

Case report

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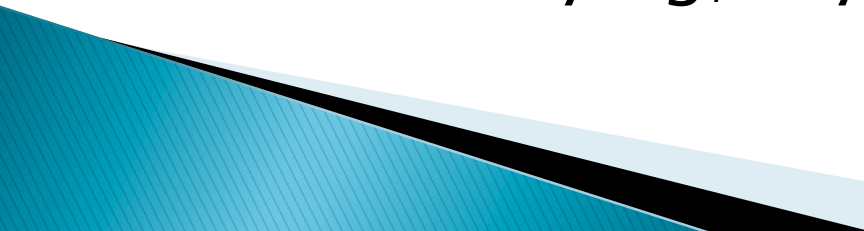
Fundeni Clinical Institute, Bucharest



Clinical History

- ▶ 27 years old women
- ▶ Smoker 8–10 cigarettes / day
- ▶ Appendectomy in 1983
- ▶ In 2000 surgery for perianal fistula and abscess

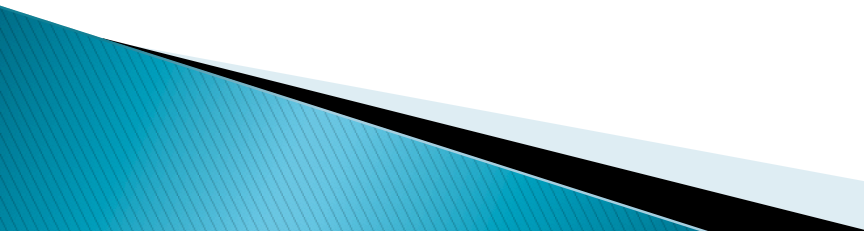
First flare

- ▶ June 2001 4–5 stools / day with blood and pus, diurnal and nocturnal, diffuse abdominal pain and weight loss (4 kg in the last two months)
 - ▶ Colonoscopy: ulcerative lesions over a wide area, with a discontinued pattern, suggestive for ileo-colonic Crohn disease
 - ▶ Treatment approach – Salofalk 4 g / day followed by 3g/day–maintaining dose
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Clinical History

- ▶ Feb. 2007 – new flare– diarrhea (10–12 stools / day) with mucus and blood; weight loss 3 kg in one month, diffuse abdominal pain
- ▶ Laboratory findings: Hb = 11.3 g / dl, Ht = 34.8%, WBC = 9200/mm³, PLT = 343000/mm³, ESR 50 mm / h

Therapy

- ▶ Solu-Medrol 60 mg/day stopped after few days because the patient didn't tolerate the steroids reporting nausea and severe abdominal pain soon after administration
 - ▶ Methotrexate (25 mg im.) and Salofalk 4 gr/day-induction therapy
 - ▶ On discharge : 4-5 stools/day, no pus or blood in the stool and no abdominal pain
 - ▶ Maintenance treatment with Salofalk 3 g/day and Methotrexate 15 mg im/wk
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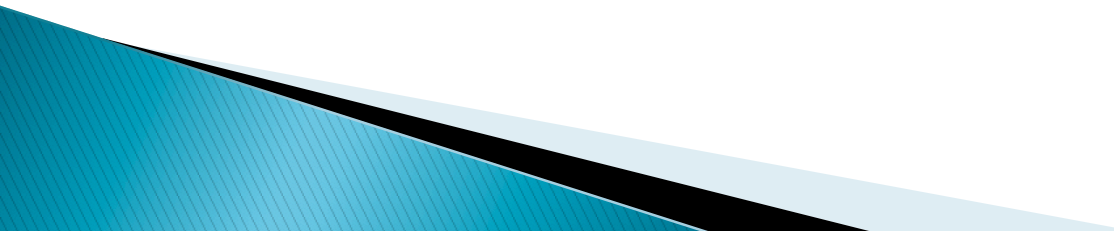
Methotrexate in CD

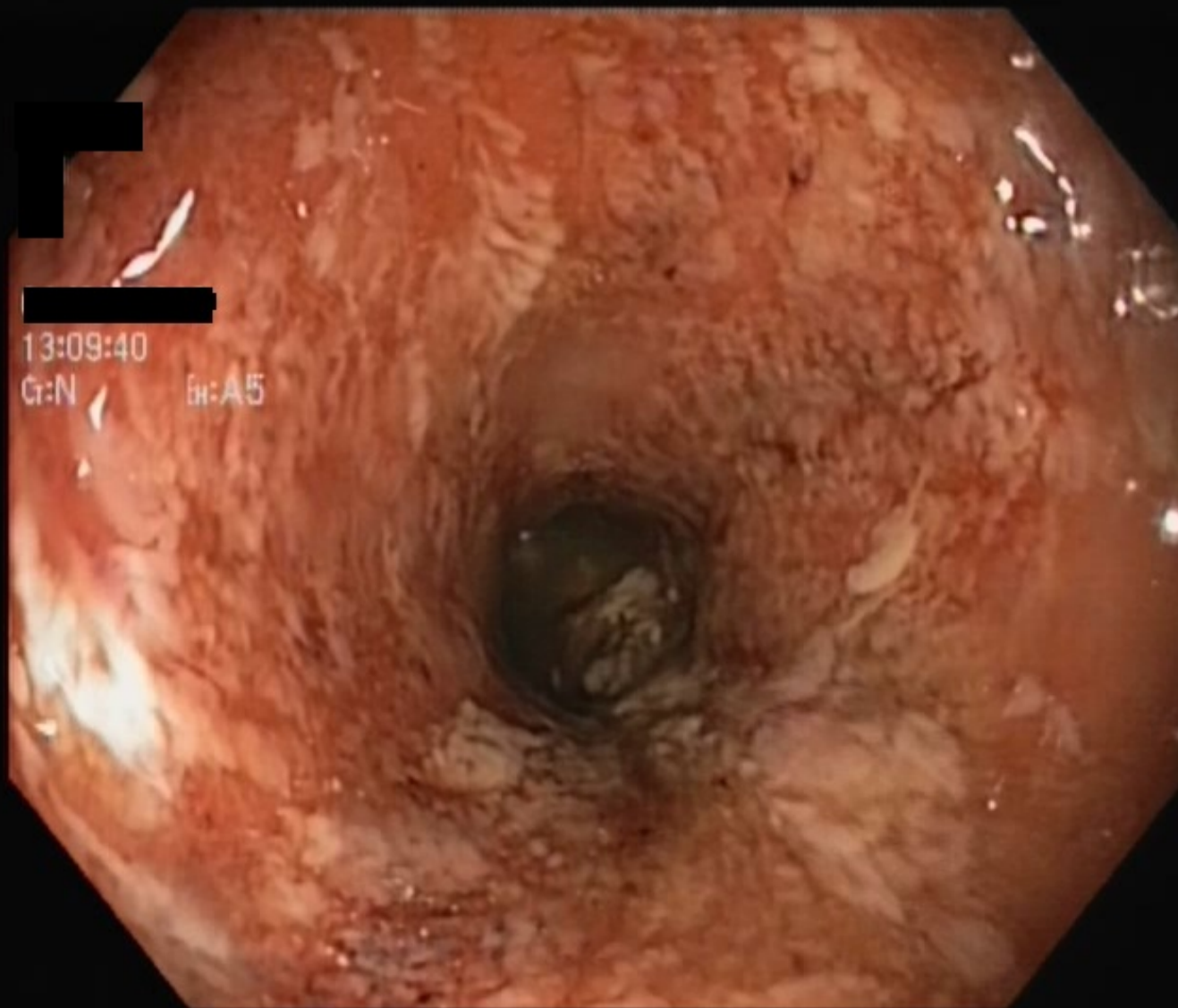
- Evidence. Two placebo-controlled trials evaluating the effectiveness of methotrexate for maintenance of medically induced remission have been published. The earlier study included only 28 patients and compared oral methotrexate 15 mg/week to placebo over 1 year. Relapse rates were 43% and 80% respectively, but because of frequent adverse events, only 31% were in remission taking methotrexate at the end of the study. A larger study included 76 patients who had achieved remission on intramuscular methotrexate (25 mg/week). Patients were randomly allocated to continue intramuscular methotrexate (15 mg/week) or placebo. After 40 weeks, remission rates were 65% and 39% ($p=0.04$) respectively. Among the 36 patients who had a relapse, 22 were then treated with open-label methotrexate 25 mg/week and 55% achieved remission. *There are no controlled studies over longer periods, but results of several open studies suggest a certain loss of efficacy of methotrexate treatment with time.*
- Summary. These data indicate that intramuscular methotrexate (15 mg/week) is effective for maintenance of remission in Crohn's disease, at least in patients of whom remission has been achieved with this agent.

Clinical History

- 11.06. 2008 severe flare
- Clinical findings: malaise, fever, >10 bloody stools/day, abdominal pain partially improved after bowel movement
- Laboratory findings: WBC 12600, NE 10000, Hb 10.2 g/dl, Ht 30 %, MCV 81 PLT 333000, Fibrinogen 678, INR 1.42, TB 0.54, TP 6.3, Cho 101, ALP 101, ALT- 27, AST 12, GGT 40

Clinical History

- ▶ Colonoscopy: longitudinal ulcers, cobblestone appearance, friable mucosa and inflammatory stenosis 6 cm above the mucocutaneous line
 - ▶ Biological therapy with Infliximab was initiated (induction doses: 5 mg / kg at S0, S2, S6)
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After induction

- Good general condition, painless abdomen, normal intestinal transit
- Biological: Hgb = 12.9 g / dl, HCT = 38.9%, L = 5100, Tr = 260000. INR = 1.08, PT = 89%, fibrinogen = 314mg/dl. Bilt = 0.45 mg / dl, TGL = 40mg/dl, Chol = 164mg/dl, ALP = 67u / l, AST = 7u / l, ALT = 29u / l, Glu = 88mg/dl, 13mg/dl urea =, GGT = 21 U / l, Cr = 0.7 mg / dl, PCR 0.43mg / l
- 6 months follow-up colonoscopy: pseudopolyps, terminal ileum without lesions

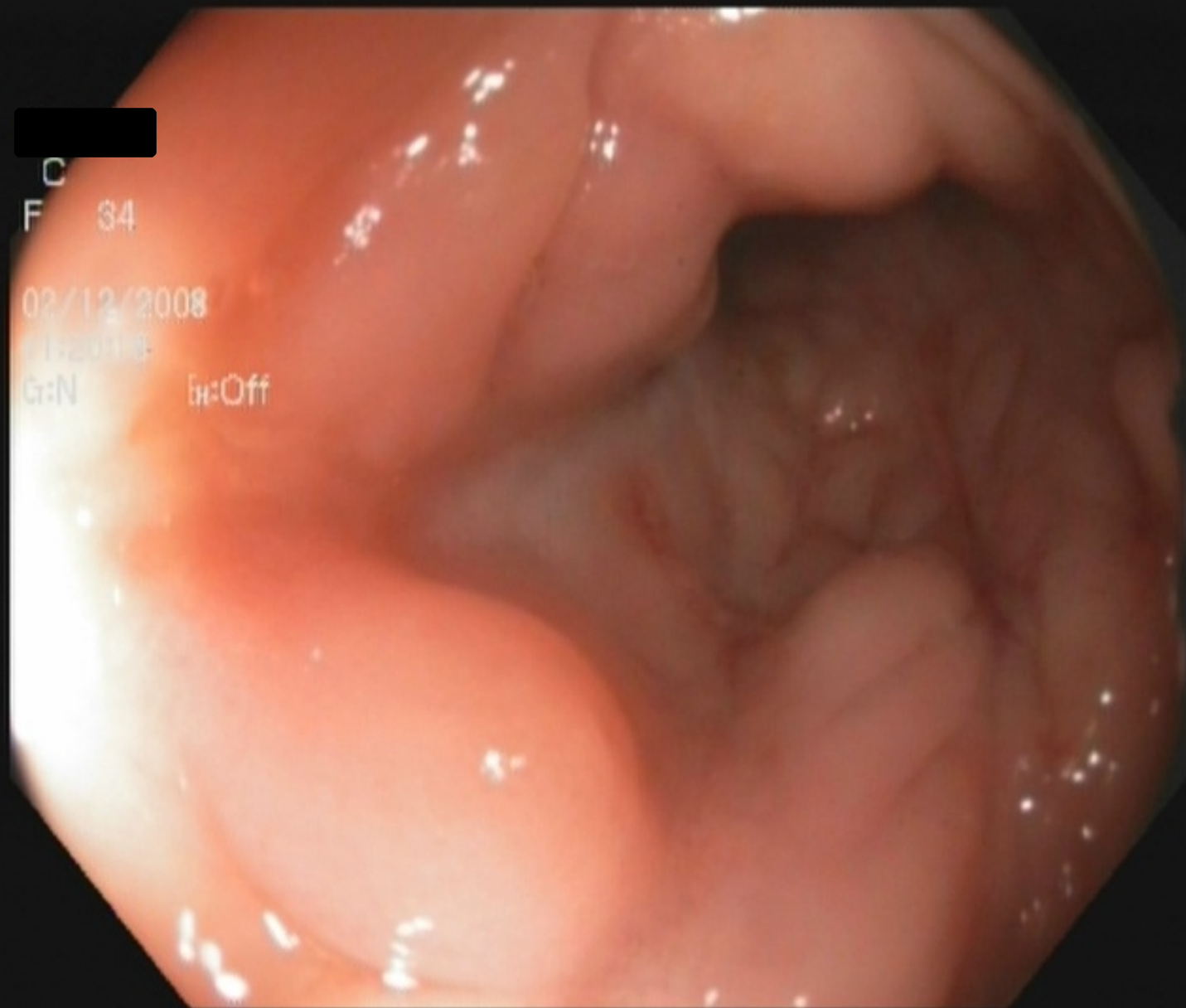
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- ▶ In 2010 the patient got pregnant
 - ▶ The disease was in clinical and endoscopy remission

Management at this point?

1. Careful monitoring because the pregnancy does' t worsen the disease in most patients who achieved remission
2. Recommend abortion because the pregnancy worsens the underlying disease
3. The risk of relapse is in 2/3 of cases
4. Abortion because of the high risk of congenital malformation

Influence of disease activity on the course and outcome of pregnancy

ECCO Statement 11B

It is advisable to strive for clinical remission before conception. Flares are best treated aggressively to prevent complications. Crohn's disease is a risk for preterm delivery and low birth weight. Insufficient data exist about maternal morbidity and fetal mortality at surgery.

The influence of pregnancy on the course of CD

- ECCO Statement 11C

1. If conception occurs at a time of quiescent disease *the risk of relapse is the same as in non-pregnant women*. If conception occurs at a time of active disease, two thirds have persistent activity and of these two thirds deteriorate. Both clinical activity and surgical interventions decline with pregnancy and parity. Nutritional status also influences parity
2. *Mothers with CD seem also to have a lower relapse rate in the years after pregnancy, compared with the years before pregnancy* but specific confounders such as smoking have not been investigated or ruled out in multivariate analyses. Pregnancy has an effect on the immune system, which may contribute to these findings.

The influence of pregnancy on the course of CD

- ▶ Spontaneous abortion is not increased in patients with CD compared to the normal background population
- ▶ Fetal mortality is very high if surgery is required, where abortion–stillbirth rates are as high as 18%–40%. Careful obstetric and medical follow up during pregnancy is indicated, especially in the third trimester

Therapy during the pregnancy?

1. No medical treatment due to the high risk of congenital malformations
2. Immunosuppressive therapy only when we deal with relapse
3. Continuation of the treatment during pregnancy
4. Discontinuation of the therapy in the first trimester because of the high risk of congenital malformations

Medical treatment during pregnancy

- *It seems that the greatest risk to mother and fetus during pregnancy is **active disease**, and not the medication used to treat it.*

ECCO Statement 11G

Medical treatment for Crohn's disease (except methotrexate) should generally continue during pregnancy, because the benefits outweigh the risk of medication.

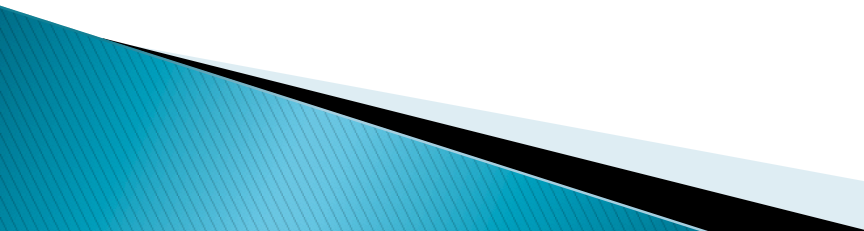
Special attention should be given to folic acid, vitamin B12 and iron deficiency and these should be corrected in women with CD wanting to conceive, since the need for these vitamins and micronutrients increases early in pregnancy

Anti-TNF therapy in pregnancy

Infliximab.

- Placental transfer of IFX occurs during in pregnancy, although it is not yet known whether this induces antibody formation in the baby. Two papers have reported the use of intentional infliximab in 92 pregnancies. No significant increase in the incidence of still births, ectopic pregnancies, spontaneous abortions and low birth weight was found. In 2 pregnancies a congenital abnormality occurred, although this may relate to the underlying increased risk for women with IBD

Anti-TNF therapy in pregnancy

- The implications of exposure to anti-TNF therapy on the newborn are unknown.
 - Patients and physicians should be aware of in utero exposure and treatment may best be avoided in the last trimester of pregnancy in order to prevent circulating anti-TNF antibodies in the neonate, because IgG1 antibodies cross the placenta barrier in late second and third trimesters.
 - Patients and partners need to be fully informed about potential risks
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Natural birth vs cesarean

Mode of delivery

ECCO Statement 11E

- The mode of delivery should primarily be governed by obstetric necessity and indication, but also in conjunction with the gastroenterologist and/or the colorectal surgeon. Patients with uncomplicated Crohn's disease without perianal disease or rectal involvement can deliver vaginally after obstetric evaluation has been performed.
- Caesarean section should be preferred in perianal disease or rectal involvement. An ileoanal pouch is regarded as an indication for caesarean section. Colostomy or ileostomy patients can deliver vaginally.

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- ▶ Cesarean at 32 week → healthy baby of 3200g

Can we recommend
breastfeeding during the
treatment?

Medical treatment when breast feeding

- Metabolites are undetectable in the few neonates studied, so it is acceptable to advise breast feeding while continuing AZA/MP.
- *IFX cannot be detected in breast milk, so can be considered acceptable. As with all drugs, the advice has to be tailored to the individual and carefully discussed*

Today..

- ▶ The patient is in clinical and endoscopy remission
- ▶ Current treatment Remicade 5 mg / kg at 8 weeks