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Cholangiocarcinoma and Sclerosing Cholangitis: Clinical Characteristics and Effect on Survival After Liver Transplantation

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ORTHOTOPIC liver transplantation (OLTx) has emerged during the last decade to be the most effective therapy for patients with advanced primary sclerosing cholangitis (PSC).[1-3] The potential risk of developing cholangiocarcinoma (CCA) in these patients triggered the current study to define the clinical characteristics of patients with concomitant CCA and its effect on patient survival after transplantation.

MATERIALS AND METHODS

Patient Population

Over a period of 9 years (December 1981 to December 1990), 169 adult patients with the diagnosis of advanced PSC underwent OLTx at the University of Pittsburgh Medical Center. Eighteen of these 169 consecutive patients were found to have a concomitant CCA, with an incidence of 10.6%. The diagnosis of CCA was known preoperatively in only 7 patients (38.9%). Standard total hepatectomy was performed, with the exception of 1 case of upper abdominal exenteration. The primary immunosuppressive drug was cyclosporine in 81% and FK 506 in 19% of the patients. Adjuvant radiotherapy and chemotherapy were given before and/or after transplantation in 11 patients.

Statistical Analysis

The sex, presence or absence of inflammatory bowel disease (IBD), and histologic stage of PSC[4] were compared in patients with PSC alone and those with PSC and CCA using Pearson's chi-square test of association. The age, duration of both IBD and liver disease, and the pretransplant serum bilirubin, alkaline phosphatase, and γ-GTP were also compared using two-tailed Student's t test. The survival curves were generated using the Kaplan–Meier method and were compared utilizing the generalized Wilcoxon (Breslow) test.

RESULTS

The age, gender, duration of liver disease, presence or absence and duration of IBD, and histologic stage of PSC were similar for patients with PSC alone and those with PSC and CCA ($P > .05$). Also, there was no significant difference between the two groups comparing the pretransplant serum bilirubin, alkaline phosphatase, and γ-GTP levels ($P > .05$).

A thorough histologic examination of the hepatectomy specimen revealed the coexistence of CCA in 11 patients in addition to the 7 who were diagnosed before OLTx. The tumor was intrahepatic in 2 patients (11.1%), hilar in 13 (72.2%), and involving gallbladder or cystic duct in 3 (16.7%). Tumor was at the resection margin in 6 cases (33%) and hilar lymph nodes were positive in 3 (16.7%). The tumor cells were well differentiated in 11 patients (61%). Patients with incidental CCA had a slightly higher incidence of positive resection margins (36.4%) than did those diagnosed before OLTx (28.6%).

The mean (±SD) post-OLTx follow-up time for all patients was 43 ± 29 months (range, 0 to 117 months). The 1-year survival rate for patients with PSC alone was 85% compared to 72% with PSC and CCA, and the survival rates at 5 years were 75.8% and 26.7%, respectively ($P = .0001$). The total mortality rate with prediagnosed CCA (85.7%) was higher than with incidental tumors (54.5%) and the actuarial 2-year survival rates were 28.6% and 54.6%, respectively ($P = .37$). The median survival time was 14 months for the prediagnosed CCA patients and 23 months for the incidental group. Only one patient in the prediagnosed group is still alive with no evidence of recurrence 26 months after OLTx. In the incidental group 5 patients are still alive, free of tumor 23 to 73 months after transplantation.

DISCUSSION

The risk of developing CCA in patients with PSC has been previously documented by different centers.[5-7] The total incidence of CCA in the PSC patients who underwent OLTx over 9 years at our institute was 10.6%. Although this estimate of prevalence may have been influenced by a referral bias to our transplant center, a similar incidence has been reported by other centers.[5-9] The epidemiologic, pathogenic, and immunologic mechanisms of such association have yet to be defined.

The current diagnostic tools are inadequate for early detection of CCA occurring in the setting of PSC. This is demonstrated in the current study by the high incidence of failure to diagnose CCA before transplantation (61.1%), despite an active attempt to do so. Comparing the preoperative data, there were no clinical distinctions between patients with PSC and CCA and those with PSC alone. Similar to other studies, no other laboratory features

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reliably distinguished patients with CCA in the setting of PSC.[5,8] Also, the histologic stage of PSC did not correlate with the presence of CCA.

The presence of CCA in patients with PSC markedly reduces survival after OLTx. In this and earlier reports published from our center,[3,10] the diagnosis or detection of CCA in PSC patients significantly influences the long-term outcome after transplantation. However, patients with incidental CCA have a better survival rate after OLTx compared to those identified before transplantation.

It is clear from these data that CCA occurring in the setting of PSC is nearly always detected at an advanced stage of the disease that precludes a cure after OLTx for most patients. In conclusion, (1) cholangiocarcinoma adversely influences the survival of patients transplanted for PSC and (2) patients with a preoperative diagnosis of CCA do worse than those with incidental CCA. An obvious need for better diagnostic tools for CCA exists in patients with PSC.

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