

Case Report

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Insidious and lethal course of duodenal perforation in crohn's disease with retroperitoneal abscess formation and right kidney necrosis**Igor Kremenevski^{1*}; Manuel Bornhof²; Markus Baehrlé²; Martin Raithe¹**¹Department of Gastroenterology, Interventional Endoscopy, Hemato-Oncology, Diabetes and Metabolic Diseases, Malteser Waldkrankenhaus St. Marien, Rathsberger Str. 57, 91054 Erlangen, Germany.²Department of General, Visceral and Thoracic Surgery, Malteser Waldkrankenhaus St. Marien, Rathsberger Str. 57, 91054 Erlangen, Germany.³Institute for Imaging Diagnostics and Therapy, Rathsberger Str. 57, 91054 Erlangen, Germany.***Corresponding Author: Igor Kremenevski**

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Abstract

A 60-year-old woman with a long history of Crohn's disease and rheumatoid arthritis was admitted to the emergency department due to progressive severe cramping with abdominal pain (right upper quadrant), subfebrile temperature, and obstipation since 3 weeks. She had been treated by her rheumatologist for rheumatoid arthritis with certolizumab pegol, prednisolone and leflunomide for at least six months before onset of the current symptoms. The physical examination revealed normal bowel sounds and tenderness in the right upper quadrant without rebound. Laboratory studies showed a normal leukocyte count, but the level of C-reactive protein was elevated. She frequently complained about pain in the right flank. Contrast-enhanced computer tomography of the abdomen performed 48 hours after admission showed circular thickening of the pars descendens of the duodenal wall compatible with an acute inflammatory manifestation of Crohn's disease with suspected spontaneous retroduodenal perforation of the colon and formation of a retroperitoneal, perinephric abscess with a large air and fluid collection around the right kidney. The patient underwent a radical nephrectomy with abscess drainage and closure of the duodenal perforation with serosal sutures. The postoperative course was complicated by sepsis, which ultimately led to multiple organ failure and death despite exhaustive intensive care management.

Keywords: Spontaneous duodenal perforation; Retroperitoneal abscess; Kidney necrosis; Immunosuppression.

Abbreviations: CD: Crohn's Disease; RA: Rheumatoid Arthritis; CT: Computer Tomography; MRI: Magnetic Resonance Imaging.

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Introduction

Retroperitoneal bowel perforation leads to a variety of complications and may be associated with mortality of up to 50% [1,2]. Among retroperitoneal perforations iatrogenic perforations after interventional endoscopy or surgery should be differentiated from perforations resulting from obvious manifest disease (e.g. ulcer disease, pancreatitis etc.), a disease condition predisposing to affect the retroperitoneum (e.g. Crohn's Disease, gallstone, etc.) or from yet unknown disease, which is often documented as spontaneous retroperitoneal perforation [3,4].

Under immunosuppression, the occurrence of spontaneous retroperitoneal perforation may be masked or atypical. Retroperitoneal abscesses following bowel perforation often constitute life-threatening conditions with insidious clinical presentations because apart of Computer Tomography (CT) and Magnetic Resonance Imaging (MRI) no reliable diagnostics instruments are readily available [5,6]. Abdominal ultrasonography is usually early performed in patients with various gastrointestinal symptoms or inflammatory markers, but diagnostic sensitivity is often very low for identification of early or ongoing retroperitoneal or retroduodenal perforation [7]. Thus, retroperitoneal perforation is up to now one of the most difficult clinical conditions to diagnose and treat.

In this context a retroperitoneal abscess developing in immunosuppressed patients or with underlying Crohn's disease poses a particular dilemma for the physician. To the best of our knowledge, we present for the first time a case of spontaneous retroperitoneal abscess formation with occurrence of total necrosis of the right kidney in a patient with Crohn's Disease (CD) and Rheumatoid Arthritis (RA) under combined triple immunosuppression.

Case presentation

A 60-year-old woman (BMI 22.4 kg/m²) with a long history of CD and RA was admitted to our emergency department due to progressive severe, painful abdominal cramping in the right and middle upper quadrant, sub febrile temperature and obstipation since 3 weeks. She reported to know similar symptoms from former exacerbation of CD and her general practitioner recently increased prednisolone dose for this clinical deterioration from 50 mg per day to 100 mg per day.

The patient denied bloody stool, nausea or vomiting. At admission, she had been treated by her rheumatologist for RA with certolizumab pegol, varying doses of prednisolone and leflunomide for at least six months before onset of the current symptoms. There were no further co-morbidities present. The physical examination revealed a reduced general condition and normal nutritional status, normal bowel sounds and tenderness without rebound of the right upper and middle abdomen as well as percussion pain of the right flank. Laboratory studies showed low Hemoglobin at 7 g/dL (reference range 12.5 - 15.0 g/dL), a normal leukocyte count, but elevated C-reactive protein at 12.64 mg/dL (reference range <0.50 g/dL). An abdominal ultrasound scan only showed altered ileum loops secondary to inflammation, while the other abdominal organs and kidney were reported as inconspicuous. The Crohn's disease activity index constituted 429 points. Accordingly, the patient was admit-

ted to our department for further diagnosis and treatment of a possible acute exacerbation of the Crohn's disease.

The patient frequently complained about progressive abdominal pain, especially in the right flank. Laboratory investigations 48 hours after hospital admission showed increasing inflammatory parameters despite ongoing antibiotic treatment. Contrast-enhanced computer tomography of the abdomen revealed circular thickening of the pars descendens of the duodenal wall compatible with an acute inflammatory manifestation of CD with suspected spontaneous retroperitoneal perforation of the colon (Panel A, arrow) and formation of a retroperitoneal, perinephric abscess with a large air and fluid collection around the right kidney (Panel A and B, asterisks).

However, neither enteroscopic nor ileo-colonoscopy investigations could identify a macroscopically visible perforation ostium. Due to the progredient clinical deterioration and rapid development of an extensive retroperitoneal and perinephric abscess leading to total right kidney necrosis, we decided to perform emergency surgery. The patient underwent a radical right nephrectomy with abscess drainage and surgical closure of the suspected duodenal perforation. In the absence of improvement in the intensive care unit, a covered enteric stent was additionally endoscopically placed. The further postoperative course was then complicated by sepsis, which ultimately led to multiple organ failure and death within 3 days despite exhaustive intensive care management.

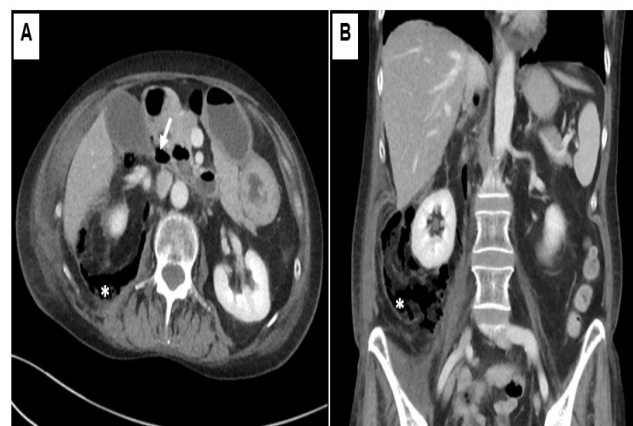


Figure 1: suspected spontaneous retroperitoneal perforation of the colon (Panel A, arrows) and formation of a retroperitoneal, perinephric abscess with large air and fluid collection around the right kidney (Panel A and B, asterisks).

Discussion

CD is a chronic transmural intestinal inflammatory process, potentially afflicting any part of the gastrointestinal tract and it is characterized as a disease predisposing to retroperitoneal complications. The disease is often associated with deep ulcers, formation of the fistulous tract into adjacent tissue and/or abscesses. It has been reported that 10% to 30 % of the patients with CD developed an abdominal abscess in the course of the disease, of which the incidence of retroperitoneal abscesses lay between 2,7 and 4,3% [8-10]. Retroperitoneal abscesses therefore constitute a rare pathology in CD, but their frequency is increased under immunosuppression. Another source is the perforation of the abdominal viscera (retrocaecal appendix, di-

verticulitis, duodenal ulcers) and pancreatitis [11]. Interestingly, the etiology of an abscess remains unknown in about 12% of cases.

Diagnosis of a retroperitoneal abscess is extremely difficult in the early stages of the illness and often recognized late in the clinical course. The delayed diagnosis leads to significant morbidity and mortality. As in the case of our patient, most patients with retroperitoneal abscess similarly present with nonspecific symptoms like abdominal pain, low grade pyrexia, and nausea/vomiting. However, there have also been a plethora of diverse clinical manifestations documented in the literature [2,4,5,8]. Therefore, the diagnosis is often delayed by weeks, which may be extremely dangerous in immunosuppressed patients. In our case a provisional diagnosis was placed within 48 hours after onset of symptoms. What is particularly insidious in this case is that the patient experienced the symptoms described in a similar way to earlier episodes of Crohn's disease and reported them to her family doctor, leading to increase of the steroid dose in an already firmly immunosuppressed patient by certolizumab and leflunomide.

CT and MRI are considered to be the investigations of choice in cases of rapid clinical deterioration of the patients. Based on a meta-analysis performed by Horsthuis et al there was no statistically significant difference between CT and MRI in terms of sensitivity in the diagnosis of inflammatory bowel diseases and their complications [12].

There are several often discussed mechanisms of abscess formation in CD, of which transmural bowel inflammation leading to fistula formation with subsequent direct penetration of bacteria from the bowel to tissue is well known. Other possible mechanisms include hematologic seeding of bacteria from the diseased bowel with contamination of the retroperitoneum, but also unnoticed damage to the duodenum or small intestine, e.g. fishbone, is conceivable as well as bowel wall ischemia [13].

The outcome of a retroperitoneal abscess depends on initial prompt diagnosis, patient general condition and importantly on comorbidity [14]. Our patient had been undergoing treatment with immunosuppressive medications for her RA with certolizumab and leflunomide, which are also effective in the therapy of CD [15,16]. The simultaneous use of prednisolone along with the anti-TNF drug certolizumab and leflunomide, which inhibits proliferation of activated T cells may be regarded as the profound risk factor leading to fulminant infectious septic course [17]. While the rate of infectious complications is clearly increased in prednisolone dose over 20 mg per day, certolizumab inhibits further TNF-action on neutrophils, mast cells, macrophages and innate immunity in the phase of an ongoing (retroperitoneal) infection. In addition, leflunomide inhibits the generation and activation of bacteria strain-specific T cell populations. Thus, this might explain -in our opinion- the insidious onset and unfavorable clinical course in this 60-year-old female without further significant other co-morbidities.

It is well known, that elderly patients with comorbidities or immune suppressed patients sometimes manifest fewer signs and symptoms after intestinal perforation and prolonged courses are documented. Several studies of retroperitoneal abscesses found that most patients had underlying immunosuppressive conditions [18-20]. After multivariate adjustment, a retrospective study of patients with CD showed a significantly higher risk for developing intra-abdominal abscesses in the group that received preoperative infliximab [20]. It has been suggested that

anti-TNF agents inhibit activation of the inflammatory cascade and recruitment of neutrophils in the bowel wall [21]. These pathways play a role in the sealing of perforations and encapsulations of infections.

However, most literature pertaining to retroperitoneal abscesses in patients with CD were published long before anti-TNF therapy became widely available for the treatment of the disease. Thus, there is a need for further study and registry documentation of immunosuppressed patients, not only in IBD when using several precisely on specific immune targets acting immune-modulators [22-24]. In addition, for general practitioners as the combined therapy with immunosuppressants and biologics may mask infections, support fulminate septic courses and endanger the life of the patient, it should be strictly differentiated between i) steroid therapy alone, either higher or lower than 20 mg per day ii) anti-TNF therapy, iii) further immunosuppressants like azathioprine, methotrexate or leflunomide etc. and iv) combinations of the forementioned drug classes [25,26]. Our patient with fatal outcome had long-term steroid dose and a high-risk situation for infectious complications due to the combined immunosuppression. Thus, in this group the threshold for performing an early CT or MRI should be set as low as possible, as these imaging modalities are most reliable for detection of an occult or masked gastrointestinal perforation [12,27].

Furthermore, for emergency departments and medical centers who get such multiple immunosuppressed patients assigned with virtual no immunity to infection or secondary immune-deficiency as in our patient one should early decide to administer immunoglobulin substitution containing IgG, IgA and IgM to support and/or substitute the lacking immune response [28,29].

Conclusion

To date, no case of total necrosis of the kidney due to retroperitoneal perforation has been described in the literature. Combined running therapy with immunosuppressants and biologics resulted in fulminant retroperitoneal spread of infection, renal necrosis and lethal sepsis. In the case of initial unremarkable abdominal ultrasonography, rapid CT or MRI imaging is indicated in the face of clinical uncertainty and the progression of symptoms. Patients with CD tend to develop an abscess during the course of the disease, with immunosuppression and intake of steroids placing them particularly under further substantial risk.

Declarations

Data availability: Data can be provided on reader's request.

Ethical approval: Not required.

Patient consent: Written consent has been obtained.

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Conflicts of interest: There are no conflicts of interest.

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