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Acute diverticulitis in heart- and lung transplant patients

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Abstract Significant gastrointestinal complications have been observed in patients following heart- and lung transplantation. These complications can occur in the immediate post-operative period or remote from the time of transplantation. We retrospectively reviewed the medical records of 268 consecutive patients who received either heart- or lung transplants at Henry Ford Hospital between 1985 and 1998. Two hundred and thirty-three patients received heart transplants and 35 underwent lung transplantation. Two patients developed acute

diverticulitis post transplant, both requiring surgery. Management of acute diverticulitis in the heart- and lung transplant population requires a high index of suspicion. Early and aggressive diagnosis is mandatory. Surgical intervention must be prompt when indicated, with meticulous attention to surgical technique. With appropriate intervention, reasonable outcomes can be expected.

Keywords Diverticulitis · Heart transplant · Lung transplant

Introduction

Significant gastrointestinal complications have been observed in patients following heart- and lung transplantation. These complications can occur in the immediate post-operative period or remote from the time of transplantation. In the immediate post-operative period, gastrointestinal complications may be secondary to cardiopulmonary bypass [12, 9] or the immunosuppressive state during induction. During the post transplantation period, disease processes are complicated by the necessity of chronic immunosuppression. With the increasing number of organ transplantations performed, acute diverticulitis has been identified as a cause of increased morbidity and mortality. There has been ongoing controversy in the literature about the need and intensity of screening for diverticular disease prior to transplantation. Authors have suggested pre-transplant screening of all patients for diverticular disease with closer observation and early surgical intervention if symptoms of diverticulitis develop post-transplant [5]. This report de-

scribes our experience with acute diverticulitis and its treatment in a group comprising 233 heart transplant- and 35 lung transplant patients over a 13-year period between 1985 and 1998.

Materials and methods

We retrospectively reviewed the medical records of 268 consecutive patients who received either heart- or lung transplants at Henry Ford Hospital between 1985 and 1998. The proposal was approved by the Internal Review Board of the Department of Research Administration of the Henry Ford Hospital. Patient charts and the Medical Information Management System (MIMS) were used for data extraction.

Results

A total of 268 patients were reviewed. Two hundred and thirty three patients received heart transplants, and 35 underwent lung transplantation. One hundred and

Table 1 Patient demographics

	Heart transplant (n = 233)	Lung transplant (n = 35)	Total (n = 268)
Men	188 (80%)	12 (35%)	200 (75%)
Mean age (men)	49.9 ± 8.2	54.7 ± 5.6	50.2 ± 7.9
Women	45 (20%)	23 (65%)	68 (25%)
Mean age (women)	46.3 ± 9.0	54.0 ± 5.5	48.9 ± 8.3

Table 2 Age distribution

	< 50 years	50–55 years	56–60 years	> 60 years
Heart (n = 233)	109	56	41	27
Lung (n = 35)	8	10	13	4

eighty eight (80%) men and 45 (20%) women received heart transplants. Twelve (35%) men and 23 (65%) women received lung transplants. The mean age of the group reviewed was 49.8 ± 9 years. (Table 1). The distribution of patients amongst different age groups is listed in Table 2.

The immunosuppression regimen most used consisted of Solumedrol 500 mg IV given during transplantation and tapered over 3 days after surgery. On post-operative day (POD)1, antithymocyte globulin (ATGAM) 10 mg/kg was given and continued for 3 days. Azathioprine 1 mg/kg every 12 h was started on POD 2. Cyclosporine in increasing doses of 50 mg, 100 mg, and 150 mg was started on POD 2 to maintain a cyclosporine level between 300 and 400 ng/ml. Prednisone was started on POD 4 (1 mg/kg) and tapered by 5 mg/day to a maintenance level of 15 mg. Pulse steroid therapy and/or OKT3 antibody therapy was applied in cases of acute rejection. If no rejection was evident, cyclosporine levels were reduced to between 200 and 250 ng/ml by the first year, Prednisone was tapered off by 18 months, and Azathioprine was maintained at the 1 mg/kg dose unless side effects required a dose alteration. Patients undergoing lung transplantation did not receive ATGAM. Patients under the age of 50 years were not screened for colonic pathology in the absence of symptoms. Of the 268 patients reviewed, only two patients developed diverticulitis. Both patients had undergone successful heart transplantation 3 years prior to the occurrence of diverticulitis. Neither patient had clinical evidence pre-transplant of diverticular disease. Both patients were maintained on parenteral or oral immunosuppression without interruption while being treated for diverticulitis. Neither patient experienced organ rejection during treatment of diverticulitis.

Patients were considered for heart transplantation if they had moderate to severe heart failure symptoms

despite ideal or maximal treatment, or if they had medical indicators of a very high risk of death (> 50%) within the next year. These indicators include repeated hospitalizations or emergency room visits, recurrent myocardial infarctions, cardiac arrest, serious arrhythmias, worsening metabolic stress tests, and progressive heart enlargement. Patients were not considered good candidates for transplantation if they were older than 65 years, suffered from a serious or terminal illness, e. g. end-stage diabetes mellitus, recent or uncured cancer, AIDS, irreversible dysfunction of other body organ systems, active psychiatric disease, or inadequate family- or financial support. Colonic screening was dependant on the patients general condition. In recent years, patients who were evaluated for transplantation in the outpatient setting usually underwent screening by flexible sigmoidoscopy and, if needed, colonoscopy with the intent of identifying polyps or cancers. Screening was deferred for patients listed for transplantation while admitted to hospital for cardiac or pulmonary failure.

Patient 1 is a 46-year-old Caucasian male who was 3 years post heart transplantation. He presented to the emergency room with a 2-day history of severe left lower quadrant (LLQ) pain and anorexia. The patient was afebrile. On examination, there were signs of diffuse peritonitis. WBC count was 9100/mm³, and abdominal roentgenograms were within normal limits. A CT scan of the abdomen and pelvis revealed a large amount of free intraperitoneal fluid and a phlegmon in the LLQ. He was given stress dose steroids, broad-spectrum antibiotics, and taken to the operating room emergently. He underwent a sigmoid colectomy with end colostomy and Hartman's procedure. He had an uncomplicated post-operative course and was discharged home on POD 9. He returned 3 months later for an uneventful laparoscopic colostomy closure.

Patient 2 is a 50-year-old Caucasian male who, at the time of presentation, was also 3 years post heart transplantation. He presented with a 1-day history of LLQ pain with no associated symptoms. On examination, he had LLQ tenderness with no evidence of guarding, rigidity, or rebound. WBC count was 8800/mm³. A CT scan of the abdomen and pelvis revealed thickening of the sigmoid colon and associated fat stranding. There was no fluid collection or evidence of abscess formation. He was treated with broad-spectrum intravenous antibiotics and discharged home after 7 days. He underwent elective sigmoid resection 6 weeks later. On post-operative day 8 he developed signs and symptoms of sepsis and was found to have an anastomotic leak. He subsequently underwent an emergent operation with creation of end colostomy and Hartman pouch. He had a complicated post-operative course with prolonged intubation and gradual recovery from sepsis. He was discharged from hospital on POD 82.

Pathologic evaluation of resected specimens from both patients showed evidence of diverticulitis with acute- and chronic inflammation, abscess formation, and significant fat necrosis. There was no evidence of cytomegalovirus infection or neoplasm.

Discussion

The incidence of diverticulosis in the United States has been reported to be between 5–45% of which 25% will develop diverticulitis. Of these, only 20% will require surgical therapy [11]. The prevalence of diverticulitis is age-related, with a significant increase in incidence after age 50 [7]. The risk of recurrent diverticulitis is estimated to be from 33–68% with each attack leading to a greater risk of developing complications [6]. Diverticulitis has long been considered a significant cause of morbidity and mortality in the immunocompromised patient. It is a complicated problem associated with a poor prognosis in the immunocompromised individuals. As early as 1950, Beck and associates [4] recognized an increased risk of colonic perforation in patients treated with glucocorticoids. Tyau et al [14] reviewed 209 patients; 169 immunocompetent patients and 40 immunosuppressed patients. They found that in the setting of acute diverticulitis there was an increased risk of free perforation in the immunosuppressed group when compared to the immunocompetent group (43% vs. 14%). They also noted that the immunosuppressed patients required surgery at a higher rate and had significantly higher post-operative morbidity and mortality.

Over the last 30 years, organ transplantation has added significantly to the number of chronically immunosuppressed patients. Our target population of heart- and lung transplant patients was maintained on Prednisone, Azathioprine and cyclosporine. Steroids cause a nonspecific antiinflammatory response by blocking IL-1 production that, in so doing, reduces macrophage chemotaxis, interferes with lymphocyte activation and reduces interleukin production. Azathioprine inhibits lymphocyte proliferation by inhibiting purine synthesis. Cyclosporines mode of action appears to target T-lymphocytes. It blocks transcription of early T-cell activation genes, especially those relating to IL-2, IL-3, IL-4, and TNF. It also inhibits IL-1 production by macrophages. These effects provide a milieu for the development of serious infections. In addition, muting of the inflammatory response alters the expected symptoms, potentially leading to a delay in diagnosis. There is no documented reduction in the incidence of infection in patients receiving the newer immunosuppressive drugs, e.g. cyclosporine and FK506, despite their narrower range of target cells. However, with regards to the effect of these immunosuppressives on diverticular disease, we

are unable to make any assumptions, based on the low incidence in our patient cohort.

The outcome of acute diverticulitis in the renal transplant population has been well examined. Recent reviews have shown that there has been a steady decline in the incidence and severity of colonic perforation in this population over the last 25 years and is currently reported as 0 to 3% [2]. This has been attributed to multiple factors including improved antibiotics, steroid sparing immunosuppressant regimens, sensitive diagnostic modalities, and aggressive surgical intervention. Currently, pre-transplant diagnosis of diverticulosis is not considered an indication for prophylactic colectomy in the renal transplant patient. However, authors have encouraged prompt aggressive medical and surgical therapy when symptoms do develop [11].

Since the advent of cyclosporine, heart- and lung transplantation have become acceptable interventions for end-stage cardiac and pulmonary disease. The incidence of diverticulitis in the heart transplant population has been reported between 0–4% [5]. In our series, of the 268 patients studied (heart- and lung transplants), two patients developed diverticulitis (0.75%). Both were males, 3 years post successful heart transplantation, their ages were 46 and 50 years. Neither patient had clinical evidence of diverticular disease pre-transplant, and thus no colonic screening was undertaken prior to transplantation. Both patients were treated with antibiotics and colectomy, either urgently or delayed. One patient had significant post-operative complications but was eventually discharged from hospital and is doing well.

The diagnosis of diverticulitis or any other intra-abdominal pathology may pose a significant challenge in the immunosuppressed patient, due to alteration of signs and symptoms of the underlying disease process [5]. Constitutional symptoms and physical examination frequently do not reflect the severity of intrabdominal disease. Signs of infection, such as fever and tachycardia, especially in the cardiac transplant patient, may be absent. Abdominal examination may be unimpressive, as clinical signs of inflammation are attenuated in the presence of immunosuppression. Laboratory testing is often unreliable and misleading in estimating the severity of disease. Abdominal radiographs may show free air but may also be non-specific. Abdominal CT scans are the most reliable testing modality in determining the location and degree of pathology [10]. Gastrograffin enema may show spasm or extravasation, but is usually not obtained as part of the initial evaluation. Endoscopy is not indicated in the initial evaluation.

Doses of immunosuppression can be reduced drastically in the face of life-threatening infection in most transplant recipients. However, this is not possible after cardiac transplantation, as there are no feasible support systems for irreversible cardiac failure. Therefore, the

management of diverticulitis in cardiac transplant population must be prompt with early attempts at determining the severity of disease via CT scanning. Broad-spectrum intravenous antibiotics should be administered early. If bowel perforation is suspected, early operative intervention is indicated. Bowel resection and colostomy are commonly required. In the setting of uncomplicated diverticulitis, it is prudent to proceed with colectomy following resolution of the acute episode, provided the patient is a reasonable operative candidate.

Several series addressing the issue of diverticulitis in the heart- and lung transplant population have been published. Between 1985 and 1996, six series reviewing a total of 986 patients are available [1, 3, 5, 8, 13, 14]. Eighteen patients developed diverticulitis following transplantation. Fifteen patients survived. In our series of patients, the incidence of diverticulitis was 0.75%. Although prophylactic colectomy has been suggested in the renal transplant population with diverticular disease prior to transplantation, this may not be a feasible

or safe option for patients awaiting cardiac transplantation. The low incidence of diverticulitis does not justify a potentially morbid operation in the setting of end-stage cardiac disease. None of our lung transplant patients developed diverticulitis, but a similar approach seems reasonable.

We can conclude that the incidence of diverticulitis in the heart- and lung transplant population is not significant enough to justify routine pre-transplant screening for diverticulosis in the absence of symptoms. Prophylactic colectomy prior to transplantation in the presence of diverticular disease is not feasible in the face of end-stage cardiac or pulmonary dysfunction. Management of acute diverticulitis in the heart- and lung transplant population requires a high index of suspicion. Early and aggressive diagnosis is mandatory. Surgical intervention must be prompt when indicated, with meticulous attention to surgical technique. With appropriate intervention, good outcomes can be expected.

References

1. Augustine SM, Yeo CJ, Buchman TG, Achuff SC, Baumgarten WA (1991) Gastrointestinal complications in heart and heart-lung transplant patients. *J Heart Lung Transplant* 10: 547-556
2. Bardaxoglou E, Maddern G, Ruso L, Siriser F, Campion JP, Le Pogamp P, Catheline JM, Launois B (1993) Gastrointestinal surgical emergencies following kidney transplantation. *Transpl Int* 6: 148-152
3. Beaver TM, Fullerton DA, Zamora MR, Badesch DB, Weill D, Brown JM, Campbell DM, Grover FL (1996) Colon perforation after lung transplantation. *Ann Thorac Surg* 62: 839-843
4. Beck JC, Brown JSL, Johnson LG (1950) Occurrence of peritonitis during ACTH administration. *Can Med Assoc J* 62: 423-426
5. Detry O, Defraigne JO, Meurisse M, Bertrand O, Demoulin JC, Honore P, Jacquet N, Limet R (1996) Acute diverticulitis in heart transplant recipients. *Transpl Int* 9: 376-379
6. Greene WW (1957) Diverticulitis of the colon: radical vs. conservative treatment. *Am J Surg* 94: 282-289
7. Hughes LE (1969) Postmortem survey of diverticular disease of the colon. Diverticulosis and diverticulitis. *Gut* 10: 336-351
8. Krana MJ, Flanbaum L, Trooskin SZ (1998) Gastrointestinal complications after cardiac surgery. *Surgery* 104: 773-780
9. Kirklin JK, Holm A, Aldrete JS, White C, Bourge RC (1990) Gastrointestinal complications after cardiac transplantation. *Ann Surg* 211: 538-542
10. Labs JD, Sarr MJ, Fishman EK, Siegelman SS, Cameron JL (1998) Complications of acute diverticulitis of the colon: improved early diagnosis with computer tomography. *Am J Surg* 155: 331-335
11. Lenderman ED, Conti DJ, Lempert N, Singh TP, Lee EC (1998) Complicated diverticulitis following renal transplantation. *Dis Colon Rectum* 1998: 613-618
12. Mercado PD, Farid H, O'Connell T, Sintek CF, Pfeffer T, Khonsari S (1994) Gastrointestinal complications associated with cardiopulmonary bypass procedures. *Am Surg* 60: 789-792
13. Steed DL, Brown B, Reilly JJ, Peitzman BP, Griffith BP, Hardesty DL, Webster MW (1985) General surgical complications in heart and heart-lung transplantation. *Surgery* 98: 739-744
14. Tyau ES, Prytowsky JB, Joehl RJ, Nahrwold DL (1996) Acute diverticulitis: a complicated problem in the immunocompromised patient. *Arch Surg* 126: 855-859
15. Watson CJE, Jamieson NV, Johnson PS, Wreghitt T, Large S, Wallwork J, English TAH (1991) Early abdominal complications following heart and heart-lung transplantation. *Br J Surg* 689-704