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Prolonged Survival After Liver Transplantation and Cancer Chemotherapy for Advanced-Stage Hepatocellular Carcinoma

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LIVER transplantation for advanced-stage hepatocellular carcinoma (HCC) has been associated with high tumor recurrence rates and poor long-term survival.[1,2] Cancer chemotherapy for HCC using standard drugs administered intravenously has also been associated with poor survival and negligible response rates.[3] However, several recent reports have indicated reproducible response rates involving greater than 50% of patients when various anticancer agents have been administered via the hepatic artery for the treatment of HCC.[4,5] We therefore investigated the feasibility of combining both treatment modalities, to determine whether chemotherapy-induced tumor cell destruction prior to surgical manipulation might decrease post-orthotopic liver transplantation (post-OLTx) tumor recurrences and thus enhance survival.

MATERIALS AND METHODS

Patients with advanced stages III and IVa HCC who were considered for OLTx because of extensive unresectable tumor or tumor that was unresectable due to underlying cirrhosis were offered pretransplant intrahepatic arterial chemotherapy if their bilirubin was less than 2.5 mg/dL, their platelets were greater than 50,000 per milliliter, and there was no uncorrectable coagulopathy. Not all patients accepted this treatment and many patients with Child's class C cirrhosis could not be considered for it. Chemotherapy was given into the right or left hepatic artery using 60 mg/m^2 doxorubicin and 100 mg/m^2 cisplatin in 100 mL of normal saline administered by slow infusion over 30 minutes. They also received 3 million units of α-interferon subcutaneously, three times per week continuously. Treatments were repeated every 4 weeks, blood counts permitting, for a minimum of three cycles. Thereafter, patients were placed on the liver transplant candidate list to await a donor liver and received continued monthly cycles of chemotherapy until the time of transplantation. All patients received FK 506 as immunosuppressant whether or not they received chemotherapy. Patients receiving chemotherapy and a transplant continued with the same chemotherapy with drugs, but administered intravenously for a nominal 12 monthly cycles after transplantation.

RESULTS

Eleven patients were treated with preoperative chemotherapy and had a minimum of 12 months' posttransplant follow-up or have died (Table 1). One patient had recurrence at 7 months and subsequently died within 1 year. There were no other new recurrences and no other deaths in this group within the first year (91% 1-year survival, 82% disease-free). A second patient had a recurrence at 14 months and died at 15 months posttransplant. A third patient had unrecognized lung metastases at the time of transplant and continues with slowly progressive disease at 16 months' post-OLTx follow-up. The second group of 14 patients had either no chemotherapy or could not tolerate the first cycle of chemotherapy so cancer chemotherapy was thus subsequently abandoned. Nine patients in this group had recurrence within 1 year and 8 patients died within 1 year of transplant (43% 1-year survival, 36% disease-free). During this study period an additional 20 patients were seen with similar advanced-stage nonmetastatic HCC who had Child's class C cirrhosis and could not

Table 1. Results of Liver Transplantation for Hepatocellular Carcinoma

Patient	Post-OLTx Recurrence (Months)	Post-OLTx Survival (Months)	HCC Stage
Chemotherapy			
1	0	25*	III
2	8	25*	IVa
3	0	21*	IVa
4	0	21*	III
5	0	17*	III
6	—†	16*	IVb
7	14	15	IVa
8	0	13*	IVa
9	0	13*	III
10	7	8	IVa
11	0	12*	III
No chemotherapy			
1	5	17	IVa
2	1	8	IVa
3	6	12	IVa
4	2	6	IVa
5	6	9	IVa
6	0	16*	III
7	5	11	IVa
8	2	5	III
9	5	9	IVa
10	20	24	III
11	0	17*	III
12	14	25*	III
13	5	6	IVa
14	23	33*	IVa

*Ongoing survival.
†Unrecognized lung metastases at the time of OLTx.

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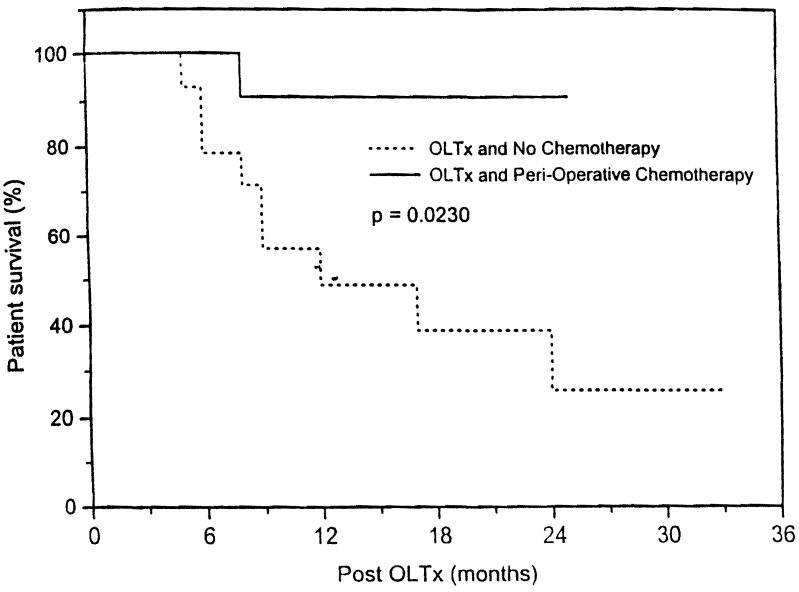

Fig 1. Post-OLTx survival rates for patients with hepatocellular carcinoma.

receive chemotherapy because of their advanced underlying liver disease. None of these patients survived long enough for liver transplantation; the median survival was 3 months (Fig 1).

DISCUSSION

This pilot study shows that it is feasible to give a subset of patients with advanced-stage HCC intraarterial chemotherapy prior to liver transplantation. This set of patients includes those without cirrhosis or with Child's class A cirrhosis. Patients with Child's class B cirrhosis were heterogeneous with regard to their ability to tolerate the chemotherapy. No patients with Child's class C cirrhosis fitted our inclusion criteria for the safe administration of chemotherapy. Although the numbers are small and the follow-up is limited, there appears to be a significant difference in the survival rates at 1 year between patients receiving a liver transplant with cancer chemotherapy and those receiving a liver transplant without chemotherapy.

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