

## Esophageal squamous cell carcinoma after liver transplantation

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The occurrence of an oesophageal squamous cell carcinoma following liver transplantation is very infrequent. Such an event has been related to a history of alcohol-induced cirrhosis, as in other squamous cell tumours of the oropharynx. We report the case of a 64-year-old male patient diagnosed as having oesophageal squamous cell carcinoma six years after having had a liver transplant due to alcohol-induced cirrhosis. The tumour was treated surgically and consisted of an Ivor-Lewis oesophagectomy. The patient is disease-free 17 months after surgery. A review of the cases reported in the literature indicated treatment with chemotherapy and radiation therapy, and with excision in some cases. Generally, despite aggressive treatment the prognosis is poor.

**Key words:** oesophageal squamous cell carcinoma, liver transplantation, alcohol-induced cirrhosis, *de novo* malignancies.

Díaz de Liaño A, Artieda C, Yáñez C, Garde C, Flores L, Ortiz H. Esophageal squamous cell carcinoma after liver transplantation. *Clin Transl Oncol*. 2005;7(11):518-20.

### INTRODUCTION

Patients undergoing liver transplantation have an increased incidence of malignant diseases following transplantation as compared to the general population<sup>1-4</sup>. However, the occurrence of an esophageal carcinoma is an exceptional event in such patients.

### CASE REPORT

A 64-year-old male with a history of alcohol-induced cirrhosis who had undergone a liver transplant six years before with a good subsequent graft function. He

was on immunosuppressive therapy with tacrolimus (3 mg/24 hours). The patient reported dysphagia for solids and a slight weight loss over the past four months. He had a history of non insulin-dependent diabetes mellitus and hyperlipidemia on drug treatment. An esophagoscopy revealed a polypoid, sessile, irregular lesion, located from 33 cm to 36 cm from the dental arcade, that involved half the esophageal circumference but did not prevent passage of the endoscope. Biopsies were reported as "squamous cell carcinoma". At echoendoscopy, a lesion of approximately 3 cm in length, of semicircular growth, was seen to involve all esophageal layers. Computed tomography showed no hepatic or pulmonary metastases, nor locoregional adenopathies. Upper gastrointestinal transit with contrast revealed a stenotic, irregular area at the junction of the middle and lower esophageal thirds. The rest of the esophagus and stomach were normal (fig. 1).

Based on the history of liver transplantation, a selective preoperative arteriography was performed of the upper mesenteric artery and celiac trunk, that showed a normal gastric vascularization.

In view of the clinical and radiological findings where no evidence of local or distant metastases were found and as the patient was fit to undergo an operation, surgical treatment was decided. A median laparotomy and a right thoracotomy were performed, and an esophageal tumor was found approximately 8 cm below the arch of the azygos vein. The tumor was approximately 4 cm in length and involved 60% of the esophageal circumference. No other findings were assessed. A subtotal Ivor-Lewis esophagectomy and two-field lymphadenectomy were performed.

The pathological examination of the surgical specimen was reported as moderately differentiated, ulcerated squamous cell carcinoma (3.4 cm) infiltrating the whole thickness of the wall, including the adventitia, and another different 8 mm squamous cell carcinoma in the cardia, which was not identified in the preoperative study and during the surgical intervention, infiltrating the mucosa and submucosa. The seventeen lymphatic nodes obtained were free of tumor (pT3N0).

The early postoperative period was uneventful. The patient tolerated well oral feeding, and was discharged from hospital with no postoperative complications.

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Received 18 May 2005; Revised 5 July 2005; Accepted 11 July 2005.



**Fig. 1. Computed tomography showing no hepatic or pulmonary metastases nor locoregional adenopathies.**

The patient did not received any kind of complementary treatment. 17 months after surgical resection, he is asymptomatic and with no evidence of relapse.

## DISCUSSION

The risk of developing *de novo* malignancies after transplantation of a solid organ is increasing. Incidence of *de novo* tumors in such patients is approximately two-fold greater as compared to the general population, ranging from 5% and 15%<sup>5</sup>. Occurrence of such malignancies following kidney and heart transplantation has been studied and is well known, whereas the incidence after a liver transplantation is less well understood<sup>6</sup>, although some papers have reported a prevalence similar to that found after transplantation of other solid organs<sup>2,6</sup>.

Esophageal squamous cell carcinoma is a condition that occurs very rarely following liver transplantation<sup>1</sup>. Esophageal squamous cell carcinoma seems to be related to chronic exposure to alcohol. This risk factor seems to be less important in patients undergoing transplantation for non alcohol-related liver diseases. Immunosuppression may enhance the oncogenic effects of pre-transplant alcohol consumption<sup>1,6</sup>. In the reported cases of esophageal squamous cell carcinoma after liver transplantation, its occurrence has been related to a history of alcohol-induced cirrhosis, however, immunosuppressive therapy has also been implicated<sup>1,5,6</sup>.

Liver transplantation may be associated to an accelerated evolution of precancerous cells towards malignization, as has been seen for some skin and colonic tumors and in Barrett's esophagus<sup>5,7,8</sup>. In the few cases reported of esophageal adenocarcinoma after liver transplantation, a rapid evolution over time from Barrett's premalignant lesions to severe dysplasia and malignization has been seen<sup>7</sup>.

In the review conducted, we have found seven cases of esophageal squamous cell carcinoma after liver trans-

plantation. Premalignant lesions had not been detected in the tests performed before symptoms occurred in any of the reported cases, and no previous lesions were known either in the case reported here. Three patients have been transplanted due to an alcohol-induced cirrhosis<sup>1,6</sup> and of the other four cases found in medical literature the cause of transplantation has not been stated, however authors reported a significant incidence of squamous cell carcinoma in those patients who underwent a liver transplantation for an alcohol - induced cirrhosis<sup>9</sup>.

The time to tumor occurrence in the published cases has varied widely, ranging from eight<sup>1</sup> to 61.7 months for a series of tumors of the upper respiratory and gastrointestinal tract and the lung<sup>5</sup>. In our case, the neoplasm was diagnosed six years after transplantation. In the reported cases, treatment consisted of surgery and/or chemotherapy with or without radiation therapy. The two cases of Kennigott et al<sup>1</sup> were treated with polychemotherapy and local radiation therapy. One of the patients died 12 months after diagnosis, and the other patient was free of relapse at five years<sup>1</sup>. In the Jiménez et al<sup>9</sup> series, including four cases of esophageal squamous cell carcinoma, in addition to 10 cases of oropharyngeal tumors and seven of lung tumors, surgery was performed in three of the cases, and no treatment was administered in the remaining patient due to the presence of distant metastases at the time of diagnosis. Only one of the patients was free of relapse at the end of the study. In the case of esophageal squamous cell carcinoma reported by Duvoux et al<sup>6</sup> in a series of five oropharyngeal tumors after liver transplantation, the treatment administered and the survival of that particular patient were not specified. While the increased incidence of tumors of the upper respiratory and gastrointestinal tract in patients undergoing liver transplantation for alcohol-induced cirrhosis is known, few cases of esophageal squamous carcinoma have been reported. Its occurrence has been related to a history of alcohol-induced cirrhosis, however, immunosuppressive therapy has also been implicated<sup>1,5,6</sup>. Prognosis is usually poor in such cases<sup>9</sup>. The case reported here is unique in that esophageal cancer occurred six years after liver transplantation, and the patient is symptom-free 17 months after surgical resection. In addition, the unsuspected finding of another esophageal squamous cell carcinoma at the level of the cardia and independent from the esophageal one, after a careful histopathologic study, suggests the influence of immunosuppression in the tumoral genesis in the case we report.

## References

1. Kennigott S, Gerbes AL, Schauer R, Bilzer M. Rapid development of esophageal squamous cell carcinoma after liver transplantation for alcohol-induced cirrhosis. *Transplant Int.* 2003;16(9):639-41.

2. Levy M, Backman L, Husberg B, et al. *De novo* malignancy following liver transplantation: a single center study. *Transplant Proc.* 1993;25:1397-9.
3. Catalina MV, de Diego A, García-Sánchez A, et al. Characterization of the *novo* malignancies in liver transplantation. *Gastroenterol Hepatol.* 2003;26(2):57-63.
4. Fung JJ, Jain A, Knawak EJ, Kusne S, Dvorchik I, Eghtesad B. *De novo* malignancies after liver transplantation: a major cause of late death. *Liver Transplant.* 2001;7: 109-18.
5. Valero JM, Rubio E, Moreno JM, Pons F, Sánchez-Turrion V, Cuervas Mons V. *De novo* malignancies in liver transplantation. *Transplant Proc.* 2003;35(2):709-11.
6. Duvoux C, Delacroix I, Richardet JP, et al. Increased incidence of oropharyngeal squamous cell carcinomas after liver transplantation for alcoholic cirrhosis. *Transplantation.* 1999;67(3):418-21.
7. Trotter JF, Brazer SR. Rapid progression to high-grade dysplasia in Barrett's esophagus after liver transplantation. *Liver Transplant Surg.* 1999;5(4):332-3.
8. Ilan Y, Shouval D, Galun E, et al. Esophageal malignancy after liver transplantation in a patient with Barrett's esophagus. *Scand J Gastroenterol.* 1996;31(4):415-6.
9. Jiménez J, Marqués E, Loinaz C, et al. Upper aerodigestive tract and lung tumors after liver transplantation. *Transplant Proc.* 2003;35:1900-1.