components did not contribute to the improvement or at least stabilization of condition severity.

The restructuring of the immune response to the anabolic scenario was carried out by introducing a DNA-containing medication. For implementation of biological activity of DNA, an important point is to maintain its native (non-denatured) form. Parenteral administration of sodium deoxyribonucleate increases the operational intensity of cells of the reticuloendothelial system and the proliferative activity of the bone marrow, which results in increasing the number of stem cells released into the blood stream [14]. When having a course of administration, sodium deoxyribonucleate is accumulated mainly in the bone marrow, lymph nodes and spleen and remains there up to 6 month [15].

Removal of autoantibodies from the blood to the liver structures, achieved when performing the plasma exchange procedure, had a synergistic positive effect and contributed to the improvement of protein synthesis and, probably, other functions of the liver. Moreover, in the presented case it was sufficient to carry out 1 plasma exchange.

4. Conclusions

The use of medications of antibodies to TNF-alpha in the treatment of patients with Crohn's disease accompanied by shown severe hypotrophy and autoimmune liver damage is associated with the risk of developing life-threatening homeostasis disorders. Procedures of extracorporeal removal of pethogenetically significant autoantibodies from the blood in combination with the administration of repair activators and immunomodulators, for example, native fragments of deoxyribonucleic acid, can have a beneficial effect in the treatment of such patient.

Consent

Written informed consent was obtained from the patient and it is available for review.

Conflicts of Interest Statement

The authors declare that they have no competing interests.

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References

[1] Adler G. Morbus Crohn Colitis ulcerosa. Spriger-Verlad, 1993. doi: 10.1007/978-3-642-97440-3.

[2] Sinenchenko G. I., Peregudov S. I., Tulupov A. N. Endolymphatic drug therapy of acute inflammatory diseases in emergency abdominal surgery [Ehndolimfaticheskaya lekarstvennaya terapiya ostryh vospalitelnyh zabolevanij v neotlozhnoj abdominalnoj hirurgii]. SPb.: DMITRIJ BULANIN, 2014. [Rus].

[3] Gomes C. A., Podda M., Veiga S. C., Cabral T. V., Lima L. V., Miron L. C., Oliveira V. L., Aranha G. L. Management of inflammatory bowel diseases in urgent and emergency scenario. *J. Coloproctol. (Rio J.)* 2020 Jan/Mar; 40 (1). doi: 10.1016/j.jcol.2019.10.012 Epub 2020 Mar 23.

[4] Belousova E. A. Ulcerative colitis and Crohn's disease [Yazvennyj kolit i bolezn Krona]. M.: "Triada". 2002. [Rus].

[5] Safi M. H., Li J. Non-alcoholic fatty liver disease in inflammatory bowel diseases patients. *IOSR Journal of Dental and Medical Sciences*. 2019 Oct; 18 (10) Ser. 15: 09-15. doi: 10.9790/0853-1810150915.

[6] Gromov M. I., Pivovarova L. P. Use of immunomodulator derinat in treatment of surgical patients with severe sepsis. *Fundamental research*. 2012; 7 (2): 289-295. [Rus]. URL: http://www.fundamental-research.ru/ru/article/view?id=30127 Epub 2020 Dec 17.

[7] Dixon W. G., Watson K., Lunt M., Hyrich K. L., Silman A. J., Symmons D. P. M. Rates of serious infection, including site-specific and bacterial intracellular infection, in rheumatoid arthritis patients receiving anti-tumor necrosis factor therapy: results from the British Society for Rheumatology Biologics Register. *Arthritis Rheum*. 2006 Aug; 54 (8): 2368-76. doi: 10.1002/art.21978.

[8] Susanna F. N. Pavesio C. A review of ocular adverse events of biological anti-TNF drugs. *J Ophthalmic Inflamm Infect*. 2020; 10 (11). doi: 10.1186/s12348-020-00202-6 Epub 2020 Apr 27.

[9] Vulliemoz M., Brand S., Juillerat P., Mottet C., Ben-Horin S., Michetti P. TNF-alpha blockers in inflammatory bowel diseases: Practical Recommendations and a User's Guide: an update. *Digestion.* 2020; 101 (suppl. 1): 16–26. doi: 10.1159/000506898.

[10] Leombruno J. P., Einarson T. R., Keystone E. C. The safety of anti-tumour necrosis factor treatments in rheumatoid arthritis: meta and exposure-adjusted pooled analyses of serious adverse events. *Ann Rheum Dis*. 2009 Jul; 68 (7): 1136-45. doi: 10.1136/ard.2008.091025 Epub 2008 Aug 27.

[11] Shah B., Mayer L. Current status of monoclonal antibody therapy for the treatment of inflammatory bowel disease. *Expert Rev Clin Immunol*. 2010 Jul; 6 (4): 607–620. doi: 10.1586/eci.10.45.

[12] Sokolove J., Strand V., Greenberg J. D. Curtis J. R., Kavanaugh A., Kremer J. M., Anofrei A., Reed G., Calabrese L., Hooper M., Baumgartner S., Furst D. E. Risk of elevated liver enzymes associated with TNF inhibitor utilisation in patients with rheumatoid arthritis. *Ann Rheum Dis*. 2010 Sep; 69 (9): 1612-1617. doi: 10.1136/ard.2009.112136 Epub 2010 May 6.

[13] Likhitsup A., Dundulis J., Ansari Sh., Patibandla S., Hutton C., Kennedy K., Helzberg J. H., Chhabra R. High prevalence of non-alcoholic fatty liver disease in patients with inflammatory bowel disease receiving anti-tumor necrosis factor therapy. *Ann Gastroenterol.* 2019 Sep-Oct; 32 (5): 463–468. doi: 10.20524/aog.2019.0405 Epub 2019 Jul 22.

[14] Pivovarova L. P., Gromov M. I., Tulupov A. N., Lapshin V. N., Osipova I. V., Ariskina O. B., Nikitin A. V., Malyshev M. E., Markelova E. V. Influence of sodium desoxyribonucleate on anti-infectious protection and hematopoiesis in patients with polytrauma (randomized prospective, double-blind, placebo-controlled study). *Medical Immunology*. 2020; 22 (4): 729-740. [Rus]. doi: 10. 15786/1563-0625-IOS-1923.

[15] Kaplina E. N., Vaynberg Yu. P. Derinat is a natural immunomodulator for children and adults. 3rd ed., rev. and corr. [Derinat - prirodnyy immunomodulyator dlya detey i vzroslykh. 3-ye izd., per. i ispr.]. M.: "Nauchnaya kniga", 2007. [Rus].