



Critical considerations for the management of acute abdomen in transplant patients

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Abstract

The number of solid organ transplantations performed annually is increasing and are increasing in the following order: Kidney, liver, heart, lung, pancreas, small bowel, and uterine transplants. However, the outcomes of transplants are improving (organ survival > 90% after the 1st year). Therefore, there is a high probability that a general surgeon will be faced with the management of a transplant patient with acute abdomen. Surgical problems in immunocompromised patients may not only include graft-related problems but also nongraft-related problems. The perioperative regulation of immunosuppression, the treatment of accompanying problems of immunosuppression, the administration of cortisol and, above all, the realization of a rapidly deteriorating situation and the accurate evaluation and interpretation of clinical manifestations are particularly important in these patients. The perioperative assessment and preparation includes evaluation of the patient's cardiovascular system and determining if the patient has hypertension or suppression of the hypothalamic-pituitary-adrenal axis, or if the patient has had any coagulation mechanism abnormalities or thromboembolic episodes. Immunosuppression in transplant patients is associated with the use of calcineurin inhibitors, corticosteroids, and antiproliferation agents. Many times, the clinical picture is atypical, resulting in delays in diagnosis and treatment and leading to increased morbidity and mortality. Multidetector computed tomography is of utmost importance for early diagnosis and management. Transplant recipients are prone to infections, especially specific infections caused by cytomegalovirus and *Clostridium difficile*, and they are predisposed to intraoperative or postoperative complications that require great care and vigilance. It is

necessary to follow evidence-based therapeutic protocols. Thus, it is required that the clinician choose the correct therapeutic plan for the patient (conservative, emergency open surgery or minimally invasive surgery, including laparoscopic or even robotic surgery).

Key Words: Acute abdomen; Abdominal emergency surgery; Transplantation; Immunocompromised patients; Immunosuppression; Posttransplantation surgery

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Core Tip: Adequate caution should be taken with patients with acute abdomen after transplantation, and these patients need constant attention because of the altered clinical course of their disease due to existing immunosuppression. Computed tomography may be valuable in diagnosis. The management of these patients must be personalized, but urgent surgical intervention is commonly needed. Specific care must be applied during the perioperative period.

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INTRODUCTION

There is an increasing number of solid organ transplantations performed annually worldwide, and these transplants include, in order of frequency, kidney, liver, heart, lung, pancreas, and, less commonly, small bowel and uterus transplantations. The increase in the number of these procedures has been accompanied by improved results, leading to a graft survival rate of more than 90% in the first year[1]. Therefore, there is a high probability that a general surgeon will be faced with the management of a transplant patient with acute abdomen[1-3].

The clinical presentation may not be similar to that of patients in the general population with acute abdomen who have not undergone transplantation; thus, a misdiagnosis or severity underestimation could occur[1]. Surgical problems in immunocompromised patients may be related to the graft, which will require referral of the patient to a transplant center [4,5] but may also not be related to the graft, allowing the patient to be treated at a nontransplant surgical department[4,6].

Particular attention must be paid to the perioperative use of immunosuppressants, and the treatment of the patient should include the correction of immunosuppression with its accompanying problems and the administration of cortisol to cope effectively with the operative stress. However, the rapid progression of acute abdomen in transplant patients and the need for specific evaluation and different interpretations of its clinical manifestations should be anticipated[1,3].

The indications for emergency abdominal surgery include gallbladder diseases (80.3%), gastrointestinal perforation (9.2%), complicated acute diverticulitis (6.2%), obstructive ileus (2%), and acute appendicitis (2%)[1].

Immunosuppression is caused by various pharmaceutical agents, such as calcineurin inhibitors (cyclosporin, voclosporin, tacrolimus, and pimecrolimus), corticosteroids (prednisone), mTOR inhibitors (sirolimus), and antiproliferative agents (mycophenolate mofetil), which are used in solid organ transplantation to prevent graft rejection. Subsequently, transplant recipients are prone to both specific infections [cytomegalovirus (CMV), *Clostridium difficile* (*C. difficile*), and neutropenic enterocolitis] and intraoperative or postoperative complications that require great caution and constant vigilance. Care must be taken during every operative procedure to completely preserve the functional capacity of the transplanted organ. Thus, it is important to avoid episodes of hypotension that may have a negative impact on the graft situation because of reduction of the graft's blood supply[1].

The treatment of acute abdomen in immunocompromised patients, including patients who have had solid organ or bone marrow transplantation, constitutes a challenge that requires specific evidence-based medicine and adequate understanding of the new directions in the treatment of these patients[2]. The sensation of pain, the main manifestation of peritonitis, in such patients is often not perceived adequately, leading to delays in early diagnosis and proper management and subsequent severe deterioration of patients, leading to severe sepsis. Thus, meticulous evaluation of the clinical course and physical examination of the abdomen are highly important. Furthermore, it is well known that emergency abdominal surgery causes more intense postoperative pain than elective surgery, affecting the patient's clinical and psychological status, which may ultimately influence surgical outcomes[7].

Moreover, immunosuppression increases the morbidity and mortality of emergency surgery[3,6,8,9].

DIAGNOSIS

A misdiagnosis of acute abdomen that causes an immunocompromised patient to undergo an emergency surgical

intervention is associated with high morbidity and mortality rates; therefore a diagnosis based on a multidisciplinary discussion is recommended[3]. Transplant patients do not exhibit the usual symptoms or clinical signs of acute abdomen because the symptoms are alleviated by immunosuppression. Additionally, a sufficient diagnostic accuracy cannot be achieved by using the clinical signs of peritonitis, the laboratory tests, or the plain abdominal radiogram and ultrasound findings. The most reliable imaging method for a definitive diagnosis is contrast-enhanced multidetector computed tomography, and thus, it should always be performed in these patients[3,10,11].

In transplant patients, the most common intraperitoneal infections include[3]: (1) Acute cholecystitis, which is the most common and occurs mainly after heart (72%), lung and kidney (30%) transplantations; (2) acute diverticulitis, which occurs mainly after kidney and liver transplantation and exhibits a more severe course than in otherwise healthy people; (3) perforation of the gastrointestinal tract (gastroduodenal ulcer, diverticulitis, acute mesenteric ischemia, severe colitis) [1,12]; (4) acute appendicitis, which is usually complicated[13,14]; (5) obstructive ileus, which is caused mainly by lymphoproliferative disorders related to immunosuppression after transplantation or intraperitoneal adhesions[1,15]; (6) acute pancreatitis, which is attributed to tacrolimus and is rare[16,17]; and (7) Meckel's diverticulum perforation[18] or acute pseudoobstruction (Ogilvie's syndrome), which are rare[19]. Additionally, a rare case of ectopic pregnancy rupture after simultaneous pancreas and kidney transplantation has been reported[20]. In addition, specific intraperitoneal infections, such as neutropenic enterocolitis, CMV colitis[8,21,22] and *Clostridium difficile* (*C. difficile*) colitis, have been reported[3].

MANAGEMENT

The perioperative assessment and preparation involve the management and correction of cardiovascular system abnormalities, hypertension, any coagulation mechanism abnormalities, thromboembolic episodes and any corticoadrenal insufficiencies caused by the suppression of the hypothalamic pituitary adrenal axis to cope with surgical stress; the safety limit of hydrocortisone is 75 mg/24 h for three days[1].

Acute cholecystitis should be managed by urgent cholecystectomy without delay. In patients who are unfit for surgery, imaging-guided percutaneous cholecystostomy may be an alternative choice[3].

Acute appendicitis should be managed by urgent appendectomy without any delay[3,13,14].

Laparoscopic cholecystectomy or laparoscopic appendectomy are not contraindicated and must be the first-line procedure[3,14].

Patients with uncomplicated cases of acute diverticulitis require conservative treatment with broad-spectrum antibiotics[3]. However, patients with complicated acute diverticulitis require urgent segmental colectomy without delay. In unstable severely ill patients, damage control surgery involving laparoscopic peritoneal lavage and drainage is preferred[23].

Surgical intervention is urgently needed for gastrointestinal tract perforation and bowel obstruction[3].

The use of minimally invasive surgery, including laparoscopic[24] and robotic surgery[25], has been documented to play an important role in the management of patients with acute abdomen, including transplantation patients. The additional advantage in the latter case is that there is no need for perioperative immunosuppressant regulation, as it is anticipated that the patients who undergo minimally invasive surgery have a shorter time to oral feeding postoperatively after these procedures.

In addition to intense monitoring and immunosuppression adjustment, the postoperative care of these patients includes multimodal pain management, *i.e.*, nonsteroidal anti-inflammatory drugs, paracetamol, COX2 inhibitors such as celecoxib, and possibly even antiepileptic gabapentinoids, thus decreasing the use of opioids[7].

The motivation of writing this article is to raise the general surgeon's awareness of the peculiarities and specific altered manifestation features of acute abdomen in the immunosuppressed patient with the caused diagnostic difficulties and the problems that arise during therapeutic management. It should be emphasized particularly, the choice of a multidisciplinary management plan and the performance of operative manipulations with great caution and gentleness.

CONCLUSION

Early accurate diagnosis and management of acute abdomen patients after transplantation is crucial. Preoperative computed tomography is necessary for precise assessment and decision-making. The therapeutic plan usually includes open or minimally invasive emergency surgery, but conservative treatment is indicated in some limited cases. Future work and perspectives, besides the improvement in immunosuppressant drugs, must be concentrated on evidence-based protocols including novel high resolution imaging modalities for precise diagnosis, more application of minimally invasive surgery, and damage control surgery in patients with severe sepsis or hypovolemic conditions.

FOOTNOTES

Author contributions: Pavlidis TE designed research, contributed new analytic tools, analyzed data, review and approved the paper; Galanis IN analyzed data, review and approved the paper; Pavlidis ET performed research, analyzed data, review and wrote the article; Tsoulfas G contributed new analytic tools, analyzed data, review and approved the paper; Katsanos G performed research, analyzed

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