However, arrest and control of the malignant process have been accomplished under some of the least likely circumstances, as with the woman who had pulmonary and peritoneal seeding from a sarcoma at the time of transplantation, the recipient with epitheloid hemangioendothelial sarcoma, and the patient with a conventional hepatoma. There has been no identifiable reason why the patients were spared recurrence and why the others were not.

Liver transplantation will have to be tied to some other kind of therapeutic effort in future trials. The usual approach of giving adjuvant chemotherapy will not be good enough, as was shown in two of our recent patients with nonfibrolamellar hepatocellular carcinomas who developed metastases within a few months in spite of very aggressive prophylactic treatment with adriamycin and other chemotherapeutic agents. Huber et al.[14] have described a novel approach in which two patients with metastatic liver disease had liver replacement as well as total body irradiation, chemotherapy, and bone marrow transplantation. One of their recipients whose original disease was a carcinoma of the breast was alive 3 years later after liver replacement and was free of tumor.[15]

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Discussion

DR. PAUL RUSSELL (Boston, Massachusetts): All of us know that the Pittsburgh experience is unique, impressive, and, from what we have heard today, quite helpful.

In Boston we are just beginning our efforts in liver transplantation. We have a combine of four hospitals (the New England Deaconness, Tufts-New England Medical Center, Children's, and Massachusetts General Hospital), which has now achieved something over 50 transplants.

At the Massachusetts General Hospital, we have four patients who received liver transplants for malignant disease. One patient with a primary cholangiocarcinoma succumbed to rapidly progressive metastatic disease less than a year after transplantation. The three others are alive within a year. It seems from the experience of Starzl and his colleagues that many of these patients, even with primary liver tumors, already have tumor outside the liver when they come for treatment.

The question is clearly whether we can better identify patients whose tumors are still confined to the liver. My questions to Dr. Iwatsuki are: What place, if any, does he think that preliminary exploration of the abdomen has? That is, should a "first look" with careful evaluation of lymph-node spread always be done? Also, are there any other diagnostic measures we might use in selecting patients with liver tumors who will most benefit from transplantation?

DR. J. P. O'LEARY (Dallas, Texas): Dr. Iwatsuki, this paper causes me to think of two things.

Number one, you suggest that further chemotherapy will be necessary. Have you had any experience with such treatment?

Number two, the new liver seems to harbor the major area for the recurrence. Is this actually recurrence from another deposit of tumor in the abdomen, or is this a new primary tumor?

DR. JAMES H. FOSTER (Farmington, Connecticut): Dr. Iwatsuki, can you tell us anything about liver transplantation for secondary or metastatic cancer?

DR. SHUNZABURO IWATSUKI (Closing discussion): Thank you very much, Dr. Russell. To answer your question as to how to select the patients, the way we usually handle the cancer patient for transplant is that we set up liver transplantation for two patients; the first patient, who is known to have a malignancy, and the second patient, who is known to have a benign disease. We start the operation earlier than the usual time and explore the cancer patient first. If the patient has extrahepatic involvement of the tumor, we stop the procedure there and call for the second patient.

Answering the question of Dr. O'Leary, as I mentioned briefly during the presentation, we have tried chemotherapy after transplant before the recurrence. Adriamycin® was used in a pretty heavy dose in a short period of time for a few patients with hepatomas. Two patients who had hepatoma suffered a recurrence within 3 months in spite of the chemotherapy. Therefore, we need more effective chemotherapeutic agents, or something else has to be added to liver replacement.

Answering the question of Dr. Foster, we have not done any transplantation for the patient with secondary metastasis. The Cambridge group and the Hanover group tried in several patients with metastatic liver malignancy, and they all died in 1 year with aggressive metastasis.

Answering the question of whether the liver tumor after transplant is actually a recurrence or a *de novo* tumor, we do not know it for sure, but histologic characteristics of the recurrent tumor were quite similar to the original tumor that the recipient had before transplant, and there was almost always extrahepatic involvement by the time liver tumor was clinically detected.