

## Perforation of Terminal Ileum as a Rare Complication of an Early Post-Transplant Course

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### Abstract

Perforations of any part of the gastrointestinal tract can occur in transplant patients, although the colon may be the most common site. We analyze the case of a 39-year-old patient after kidney transplantation who suffered perforation of terminal ileum with peritonitis on the 7th day after transplantation. We histologically confirmed presence of a foreign body in the intestinal wall – a rare cause of intestinal perforation in a patient after kidney transplantation. We have not noticed a significant worsening of graft function or development of sepsis mainly because of quick evaluation of the patient's clinical state, prompt surgical intervention and a combined antibiotic treatment. Gastrointestinal perforations have rarely been noted in large studies involving transplant recipients.

**Keywords:** Kidney transplantation; Intestinal perforation; Antibiotic treatment; Immunosuppression

### Introduction

Organ transplantation has emerged as the preferred treatment modality for end-stage liver, kidney, heart and lung diseases. The gastrointestinal tract accounts for a large component of non-allograft-related complications seen after all types of solid organ transplantation and is responsible for considerable morbidity and mortality associated with transplantation [1- 4].

Upper bowel perforation can be described as either free or contained. Free perforation occurs when bowel contents spill freely into the abdominal cavity, causing diffuse peritonitis (eg, duodenal or gastric perforation). Contained perforation occurs when a full-thickness hole is created by an ulcer, but free spillage is prevented because contiguous organs wall off the area (as occurs, for example, when a duodenal ulcer penetrates into the pancreas). Lower bowel results in free intraperitoneal contamination [5].

Thompson et al. first described ileocolonic perforation in patients after kidney transplantation in 1975. Out of 248 patients after kidney transplantation, eleven patients developed ileocolonic perforation. Only three of the patients survived this complication and in each case the perforation was localized [6]. Perforations of any part of the gastrointestinal tract can occur in transplant patients, although the colon may be the most common site. Perforation occurs most commonly in patients with renal failure who are undergoing dialysis and have had heavy immunosuppression, particularly with corticosteroids. Early perforations are considered to be largely attributable to diverticulitis or CMV colitis [7].

Symptoms of gastrointestinal perforation may include severe stomach pain, chills, fever, nausea and vomiting. When peritonitis occurs, the abdomen feels very tender. In addition to the general symptoms of perforation, symptoms of peritonitis may include exhaustion, shortness of breath or tachycardia.

The goals of surgical therapy are as follows:

- To correct the underlying anatomical problem
- To correct the cause of peritonitis
- To remove any foreign material in the peritoneal cavity that might

inhibit WBC function and promote bacterial growth (eg, feces, food, bile, gastric or intestinal secretions, blood) [5].

•However, if symptoms and signs of generalized peritonitis are absent, a nonoperative policy may be used with antibiotic therapy directed against gram-negative and anaerobic bacteria.

The causes of intestinal perforation in patients following organ transplantation are well known and are mainly related to administered immunosuppression after transplantation. In our case report which describe terms of intestinal perforation in a short post-transplant period, where the foreign body causing perforation.

### Case Presentation

In the set of patients who underwent kidney transplantation in Transplant Center Martin from 2003 to 2015 (n=250) we identified only one patient who had developed perforation of the gastrointestinal tract in the post-transplant period.

We present the casuistics of a 39-year-old man patient who underwent primary kidney transplantation from a living donor (58-year-old mother) in 04/2015. The recipient was in a regular hemodialysis program from 03/2015 and the cause of native kidney failure was a suspected chronic glomerulonephritis of the solitary kidney (biopsy of the native kidney was not carried out). The patient was prepared for transplantation already in pre-dialysis period, so the patient could undergo a transplant very short time (1 month) after initiation of dialysis program. Cross match test (by using flow cytometry) before transplantation was 2 times negative and PRA were 0%. In case of induction we chose basiliximab due to the

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low immunological risk of the recipient (1 mismatch in HLA A) in combination with methyl-prednisolone (500 mg intravenous on D0 and D1), immunosuppressive regimen consisted of tacrolimus (target level 5-10 ng/ml), everolimus (target level 3-8 ng/ml) and 20 mg prednisone/day (regimen was adjusted according to the protocol of the clinical study in which the patient is engaged). After transplantation we noticed only small decrease in creatinine and diuresis was around the level of residual diuresis. On the second post-surgery day we have proven positivity in B-lymphocyte cross-match test (it is highly unlikely that cross match after transplantation was a false positive, donor specific antibodies by using flowPRA were negative, so we supposed an nonHLA acute antibody-mediated rejection) and consequently realized 3 high-volume plasmaphereses with 5% albumin in combination with intravenous immunoglobulins (total dose 94.5 grams). Diuresis

had developed after this treatment, and a decrease in nitrogenous substances was noticed as well. The check cross-match test on the 6th post-surgery day was negative.

On the 7th day after surgery an acute abdomen pain and vomiting appears, accompanied by tachycardia, hypotension and shiver. An x-ray image of the abdomen was urgently made and pneumoperitonea was diagnosed. The patient was immediately taken to the operating theatre. During the examination of abdominal cavity perforation of terminal ileum with peritonitis was discovered. During the surgical procedure was realized wash-out of the abdominal cavity and end to end anastomosis of ileum. There was just one drain placed and we removed it after 2 days.

We have also laboratory recorded a significant rise in inflammatory parameters and a slight deterioration of graft function (Graph 1). We have confirmed presence of *Klebsiella pneumoniae* and *Enterococcus faecium* by cultivation (sensitivity to antibiotics is shown (Tables 1 and 2). We immediately started with combined antibiotic treatment (meropenem – reduced dose according to the actual glomerular filtration, linezolid 600 mg intravenous 2x per day and natamycin per os 3x per day). Three fragments of the perforated part of the intestine were histologically analyzed and a complex of reactive changes such as vascular congestion, bleeding and coagulative necrosis was discovered, inside we found remains of foreign material accompanied by a purulent inflammation without signs of a neoplastic process (Figure 1). We have not proven CMV infection in the patient (CMV viremia established by

PCR was negative at the time of perforation).

Further post-surgery course was not complicated. The antibiotic treatment lasted 10 days and immunosuppression was not interrupted or reduced. The patient is currently in an excellent condition without any problems. After completion of history regarding foreign body as a cause perforation of the ileum, we can assume that it could be the nucleolus of apples or cherries.

## Discussion

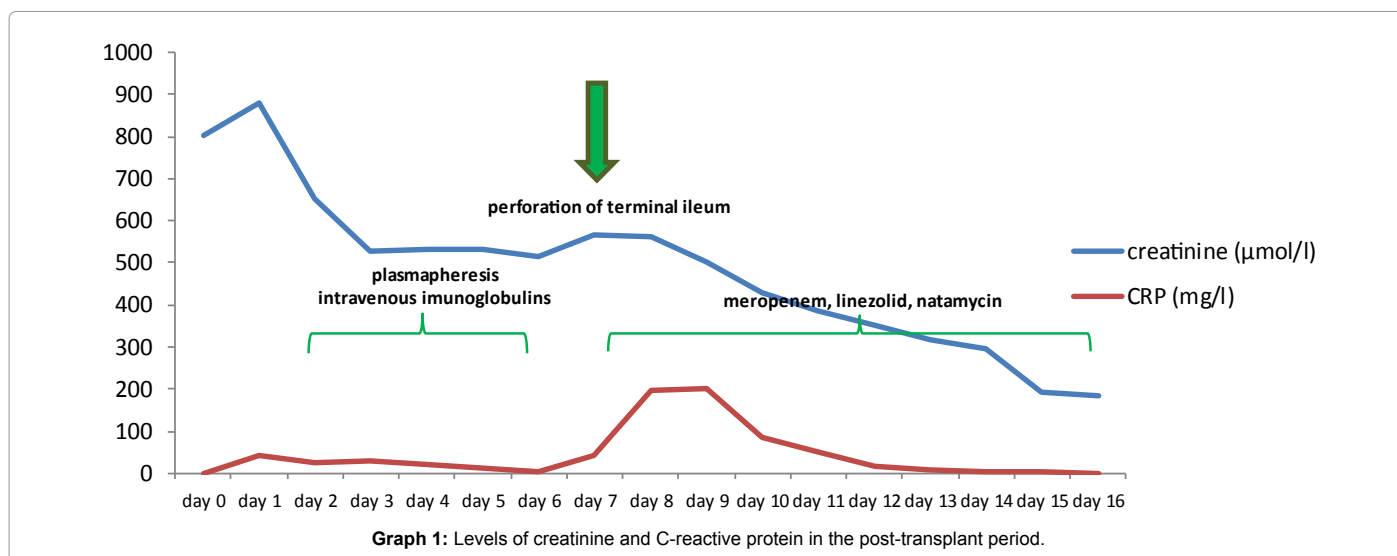
Perforation of the colon is the most feared consequence of these complications, because the mortality rises to over 50% in transplanted group of patients [8]. A delay in the diagnosis in patients after transplantation is common, as the symptoms and signs are sparse and often masked by immunosuppression [9]. The incidence of colon perforations is 1-2% in kidney transplantation patients [10,11]. Diverticulitis is the most common cause [9,12]. Other causes can be ischaemia or CMV colitis [12].

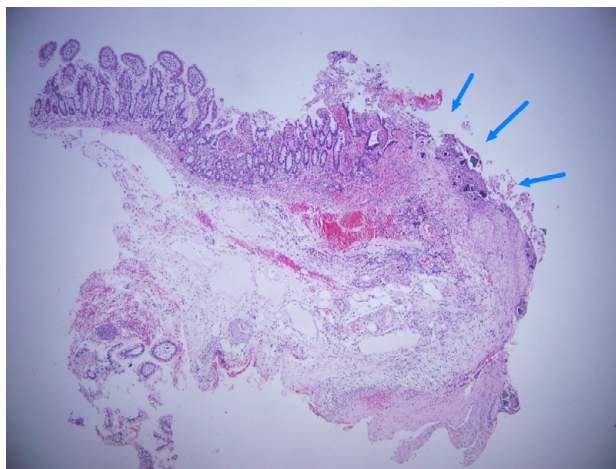
Large, prospective, randomized trials with gastrointestinal complications or intestinal perforation as the primary endpoint do not exist and data found in literature are only at the level of case reports.

Authors retrospectively evaluated gastrointestinal complications in more than 1500 patients. Out of this number of patients, only 8 of them suffered intestinal perforation after transplantation (0.53%).

Half the perforations were caused by diverticulitis. Although they were few in number, 25% of these complications were fatal. The diagnosis was often delayed because immunosuppressive drugs might have masked symptoms and affected the patients' responses to the septic condition. All fatal colon perforations in these series occurred during the first year after the transplantation [1].

Similarly, in the study of authors Catena et al., perforation of gastrointestinal tract was a very serious complication of the post-transplant course with high mortality. This study reports major gastrointestinal complications among a group of 1611 patients following kidney transplantation. The immunosuppressive regimen changed somewhat during the course of the study but included azathioprine, prednisolone, antilymphocyte globulin, cyclosporine, tacrolimus, mycophenolate mofetil, and sirolimus. Perforations occurred in the colon (n=21), small bowel (n=15), duodenum (n=6),





**Figure 1:** Hematoxylin and Eosin shows small intestine specimen with perforation and basophilic crystals in the fibrinopurulent material (blue arrows).

Amikacin	Sensitive	Amoxicillin+Clavulanate	Resistant
Ampicillin	Resistant	Aztreonam	Resistant
Cefalexin	Resistant	Cefepime	Resistant
Cefoperazone + Sulbactam	Sensitive	Cefotaxime	Resistant
Cefoxitim	Sensitive	Ceftazidime	Resistant
Ciprofloxacin	Resistant	Ertapenem	Sensitive
Levofloxacin	Resistant	Imipenem	Sensitive
Piperacillin+ Tazobactam	Intermediarysensitive	Meropenem	Sensitive

**Table 1:** Sensitivity to antibiotics *Klebsiella pneumoniae* –cultivation from the wound after perforation of terminal ileum.

Amoxicillin+Clavulanate	Resistant	Vancomycin	Sensitive
Cefepime	Resistant	Ampicillin	Resistant
Cefotaxime	Resistant	Cefoperazone+Sulbactam	Resistant
Ciprofloxacin	Resistant	Ceftazidime	Resistant
Gentamicin	Resistant	Ertapenem	Resistant
Imipenem	Resistant	Chloramphenicol	Sensitive
Meropenem	Resistant	Linezolid	Sensitive
Teicoplanin	Sensitive	Piperacillin+ Tazobactam	Resistant
		Tetracycline	Resistant

**Table 2:** Sensitivity to antibiotics *Enterococcus faecium* – cultivation from the wound after perforation of terminal ileum.

and stomach (n=4). Nearly 50% of the complications occurred while patients were being given high-dose immunosuppression to manage either the early post-operative period or acute rejection episodes. Of the 46 patients affected, 11 (24%) died as a direct result of the gastrointestinal complications. This high mortality appeared to be related to the effects of the immunosuppression and the associated response to sepsis [13].

In case of our described case we excluded diverticulosis and CMV infection from the possible risk factors for perforation of the intestine after kidney transplantation (by inspection during operation). Perforation might have been caused by the immunosuppressive therapy; however, we have rarely diagnosed presence of a foreign body (probably a seed, or a pip) by a histological examination.

Due to the prompt diagnostics and a quick surgical intervention

the patient had not developed sepsis in the immunosuppressive environment. The patient was afebrile and with a targeted antibiotic treatment a prompt decrease in inflammatory parameters was recorded. During the post-transplant period it was not necessary to discontinue or reduce the immunosuppressive therapy (per os intake was maintained due to localization of the perforation), this made it possible to maintain stabilized graft function, moreover, we later recorded a decrease in the creatinine level.

## Conclusion

Perforation of intestine in a patient after kidney transplantation is a serious complication with high mortality. Perforation of the intestine caused by presence of a foreign body is not currently mentioned in any literature, it is considered to be a very rare complication. In case of development of perforation of the intestine during the post-transplant period a prompt diagnosis and a quick surgical solution are important, as well as a targeted combined antibiotic treatment.

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