Acute Appendicitis After Kidney Transplantation: Experience at a Tertiary Care Hospital in Mexico City

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Abstract

Objectives: Here, we describe the presentation, treatment, and outcomes of acute appendicitis in kidney transplant recipients at a tertiary care hospital in Mexico City.

Materials and Methods: We conducted a retrospective case series study at a tertiary care hospital in Mexico City from January 2000 to January 2015.

Results: During our study period, 1186 patients received a kidney transplant; among these patients, we identified 10 cases of acute appendicitis (0.008%). Four patients (40%) were diagnosed on day 5 of symptom onset. Nine patients (90%) showed abdominal pain, 2 patients (20%) presented with a typical migratory pattern, and 2 patients (20%) showed symptoms of small bowel intestinal obstruction. Thirty percent of patients (3/10) presented a rule-out Alvarado score (≤ 3 points). A computed tomography scan was performed in all but one patient; among these 9 patients, 1 (11.1%) had a false-negative result. Among all patients with acute appendicitis, 50% (5/10) presented with a periappendiceal abscess and 40% (4/10) showed localized peritonitis. An open and laparoscopic appendectomy was performed in 7 of 10 patients (70%) and 3 of 10 patients (30%), respectively. All patients received ceftriaxone plus metronidazole or ertapenem for 5 to 7 days. There were no reported treatment failures or recurrence of symptoms.

Conclusions: The diagnosis of acute appendicitis in kidney transplant recipients requires a high index of suspicion. Kidney transplant recipients with acute appendicitis had good outcomes with a therapeutic approach similar to that used in the general population.

Key words: Kidney, Renal, Solid-organ transplantation, Transplant

Introduction

Acute appendicitis (AA) is the most common surgical emergency in the general population. Although it is thought to be less prevalent in recipients of solid-organ transplant, their incidence may increase given the growing number of patients with functioning allografts. Due to immunosuppressive therapy, solid-organ transplant recipients with gastrointestinal complications display a blunted immune response and, consequently, a mild and delayed clinical presentation. These patients may even present with complete absence of symptoms or physical findings. Moreover, the allograft localization in the right lower quadrant leads to a greater diagnostic challenge because of the impaired physical examination and the broader possibility of differential diagnosis. Therefore, these patients are prone to developing an unusual clinical presentation and an indolent clinical course. The primary objective of this study was to describe the clinical presentation, treatment, and outcomes of AA in kidney transplant recipients at our center.

Materials and Methods

We conducted a retrospective case series study at the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán. This institution is a 200-bed tertiary care teaching hospital in Mexico City, where adult patients are referred from all over the country for solid-organ transplant. We searched our electronic database for patients with AA diagnosis.
after a kidney transplant from January 2000 to January 2015. We retrieved additional baseline characteristics, clinical features, and outcomes from the medical records. This study was approved by our internal review board. We assessed the comorbidities based on the Charlson comorbidity index, and we used the Alvarado score to evaluate the probability of AA diagnosis.6,7

Results

Baseline characteristics and description of episodes
During our study period, 1186 patients received a kidney transplant at our center; among these, we identified 10 cases of AA (0.008%). The median age at diagnosis was 42.5 years (interquartile range [IQR], 30-52 y), 60% (6/10) were male, and 70% (7/10) had the kidney allograft located in the right lower quadrant. The median body mass index was 25.8 kg/m² (IQR, 25.2-29.0 kg/m²). All cases had a Charlson comorbidity index of ≤ 3, and patients received a median of 3 immunosuppressive drugs (IQR, 2-3). The median time elapsed between kidney transplant and AA diagnosis was 4.9 years (IQR, 2.8-12.9 y) (Table 1).

Clinical presentation and diagnostic approach
Forty percent (4/10) of the cases were diagnosed on day 5 of symptom onset. Abdominal pain was present in 9 of 10 patients (90%), with only 2 patients (20%) showing a typical migratory pattern. Nausea was present in 70% (7/10), anorexia in 30% (3/10), and fever in 20% (2/10) of patients. Two patients (20%) presented with symptoms of small bowel intestinal obstruction, with 1 patient having diagnosis delayed for 15 days. At physical examination, 20% (2/10) showed positive McBurney sign, 10% (1/10) showed abdominal wall rigidity, and 20% (2/10) showed rebound tenderness.

The median serum creatinine level at diagnosis was 1.4 mg/dL (range, 1.1-1.6 mg/dL), with 3 patients presenting with acute kidney injury (defined as a serum creatinine increment of ≥ 0.3 mg/dL above baseline). The median white blood cell count at diagnosis was 10.1 × 10⁹/L (IQR, 8.3-14.8 × 10⁹/L), and median C-reactive protein level was 8.7 mg/dL.

<p>| Table 1. Description of 10 Patients with Acute Appendicitis After Kidney Transplant |
|---------------------------------|---------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Case</th>
<th>Sex/Age, y</th>
<th>Primary Diagnosis</th>
<th>Immunosuppressive Therapy</th>
<th>Time Elapsed (SOT to AA/ SO to AA Diagnosis)</th>
<th>Histopathologic Diagnosis</th>
<th>Type of Surgery</th>
<th>Therapy (Days)</th>
<th>Complication (Follow-up)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M/52</td>
<td>Diabetic nephropathy</td>
<td>PND 5 mg/d, AZA 100 mg/d, CIsA 180 mg/d</td>
<td>10.3 y/0 d</td>
<td>AA + localized peritonitis</td>
<td>Laparotomy</td>
<td>CRO+MTZ (7)</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>M/61</td>
<td>Acute tubulointerstitial nephropathy</td>
<td>Tacrolimus 4 mg/d, PND 5 mg/d, MWF 1 g/d</td>
<td>3.7 y/0 d</td>
<td>AA + localized peritonitis</td>
<td>Laparoscopic appendectomy</td>
<td>CRO+MTZ (7)</td>
<td>Surgical site infection</td>
</tr>
<tr>
<td>3</td>
<td>M/54</td>
<td>Acute tubulointerstitial nephropathy</td>
<td>AZA 125 mg/d, PND 5 mg/d</td>
<td>17.0 y/1 d</td>
<td>AA + peripancreatic abscess</td>
<td>Open appendectomy</td>
<td>ETP (5)</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>F/44</td>
<td>Idiopathic CKD</td>
<td>Tacrolimus 2 mg/d, PND 5 mg/d, AZA 75 mg/d</td>
<td>12.9 y/0 d</td>
<td>AA + peripancreatic abscess</td>
<td>Open appendectomy</td>
<td>CRO+MTZ (7)</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>M/50</td>
<td>Idiopathic CKD</td>
<td>Tacrolimus 3 mg/d, PND 5 mg/d, MMF 2 g/d</td>
<td>89 d/15 d</td>
<td>AA + peripancreatic abscess</td>
<td>Open appendectomy</td>
<td>ETP (7)</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>M/22</td>
<td>Idiopathic CKD</td>
<td>AZA 100 mg/d, PND 15 mg/d</td>
<td>3.2 y/6 d</td>
<td>AA + peripancreatic abscess</td>
<td>Open appendectomy</td>
<td>CRO+MTZ (7)</td>
<td>None</td>
</tr>
<tr>
<td>7</td>
<td>F/37</td>
<td>Idiopathic CKD</td>
<td>AZA 100 mg/d, PND 5 mg/d</td>
<td>17.6 y/0 d</td>
<td>AA + localized peritonitis</td>
<td>Laparoscopic appendectomy</td>
<td>CRO+MTZ (7)</td>
<td>None</td>
</tr>
<tr>
<td>8</td>
<td>M/72</td>
<td>Idiopathic CKD</td>
<td>Tacrolimus 60 mg/d, PND 7.5 mg/d, MWF 1.5 g/d</td>
<td>2.8 y/5 d</td>
<td>AA + localized peritonitis</td>
<td>Open appendectomy</td>
<td>CRO+MTZ (7)</td>
<td>None</td>
</tr>
<tr>
<td>9</td>
<td>F/24</td>
<td>Idiopathic CKD</td>
<td>Tacrolimus 5 mg/d, PND 5 mg/d, MMF 500 mg/d</td>
<td>6.1 y/1 d</td>
<td>AA + peripancreatic abscess</td>
<td>Laparoscopic appendectomy</td>
<td>CRO+MTZ (7)</td>
<td>None</td>
</tr>
<tr>
<td>10</td>
<td>M/51</td>
<td>Idiopathic CKD</td>
<td>AZA 100 mg/d, Tacrolimus 6 mg/d</td>
<td>23 d/9 d</td>
<td>AA + localized peritonitis</td>
<td>Open appendectomy</td>
<td>CRO + MTZ (7)</td>
<td>None</td>
</tr>
</tbody>
</table>

Abbreviations: AA, acute appendicitis; ADPKD, autosomal dominant polycystic kidney disease; AZA, azathioprine; CIsA, cyclosporine; CRO, ceftriaxone; E, female; M, male; MMF, mycophenolate mofetil; MTZ, metronidazole; PND, prednisone; SO, symptom onset; SOT, solid-organ transplant; T2DM, type 2 diabetes mellitus
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(range, 3.65-12.6 mg/dL). Severe sepsis and septic shock were present in 3 patients (30%), with only 20% of patients fulfilling the systemic inflammatory response diagnostic criteria. The median Alvarado score was 3 points (IQR, 2-4), with 30% of patients (3/10) having a rule-out score (≤ 3 points) and 20% (2/10) having a rule-in score (≥ 6 points) (Table 1).

A computed tomography (CT) scan was performed in all but 1 patient. Among these patients, 8/9 (88.8%) had imaging findings compatible with AA diagnosis, 6 patients (66.7%) presented with fat stranding, and 1 patient (11.1%) presented with an appendicolith. The median appendiceal diameter by CT scan was 11.5 mm (range, 8.5-12 mm). Fifty percent of patients (5/10) presented with periappendiceal abscess, and 40% (4/10) showed localized peritonitis. Blood and peritoneal fluid cultures were obtained in 3 of 10 patients (30%); of these patients, an Escherichia coli susceptible to all β-lactams was isolated in 1 patient.

Treatment and outcomes
The median elapsed time between symptom onset and surgery was 33.3 hours (IQR, 17-124 h). Open appendectomy was performed in 7 patients (70%), with the other 3 patients having a laparoscopic approach performed, with median surgery time of 1.75 hours (IQR, 1.5-4 h). One patient required right hemicolectomy and another required cecectomy. No patients with a laparoscopic approach required conversion to open laparotomy. Seven patients (70%) received treatment with a third-generation cephalosporin plus metronidazole, and 3 patients (30%) received ertapenem; the median duration of therapy was 7 days (IQR, 7-7 d). All patients continued their immunosuppressive therapy scheme during the acute event, even the patients with a mammalian target of rapamycin inhibitor-based immunosuppressive therapy (ie, sirolimus). There were no reports of treatment failures or symptom recurrence. One patient presented with a follow-up complication (surgical site infection). All patients returned to their baseline serum creatinine level (Table 1).

Discussion
Our case series shows that patients with AA after kidney transplant have an atypical presentation with a subacute clinical course and a high incidence of complications. Although almost every patient had abdominal pain, only a few presented with typical clinical features (ie, right lower quadrant pain, migratory pain, McBurney sign, guarding, and rebound tenderness). Remarkably, 2 patients presented with symptoms that were compatible with small bowel obstruction, an unusual presentation of AA that has been associated with a delayed diagnosis.8

Many factors may be responsible for these findings, including the distorted anatomy and the immunosuppressive therapy, which in turn may lead to symptom masking, impair the physical examination, and lead to a broadened differential diagnosis.4,9 These findings were reflected in a poor prediction ability of the Alvarado score compared with reported sensitivities of up to 99% in the general population.10 On the other hand, we found only 1 false-negative result with CT scan. This imaging technique has been shown to be the most useful clinical aid in nonimmunosuppressed patients, and it was performed in almost all reported cases of AA after solid-organ transplant with sensitivities of up to 90%.5,11 Therefore, it seems reasonable to perform an abdominal CT scan in the event of suspicion of AA.

The optimal surgical approach and antimicrobial therapy necessary for patients with immunosuppressive treatment are unknown. Although we found a high incidence of periappendiceal abscess and localized peritonitis, all of our patients had an excellent response to laparoscopic or open appendectomy approach, consistent with previous reports. Similarly, although we could not find a causative agent in most cases, in our study all patients received an antimicrobial regimen that covered a mix of aerobic and anaerobic bacteria, mostly Enterobacteriaceae and Bacteroides species with good outcomes (ie, ceftriaxone plus metronidazole, ertapenem). Notwithstanding, opportunistic organisms (eg, Cytomegalovirus) should also be considered as a possible cause of AA in solid-organ transplant recipients.12,13

Regarding duration of antimicrobial therapy, because all patients in our study had evidence of localized peritonitis or a periappendiceal abscess, every patient had an excellent response with a 5- to 7-day antibiotic course as recommended by current guidelines.14 Although every patient continued their basal immunosuppressive therapy, further studies are required to determine whether there is any benefit in withholding or substituting some of them, particularly for patients under mammalian target of
rapamycin inhibitor (sirolimus, everolimus) therapy and wound healing.\textsuperscript{15}

In conclusion, the diagnosis of AA in kidney transplant recipients supposes a clinical challenge that requires a high index of suspicion. However, the therapeutic approach seems not different from the general population.

References