https://doi.org/10.31689/rmm.2024.31.1.79

CASE REPORTS

Not Your Typical Ulcerative Colitis Patient

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Abstract

Background: Extraintestinal manifestations (EIMs) of inflammatory bowel diseases (IBDs) are a common and debilitating feature of disease, occurring in up to 40% of patients with IBD. Despite the huge therapeutic progress of the last decade, one must not forget about the side effects that currently available medications might have and the challenges to both patient and physician.

Case presentation: We present the case of a 33-year-old woman, that initially was admitted for diffuse abdominal pain, nausea and bloating. After careful investigation she was diagnosed with a drug induced acute pancreatitis, caused by sulfamethoxazole/trimethoprim taken for UTI. Further investigations established a diagnosis of ulcerative colitis. Initial treatment with mesalamine resulted in another acute pancreatitis event that required hospitalization. An anti-TNF therapy with infliximab was started with initial clinical remission but then she developed another adverse reaction, this time paradoxical psoriasis, while having an IBD flare. So, this begged the question, how do we treat a patient that had an adverse reaction to every prior treatment?

Conclusion: Developing newer and newer therapies will bring also different possible adverse events that should be carefully diagnosed and managed.

Keywords: Inflammatory bowel disease, ulcerative colitis, pancreatitis, psoriasis, paradoxical, mesalamine

Rezumat

Introducere: Manifestările extra intestinale ale bolilor inflamatorii intestinale (BII) reprezintă o caracteristică comună și debilitantă ale acestei patologii, ce poate apare la până la 40% dintre pacienți. Acestea nu sunt singurele probleme cu care se confruntă pacienții cu această BII, având în vedere și numeroasele efecte adverse pe care le pot avea tratamentele disponibile.

Prezentare caz: Va prezentam cazul unei paciente în vârsta de 33 de ani, care a fost inițial internată în clinica noastră pentru dureri abdominale difuze, greață, meteorism abdominal. În urma investigațiilor amănunțite, am diagnosticat pacienta cu pancreatită acută medicamentoasă, cauzată de tratamentul cu sulfametoxazol/trimethoprim, administrat pentru o infecție de tract urinar. Investigațiile ulterioare au depistat și o boală inflamatorie intestinală, colita ulcerativă. Tratamentul inițial cu mesalazină a declanșat un nou episod de pancreatită acută, ce a necesitat spitalizarea. Ulterior a fost începută terapia cu anti-TNF – infliximab, cu răspuns inițial favorabil și remisiune clinică, însă și în urma acestui tratament pacienta a prezentat o reacție adversă, de această dată psoriazis paradoxal, însoțit cu un puseu de acutizare a bolii inflamatorii intestinale.

Astfel, cazul acesta, a ridicat întrebarea "Cum tratăm un pacient care a prezentat o reacție adversă la fiecare medicament încercat?"

Concluzie: Dezvoltarea de noi terapii aduce nu numai soluții, ci și diverse posibile efecte adverse cu care ne putem confrunta, inclusiv afecțiuni imun-induse.

Cuvinte cheie: Boli inflamatorii intestinale, colita ulcerativa,pancreatita, psoriazis, mesalazina

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INTRODUCTION

Inflammatory bowel disease (IBD) are idiopathic, chronic and recurrent inflammatory diseases affecting the GI tract. The course of IBD, both ulcerative colitis (UC) and Crohn`s disease (CD) is characterized by periods of relapse and remission with the possible occurrence of extraintestinal manifestations and sometimes iatrogenic complications as well.

Acute pancreatitis may be a problem encountered in IBD patients with various etiologies such as drugs, gallstones, duodenal inflammation, endoscopic procedures, autoimmune, primary sclerosing cholangitis or it may be idiopathic.[1]

Other complications that may occur in the evolution of IBD are caused by the medical or surgical therapies.

Anti-TNF agents are effective for induction and maintenance of remission of this pathology, however, usage of this type of therapy may come with adverse events such as infection, post-operative complications of wound healing, malignancy and immune-mediated manifestations. As a paradox, psoriasis may be one of the immune-mediated diseases that can appear, although anti-TNF agents are being used as therapy for psoriasis. The cause of this paradoxical reaction has not been clearly identified yet.[2,3]

CASE PRESENTATION

A 33-year-old female, smoker, with no prior medical history, presented to our department with severe upper-quadrant abdominal pain, that radiated to the back, diarrhea, and bloating. The symptoms started a few days earlier after she received antibiotics (sulfamethoxazole/trimethoprim) from her family doctor for a urinary tract infection.

The clinical examination showed an overweight patient, with abdominal pain in the epigastric region, no palpable masses, no ascites and no other pathological findings.

The blood tests showed increased levels of leukocytes (WBC 12,2 - 10*3/UL), inflammatory syndrome with increased C reactive protein (12XN) and erythrocyte sedimentation rate (ERS) (3xN) levels, thrombocytosis, high lipase (8XN), high gamma-glutamyl transferase (GGT 90U/L), slightly high triglycerides (180mg/dL), high LDL-cholesterol (140mg/dL), normal calcium levels (Ca 4,8mg/dL), glycated hemoglobin above the normal level (HbA1C – 6.2%), negative tests for hepatitis B, C. The *Clostridioides difficile* test was negative.

Acute pancreatitis diagnosis was diagnosed based on clinical and biological criteria and imaging tests were also performed.

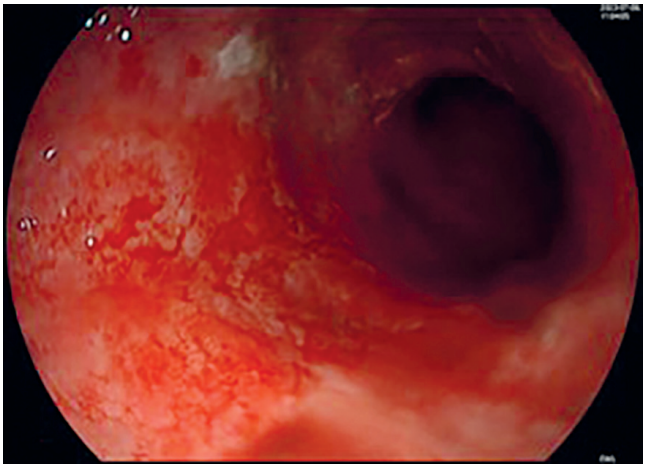
The abdominal ultrasound showed hepatic steatosis -S3 and minimal biliary sludge. The pancreas was not visible due to increased abdominal gas.

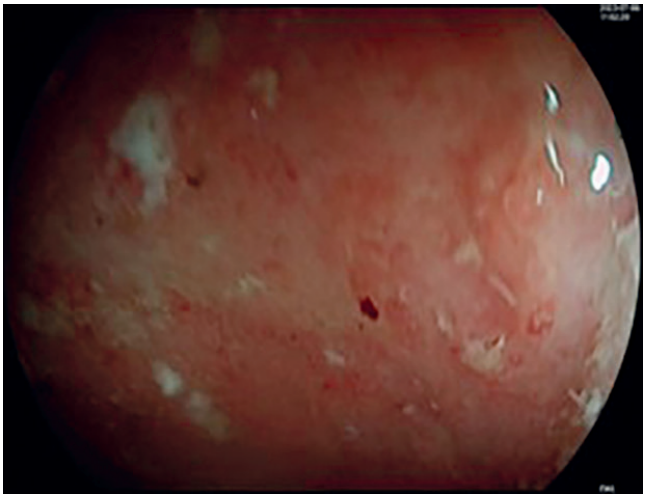
A CT scan showed pancreatic and peripancreatic fat inflammation, with no dilatation of the main pancreatic duct nor its branches, normal gallbladder, and no obstructions of the bile ducts, with grade C Balthazar score and low degree CT severity index (CTSI). An MRI-cholangiography was performed in order to search for eventual malformations or lithiasis. To complete the etiological quest a serum IgG4 level was performed but the tests came back negative.

A diagnosis of drug induced pancreatitis was made, the sulfamethoxazole/trimethoprim being one of the most common medications involved[4,5].

Two years later, the patient was admitted for chronic diarrhea (more than 7 stools per day with blood and mucus) and abdominal pain. Blood tests showed inflammatory syndrome (C reactive protein 3XN, thrombocytosis), low iron levels, normal lipase, high fecal calprotectin – 5980 micrograms per milligram. We performed an ileo-colonoscopy, which showed continuous inflammation of the left colon and rectal mucosa with edema, erythema, granular appearance, ulcerations and a loss of vascular pattern, highly suggestive of ulcerative colitis with an endoscopic Mayo 2 severity score. Multiple biopsies and the histopathological results confirmed the diagnosis of ulcerative colitis.

Systemic and topical enemas with mesalamine treatment was initiated.





After a few days of 5-ASA treatment, the patient presented intense upper-middle abdominal pain, nausea and vomiting. Blood tests showed a lipase level of 6XN, inflammatory syndrome (CRP 8XN) and the CT scan showed pancreatic inflammation (Balthazar grade 2). The patient was diagnosed with another episode of acute pancreatitis due to medication, most probably related to 5-ASA. We treated her IBD flare with corticosteroid therapy and after resolution of the pancreatitis an anti-TNF therapy with infliximab was initiated.

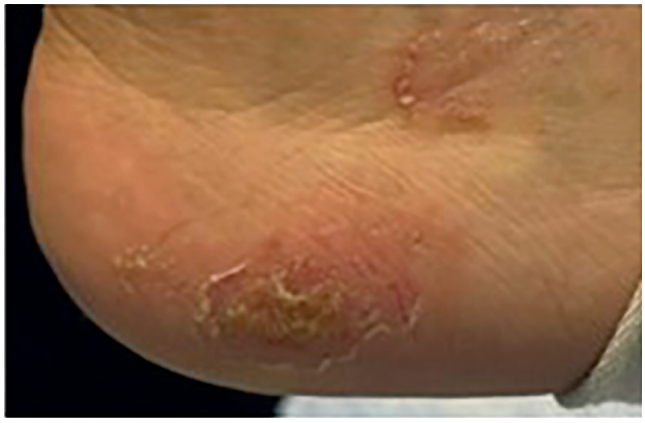
Post-induction evaluation showed clinical remission, no inflammation on blood tests and fecal calprotectin levels of 60 micrograms per milligram and she continued the therapy with 5mg/kg every 8 weeks.

Six months after the initiation of anti-TNF therapy, the patient had had another flare of her UC with 5 stools per day. Colonoscopy revealed a left side colitis, Mayo 2 score.

The infliximab serum levels were low at 1,95 micrograms per milliliter and anti- infliximab antibodies were negative. The patient also had few erythematous plaques highly suggestive for psoriasis and she was referred to a dermatologist, that confirmed our suspicion of infliximab-induced psoriasis. Topical treatment was prescribed.

Due to her low serum levels of infliximab, and also taking into consideration the psoriasis remission, we decided to optimize treatment by switching to subcutaneous administration of a weekly dose of 120mg. We based our option on studies that show effectiveness in switching from iv to subcutaneous administration of infliximab in patients who experience iv infliximab failure.[6]

Currently the patient is in emission without any skin manifestations.



DISCUSSION

Pancreatic disorders are not uncommon in IBD patients. Although inflammatory bowel diseases affect mainly the digestive tract, other systemic manifestations can occur. An increased number of either acute or chronic pancreatitis has been recorded in IBD patients compared to the general population.[7] In our patient the two episodes of pancreatitis were probably drug induced appearing after few administrations of medications known to cause pancreatitis. The 5-aminosalicylic acid formulations are a commonly used in induction and maintenance care in mild-to-moderate ulcerative colitis with an acceptable safety profile. Pancreatitis has a significantly low prevalence in 5-ASA therapy but is cited (0,3-1,8%) (8)(9). A diagnose of 5-ASA induced pancreatitis has important implications in ulcerative colitis treatment, demanding escalation to immuno-

modulators or biologic therapies. Since azathioprine is a well-known cause of pancreatitis, biologic therapy with infliximab was initiated.

Although the therapy was initially effective after six months the patient presented a flare requiring optimization of therapy concomitant with a paradoxical reaction to the drug. Although anti-TNF agents are approved for treatment of psoriasis in some patients a paradoxical reaction can occur. Most commonly the paradoxical psoriasis is a palmoplantar psoriasis phenotype (33,3%- 45%) and infliximab and certolizumab are the most reported anti-TNF agent to elicit this type of reaction[10,11].

The infliximab induced psoriasis was even more challenging since currently there is no standard approach for the management of TNF-inhibitor induced psoriasis: steroid administration, switch to another anti TNF or swap to anti IL17 blocker ustekinumab which is effective in both conditions[10]. However, there are some reports of resuming the same anti TNF without the reoccurrence of the psoriatic reaction. We decided to switch to subcutaneous form of infliximab which has a better profile in terms of effectiveness and side effects and was recently shown to be an affective choice after failure of intravenous infliximab[12].

CONCLUSION

The 5-ASA induced pancreatitis in UC patients is a rather rare adverse reaction, that needs to be carefully diagnosed, excluding the more frequent etiologies, especially because this type of reaction will most likely change the course of treatment.

Anti-TNF induced psoriasis is another rare adverse event that can occur in the evolution of an IBD patient, and needs a proper diagnostic, proper treatment and close monitoring. A treatment switch to another anti TNF or a swap to ustekinumab is necessary in these cases.

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