

Cancer in Transplantation: Prevention and Treatment

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Primary Bronchogenic Carcinoma in Transplant Recipient

Delcambre F., Ramon P., Noel C., Pol A., Declercq N., Gosselin B., Wautz A., Laffite J.J., Dracon M. and Pruvot FR. CHU-Lille France.

The risk of malignancy is a well-recognized event in long term transplant recipients. Incidence, average age of appearance, evolution, and response to treatment may differ from the general population and depend on varieties of neoplasms. Lung cancer has been reported as a specific risk of heart transplant recipients. We present 8 cases of lung cancer from 892 kidney, heart, and liver transplant recipients in which risk factors and management are discussed.

Patients and methods. Among kidney (n = 564), heart (n = 240), and liver (n = 88) recipients transplanted from January, 1986 to December, 1994, eight cases of primary bronchogenic carcinoma were included in this study. All transplanted patients received cyclosporine. No correlation could be made between immunosuppression, rejection, CMV infection and appearance of cancer (table 1).

Table 1	organ	age (1)	smoking	ALG(3)	Immunosuppression (4)	Rejection crisis (n)	Rejection treatment	Rejection disease	CMV
obs 1	kidney	64	20	+	CSA+ IM+ CS	0	-	-	-
obs 2	kidney	56	0	+	CSA+ CS	0	-	-	-
obs 3	liver	52	60	-	CSA+ IM+ CS	2	ALG	+	+
obs 4	liver (*)	50	50	-	CSA+ IM+ CS	2	OKT3+SAL	-	-
obs 5	heart	46	60	+	CSA+ IM+ CS	0	-	-	-
obs 6	heart	50	60	+	CSA+ IM+ CS	2	ALG	-	-
obs 7	heart	62	50	+	CSA+ IM+ CS	1	CS	-	-
obs 8	heart	54	60	+	CSA+ IM+ CS	0	-	-	-

(1): age at time of transplantation (years), (2): packs of cigarettes per day per years, (3): induction therapy, (4): CSA: cyclosporine; IM: Imurel; CS: Prednisone; (*) retransplantation for chronic rejection before cancer.

Results. The delay between transplantation and diagnosis of lung cancer was either <1 year (n=3) or > 4 years (n=5). A majority of patients (n=4, 3/4 heart recipients) had small cell lung cancers with high TNM stage of which three died from early (< 230g) dissemination. Four non small cell cancers could be resected with no post-operative death. Five patients survived more than 6 months (table 2).

Table 2	Symptoms	Delay (1)	Histology	Stage (2)	Treatment	Survival
obs 1	chest X ray	6	epidermoid	pT2N2M0	lobectomy + RT (3)	alive 8 months
obs 2	chest X ray	48	small cell	T4N2M1	chemotherapy	alive 6 months
obs 3	fever	6	adenocarcinoma	pT2N0M0	lobectomy	died 21 months (4)
obs 4	chest X ray	57	epidermoid	pT2N0M0	lobectomy	alive 20 months (4)
obs 5	chest X ray	57	small cell	T1N2M0	chemotherapy	died 4 months
obs 6	dyspnea	69	epidermoid	pT2N1M0	pneumectomy + RT	alive 10 months (4)
obs 7	chest X ray	11	small cell	T3N2M1	none	died 2 months (4)
obs 8	cough	82	small cell	T4N3M1	none	died 2 months

(1): months (2): at diagnosis (3): radiotherapy (4): with bone dissemination

Discussion. Incidence of bronchogenic cancer is high (0.9% in transplanted patients and occurs at a younger age as compared to general population. Diagnosis is often made by chest X ray especially in small cell cancer. Pulmonary resection in non small cell cancer is a safe procedure in spite of immunosuppression, but prognosis is altered by secondary dissemination. Recipients with smoking history should be submitted to a special high frequency broncho-pulmonary investigation program.

MISDIAGNOSED MALIGNANCY IN TRANSPLANTED ORGANS.

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Organ transplantation has become the treatment of choice for a growing number of terminally ill patients. The increase number of procedures increase the number of complications related to transplantation and to the immunosuppression. We report our experience in the transferral of malignancy by grafting cancerous organs into recipients, which is a rare but disastrous complication of transplantation.

CASE REPORTS

Donor 1 was a 50-year-old female died from nontraumatic cerebral hemorrhage. A multiorgan harvest was performed, and the liver and the left kidney were explanted and transplanted to recipient 1 and 2, respectively. The right kidney was rejected for vascular and urological abnormalities. Necropsy revealed a nodule in the right kidney, and three hemorrhagic nodules in the right lung. Histopathological analysis of these nodules demonstrated the presence of a choriocarcinoma. Later serum analyses revealed very high levels of β -HCG.

Recipient 1 was a 20-year-old female who received the left kidney from donor 1. Graft CT-scan demonstrated a 2-cm nodule, and the immunosuppression was interrupted. Transplantation was performed on postoperative day 12 but β -HCG levels rose. A chemotherapy was undergone, which succeeded in normalizing the β -HCG level. Two years later, the patient was retransplanted and since then shows no evidence of recurrence.

Recipient 2 received the liver from donor 1. His β -HCG levels rose despite normal graft CT scan. The patient died on day 39 from pulmonary complications, and autopsy showed 3 choriocarcinoma metastasis in the hepatic graft.

Donor 2 was a 35-year-old female died from a nontraumatic cerebral hemorrhage. Paraortic adenopathy was noticed during multiorgan harvesting. The liver, the heart and the kidneys were transplanted in 4 different centers. The results of the histopathological examination conducted that the paraortic and pulmonary nodes were positive for a disseminated epidermoid epithelioma, originating from the cervix uteri.

Recipient 3 was a 25-year-old man who received the liver from donor 2 in our department. The patient was retransplanted on postoperative day 7 and no evidence of malignancy was detected on histopathological analysis examination on the graft.

Donor 3 was a 55-year-old female who died from cerebral hemorrhage in another country. We received one kidney, and we found a 4-cm nodule in this organ. Frozen section of this lesion showed a renal adenocarcinoma and transplantation was aborted in our center and in the centers which received the other kidney and the heart from the same donor.

DISCUSSION
As these cases demonstrate, the transferral of malignancy with organ transplantation may rarely but dramatically complicate the postoperative outcome of recipients. Its medical management is difficult, and its psychological impacts on the recipients may be disastrous. The transplant centers, both small and large, must be prepared for such an eventuality. Due to the organ shortage, the transplant teams must be avoided. The use of donors with previously successfully treated cancer should be totally excluded, excepted the primary supratentorial cerebral tumors. However, as in our cases, the donor's cancer is often non diagnosed. Careful examination of the abdomen and the thorax must be performed during the harvesting, and histopathological analysis of suspected nodules must be available before the transplantation. Postoperative echography and postharvesting autopsy may be helpful. If a recipient was transplanted with a kidney harvested from a cancerous patient, the immunosuppression must be discontinued and the graft must be explanted. Specific chemotherapy must be initiated if primary tumor is proven sensitive to treatment. Hepatic allografts are not immediately expandable, and they must remain in situ until another graft is available.