Original Article

Colon cancer in lung transplant recipients with CF: Increased risk and results of screening

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Received 8 April 2011; accepted 17 May 2011
Available online 12 June 2011

Abstract

Objective: To determine the incidence of colon cancer in lung transplant recipients with cystic fibrosis (CF) and review screening colonoscopic findings in other recipients with CF.

Methods: A retrospective chart review was performed for all patients with CF transplanted at the University of Wisconsin Hospital and Clinics (January 1994 through December 2010).

Results: Four of 70 transplant recipients with CF developed fatal colon carcinoma following transplantation, and the cancer was advanced in all 4 recipients (age 31, 44, 44, 64) at the time of diagnosis. In contrast, only one of 287 recipients transplanted for non-CF indications developed colon cancer. Of all recipients with CF who did not develop colon cancer, 20 recipients underwent screening colonoscopy at 1 to 12 years following transplantation. Seven (35%) of the screened transplant recipients (ages 36, 38, 40, 41, 43, 49, 51) had colonic polyps in locations ranging from cecum to sigmoid colon and up to 3 cm in diameter.

Conclusions: In contrast to non-CF recipients, patients with CF displayed a significant incidence of colon cancer (4 of 70 recipients; 5.7%) with onset ranging from 246 days to 9.3 years post-transplant, which may be due to a combination of their underlying genetic disorder plus intense, sustained immunosuppression following lung transplantation. Colonoscopic screening may identify patients with pre-malignant colonic lesions and prevent progression to colonic malignancy.

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Keywords: Colon cancer; Cystic fibrosis; Lung transplant

1. Introduction

Cystic fibrosis of the pancreas (CF) is a genetic disorder caused by various mutations of the cystic fibrosis transmembrane regulator (CFTR), which causes dysfunction of epithelial membranes of the gastrointestinal and respiratory systems [1]. Most adults with CF will eventually develop advanced bronchiectasis and respiratory insufficiency, and CF is the third most common indication for which lung transplantation is performed and the most common indication for bilateral lung transplantation [2]. As more patients with severe CF lung disease undergo lung transplantation, several issues that are somewhat unique for this transplant indication can present significant management issues [3,4]. These complications include diabetes mellitus, liver disease, paranasal sinus disease, osteoporosis and gastrointestinal dysfunction (pancreatic insufficiency, biliary tract dysfunction, and impaired intestinal motility).

Colorectal cancer is the third most common malignancy diagnosed in the general population of the United States, and it ranks second in mortality [5]. The risk of gastrointestinal malignancy has been reported to be increased in patients with CF [6], and colonic adenocarcinoma has been reported in patients ranging in age from 13 to 41 [7-11]. Sustained, intense
immunosuppression may also increase the risk of malignancy in lung transplant recipients. Although colonoscopy has been shown to decrease the risk of colonic malignancy in the general population by detecting pre-neoplastic polyps that can be endoscopically removed [12-14], screening colonoscopy may not be performed in relatively young patients with CF who undergo lung transplantation. Guidelines for colorectal cancer screening usually recommend the first screening at age 50 years [12].

2. Methods

We performed a retrospective chart review of all CF LTX recipients with CF at University Hospital and Clinics who were transplanted from 1994 through 2010. We identified all patients who developed colon cancer, and we reviewed screening results for all CF patients who had colonoscopy performed at various time points post-transplant. This study was approved by the University of Wisconsin Human Subjects Committee (Approval #M-2008-1093).

3. Results

Demographics of all patients (CF and non-CF indications) transplanted at UWHC are given in Table 1. Four of the 70 recipients with CF followed by the University of Wisconsin Hospital and Clinics from 1994 to 2008 developed metastatic cancer of colonic origin, and none of these individuals had undergone colonoscopic screening (Table 2). In contrast, only one patient transplanted for other indications (N=287) through December 2010 had developed colon cancer. Three of the 4 recipients with CF were under age 50 years at the time they developed bowel symptoms and were diagnosed with colon cancer. Diagnoses were made after the onset of abdominal symptoms in all 4 patients, and diagnostic studies consisted of radiologic imaging and colonoscopy in all. All patients who developed colon cancer were receiving tacrolimus as their immunosuppressive drug regimen that recipients must receive to prevent allograft rejection. In contrast to our recipients with CF due to impaired tumor surveillance as a consequence of the intense immunosuppression required to prevent lung allograft rejection. In contrast to our recipients with CF, only one of our non-CF recipients has been diagnosed with colon cancer.

When the third patient with colonic adenocarcinoma was diagnosed, we recommended post-transplant colonoscopic screening for all recipients with CF who were willing to give consent for such. Colonic polyps were identified in 7 of the 20 (35%) recipients who underwent screening colonoscopy at various time intervals ranging from 1 to 12 years after undergoing lung transplantation (Table 3). One patient had 7 polyps at the first screening procedure including a 3 cm diameter sessile tubulovillous adenoma, and this patient had another polyp at repeat colonoscopy 425 days following the first procedure, and 8 new polyps were found 337 days following the second colonoscopy. All seven patients in whom polyps were identified had multiple polyps, and two other patients had tubulovillous adenomas up to 1 cm diameter.

4. Discussion

Patients with CF can develop numerous GI complications that are linked to CFTR dysfunction. These include complications of intestinal dysmotility (gastric bezoars, distal intestinal obstruction syndrome), biliary tract dysfunction (gastroesophageal reflux, mucosal ulcerations, hepatic cirrhosis, cholelithiasis, cholecystitis, biliary obstruction, acute pancreatitis, pseudomonas colitis, fatty liver), and gastrointestinal malignancy [15-20]. These potential complications can complicate the post-transplant course of patients and cause significant morbidity or death, and the immunosuppressive drug regimen that recipients must receive to prevent allograft rejection can cause adverse GI reactions (nausea, diarrhea) or increase the risk of infectious complications (enteric cytomegalovirus infection, pseudomembranous colitis, other GI tract infection).

It is estimated that 20–35% of the general population will have a colorectal adenoma detected at age 50 or beyond [14], and 20–50% of these individuals will have additional lesions detected at followup examinations performed within 3–5 years of the initial colonoscopy [14]. The presence of colorectal adenomas predicts an increased risk of developing colorectal cancer [14], and it is widely accepted that colon adenocarcinomas arise via conversion of a subset of adenomas to cancerous lesions [14,21-24].

Although the overall incidence of malignant disease in patients with CF has been reported to be within the expected range [24], patients with CF appear to have an increased risk of developing gastrointestinal malignancies [6,24]. Patients of age 13, 18, 30, 31, 41 at the time of diagnosis of colon cancer have been reported in the medical literature [7-11]. The risk for developing colon cancer at a young age may be increased for lung transplant recipients with CF due to impaired tumor surveillance as a consequence of the intense immunosuppression required to prevent lung allograft rejection. In contrast to our recipients with CF, only one of our non-CF recipients has been diagnosed with colon cancer.

5. Summary and conclusions

Carcinoma of colonic origin can be a devastating complication following successful bilateral lung transplantation for end-stage lung disease in patients with CF. Four of 65 (6.2%) lung
transplant recipients for CF at our institution who survived beyond 6 months post-transplant developed fatal colonic adenocarcinomas, and 7 of 20 recipients (35%) who underwent screening colonoscopy had polyps that ranged from 2 to 30 mm in diameter. We suggest that lung transplant programs should consider early (and perhaps sequential), screening colonoscopy regardless of age for adult patients with CF following lung transplantation to detect and remove pre-malignant lesions. Individuals found to have colonic polyps at screening colonoscopy should likely have more frequent followup colonoscopic procedures, as these individuals may be at considerable risk to develop additional adenomas that may undergo malignant transformation.

References


