AN INTERDISCIPLINARY APPROACH TO THE TREATMENT OF CROHN’S DISEASE – GASTROENTEROLOGY, INTENSIVE CARE, ABDOMINAL AND PLASTIC SURGERY. CASE REPORT

N. Mladenov1, M. Doitchinova-Simeonova1, K. Kazarov1, N. Petrov1, X. Gelev1, N. Vladov1, L. Voinov2
Military Medical Academy, Department of Anesthesiology and Intensive Care, Sofia, Bulgaria
Military Medical Academy, Department of Ophtalmology, Sofia, Bulgaria
Correspondence to: Nikolay Mladenov
Email: nikidoc@abv.bg

ABSTRACT
Crohn’s disease is known for its various complications and affection of systems other than the GI-tract, which altogether can seriously impair organ function or even lead to life-threatening conditions, especially in children. There are a variety of indices, created for evaluation of disease activity and severity, such as VCCD, CDEIS and CDAI. The case report is showing the practical use of such evaluation and the consequences drawn as well as the practical approach of interdisciplinary cooperation, stating diagnostics, drug therapy (following therapy protocols as well as the use of anti-TNF-α antibodies), monitoring nutritional status and providing both enteral and parenteral nutrition therapy, intensive care monitoring, surgery, as well as pre- and postoperative care. As shown in the case of a 13-year-old severely affected boy with a long history of the disease, manifesting a great lot of all possible complications, this approach results in reversal of the course of the disease or even decides its outcome.

Keywords: interdisciplinary approach, VCCD, CDEIS, CDAI, PEG, anti-TNF-α antibodies, long-term parenteral nutrition catheter

Introduction
Crohn’s disease is a chronic inflammatory disease of the GI-tract and can involve any part of it, from the mouth to the anus. Incidence varies from 1:1200 in Europe to 1:300 in the United States (12, 13, 14, 16). It typically affects the terminal ileum and demarcated areas of the large bowel. Crohn’s disease is often associated with autoimmune disorders outside the digestive tract, such as rheumatoid arthritis (17). It is also accompanied by other extraintestinal manifestations such as osteoporosis, joint involvement, ophtalmologic and biliary tract diseases (23).

It is characterized by chronic diarrhea and disrupted digestion (9). The inflammation can be extremely painful. Other common complications include fistulae and fissurae of the colon, ulcerations, fibrosis and strictures, lipid absorption problems and anemia (24). Children with Crohn’s disease often suffer delayed development as a consequence of malnutrition (11). Further, side-effects of all drugs, used in the course of therapy, must be considered (1, 3, 4, 5, 6, 7, 8, 10, 18, 19, 21, 22).

Such a variety of symptoms and possible complications imply the necessity of an interdisciplinary approach, where gastroenterology meets intensive care and surgery to provide the best possible quality of life for the patient. This we want to demonstrate by the following case report (15).

Case report
A 13-year-old boy with the diagnosis of Crohn’s disease in a progressive state over the last 9.5 years. Upon admission the patient was in a state of malnutrition (marasmus) with a body weight of 22 kg. Further clinical findings included sepsis, a previously created transversostomy with multiple fistula paths as well as anorectal fistulae and a chest wall deformity due to a compulsory right recumbent posture.

We used the following criteria to evaluate the disease activity and severity:
1. Vienna Classification of Crohn’s Disease /VCCD/, 1998
   • Age at diagnosis < 40 – A1
   • Location – rectum, sigmoid colon, descendent colon, transverse colon, ascendent colon, i.e. 5 anatomical regions – L2
   • Intraabdominal fistulæ /in the region of the transverse colon/, abscesses, perianal fistulæ, perirectal fistulæ and rectal ulceration – B1
2. Crohn’s Disease Endoscopic Index of Severity /CDEIS/ - lesions of the rectum, sigmoid colon, descendent colon, transverse colon, ascendent colon - scoring 37 from a maximum of 44 points declared. Accomplished gastroscopy. Terminal ileum sighted by passing through the transversostomy up to the Bauhini’s valve and further. Standard colonoscopy was performed through the rectum up to the site of the stoma.
3. Crohn’s Disease Activity Index /CDAI/ > 450 points. In the course of the examination multiple polyposis was found in the following anatomical regions – sigmoid colon, left colon and ½ transverse colon.
4. Present intestinal/extraintestinal manifestations

- intestinal – diarrhea, weight loss, abdominal pain, perianal disease /abscesses, fistulæ, fissuræ/.
- extraintestinal – joint involvement /peripheral arthritis, sacroilitis, ankylosing spondylitis/, osteoporosis, gallstones, iritis and uveitis.

5. Paraclinics. The paraclinics constantly monitored included ESR, differential count, C-reactive protein, iron- and B12-deficiency, folic acid deficiency, α1-acid glycoprotein, α2-globulin, hypoproteinaemia and low albumin caused by protein-losing enteropathy. In the course of preoperative intensive care following parameters, related to the metabolic stability of the patient were monitored closely /by protocol/- glucose, lactate, K+, PO 4, Na+, Cl-, triglycerides, creatinine, urea, coagulation status, haemogram, urine, liver enzymes, NH3, bilirubine, cholinesterase, lipase, amyrase, total protein, high transferrine, prealbumin, microelements, vitamins and capacity utilization. Immunohistologically the mucous changes during the acute phase were characterized by infiltration of granulocyte and mononuclear cells with regions of epithelial cell necrosis. These areas were alternated by fibrosis and intestinal strictures. The mucous infiltration was confirmed by predominating CD4+ Th1 (helper type 1) lymphocytes, which determine the production of interferon-γ and interleukin-2 (IL-2). A decrease in Bax expression was noted with a high Bclx/Bax correlation in the isolated mucosal T-cells /in the context of the particularly crucial position they occupy in the process of balance between death and survival signals and hence in the regulation of immune homeostasis/. Monitoring of the GIT through coproculture. A symptomatic therapy of metabolic disorders and diarrhea was pursued. In the ICU control over the patient’s metabolic state was primarily based on the principle of indirect calorimetry [S5 „manufactured by Datex-ohmeda Inc.”]. The therapeutic aspect involved the following techniques and drugs – tunneling technique for venous catherization of V. subclavia dexter for long-term parenteral nutrition therapy [double-lumen Hickmann catheter „manufactured by C.I. Bard Inc.“, size 7F/], primary use of Kabiven [manufactured by Fresenius Kabi Inc.] emulsion for intravenous nutrition in a three-chamber-bag containing 1026 ml and additionally alanil-glutamine dipeptide supplement [Dipeptiven 20% 100 ml „manufactured by Fresenius Kabi Inc.”], microelements Tractitol 10 ml [confirmed low levels for Se, Mg and Zn „manufactured by Braun Melsungen AG"], venous polyvitamines Cervid [manufactured by Baxter Inc.], PEG-G18 [manufactured by Fresenius Kabi Inc.], using mainly Survimed OPD [manufactured by Fresenius Kabi Inc.] for enteral nutrition. We achieved a reduction in defecation (not more than 2 times daily) and thickening of fecal masses. The child’s oral diet was preserved as developed by the hospital’s diet assistant.

6. Stages of preoperative gastroenterological behaviour /by protocol/. The patient had gone through different phases of clinical manifestation of the disease - from mild to severe - before reaching our clinic. The choice of drugs is determined by the localization of lesions. Initially a mild form of the disease required treatment with 5-aminosalicylates - sulfasalazin [Azulfidine “manufactured by Kabi Pharmacia Inc. “] or olsalazin [Dipentum “manufactured by Kabi Pharmacia Inc.”] combined with metronidazol [Flagyl „manufactured by Rhône-Poulenc Rorer Inc.”] antibacterial therapy /literature research shows less than 25% success rates for this antibiotic treatment/, which was later replaced by quinolones [Ciprobay “manufactured by Bayer AG”].

Because of the frequent relapses in the course of the disease and its transition to a more serious condition, a corticosteroid [Prednisolon “manufactured by Pharmacia Co Inc.” “] had been added. Optimal therapeutical drug-levels had been achieved, but the patient grew corticoid-dependent as relapses became more frequent and remission phases even shorter. Therapy side-effects /such as osteoporosis/ added as a result from long-term corticoid treatment /more than 7 years/ and the child entered a late phase of the disease, marking high activity and severity. Azathioprine/6-mercaptopurine [Imuran „manufactured by Borroughs Wellcome Inc. “] were added according to the therapy protocol. Surgical treatment and optimized pre-operative preparation by the intensive-care team were discussed, since conservative therapeutical approaches were exhausted and complications were present, which were likely to develop into a life-threatening condition. Preoperative preparation included the use of anti-TNF-α antibodies infliximab [Remicade „manufactured by Schering-Plough Inc.”], administered at a dose of 5mg/kg as an intravenous infusion over a time-interval of 2 hours. As positive response to treatment was observed /local status at the site of the perianal fistulae had improved tremendously/, infusion of another 5mg/kg dose during the 2nd week was justified. The patient underwent immunologic monitoring during and before the course of treatment – chiefly regarding cell-mediated immunity and antibacterial protection /high risk of developing infection, opportunistic or other/, since TNF-α mediates the inflammatory process and modulates the cell-mediated immune response. An active or latent form of
tuberculosis was excluded. Treatment considered the unwanted effects caused by the drug, as described in clinical studies.

During week 6 after admission to the clinic surgical treatment was discussed, involving colectomy with definite ileostomy, closure of the transversostomy and cholecystectomy, since according to the patient’s condition, a maximum stabilization of vital functions and a reasonable operative and postoperative risk were established.

7. Indications for surgical treatment (2, 20)
   A. Exhausted effect of conservative treatment
   B. Recurrent periods of intestinal obstruction
   C. Inadequate growth and physical development – the patient had been in a compulsory recumbent position for the last 3 years
   D. Complications imposed by bowel impairment – melena, large-bowel obstruction, bowel perforation
   E. Complications imposed by the pararectal inflammatory process /pararectal abscesses and fistulae/
   F. The presence of multiple intestinal polyposis was an additional finding, complicating the patient’s condition and even more so the local status

8. As specified preoperatively, surgical treatment was carried out under the conditions of multicomponent endotracheal anesthesia (2.5 h) and an installed peridural catheter, which was effectively used for postoperative dressing during the following month. Secondary wound healing of the anorectal canal occurred. Intraoperatively an ileoscopy was performed through the ileostomy, confirming preoperative judgment that no small-bowel segment of the GI-tract is affected by the disease (Fig. 1).

Results and Discussion
Hospital treatment continued for a year with surgical dressing changes in the sacroglateal region twice a week under venous propofol [Diprivan „manufactured by Braun Melsungen AG”] anesthesia and two more surgical interventions in the same area under spinal analgesia (Figs. 2, 3), which led to complete closure of all postoperative tissue defects.
using a walking assist device and able to sit in the wheelchair in an upright position. Repeated gastroscopy and ileoscopy did not show disease activity in the observed areas of the GI-tract. Psychological tests after discharge from the hospital testified a normal psychoemotional status and intellectual development. At the moment the boy is successfully attaining high school education.

This comes to show that providing a smooth and resolute interdisciplinary cooperation can reverse the course of the disease to a very great extent and improve much of life’s quality for the affected patient.

REFERENCES