Ten years survival with excellent outcome after living donor liver transplantation from 70 years old donor for primary hepatic neuroendocrine carcinoma: Case report

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BACKGROUND: Primary hepatic carcinoid tumors (PHCT) are rare entities; they are even rarer than extrahepatic neuroendocrine gastrointestinal tumors with only about 95 cases reported in the literature. An extrahepatic primary tumor must be excluded to confirm the diagnosis of PHCT.

CASE PRESENTATION: We report a case of a 42-year-old male patient with a primary hepatic neuroendocrine carcinoma, who successfully underwent living donor liver transplantation from his 70 years old mother with 10 years follow-up. Both donor and recipient are still alive and in the good health.

CONCLUSION: Living liver donation from elderly donors for the patients with irresectable neuroendocrine liver malignancies can be as safe as deceased donation or liver donation from young donors (age <50). Living donation from elderly donors might significantly expand the donor pool for patients with liver neuroendocrine tumors (NET) and potentially reduce waiting list mortality. Especially young patients with irresectable NET can benefit from this option. However, case-control studies are needed to verify the advantage of living liver transplantation (LDLT) for the patients with irresectable liver NET and to define selection criteria for these patients.

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1. Introduction

Primary hepatic carcinoid tumors (PHCT) are even rarer than extrahepatic gastrointestinal neuroendocrine tumors with only about 95 cases reported in the literature. This entity is not included to a current WHO classification of neuroendocrine tumors (NET). There are few or none neuroendocrine cells in the liver compared to other organs, therefore an exact derivation of these tumors remains unclear. Nevertheless, there are several theories for the origin of PHCT. According to first hypothesis the neuroendocrine tumors of the liver arise from ectopic pancreatic cells. However, the majority of these tumors showed no pancreas specific endocrine function. Some investigators suggest that the origin of PHCT can be omnipotent hepatic cells. Alternatively, the endocrine hepatic tumors arise from endocrine cells scattered in the intrahepatic biliary epithelium. These cells are also observed in hepatobiliary cystadenomas. Case reports concerning NET of the extrapancreatic ducts confirm this hypothesis. It is supposed, that chronic inflammation in the biliary system may result to the development of neuroendocrine tumor by initiating intestinal metaplasia.

2. Presentation of case

A 42-year-old male patient was admitted at the end of August 2000 to our hospital for evaluation of hepatomegaly. The symptoms such as light abdominal distension and fever accompanied with diarrhea started three weeks ago and were intermittent. Liver function tests showed a serum bilirubin of 1.6 mg/dl (normal <1.2 mg/dl), gamma-glutamyl transferase (GGT) of 504 U/l (normal <55 U/l), and alkaline phosphatase (AP) of 447 U/l (normal 60–180 U/l), carcinoembryonic antigen (CEA) 9.4 (normal <5 µg/l), CA 19–9 66 kU/l (55 kU/l) whereas alamin–aminotransferase (ALT), aspartate–aminotransferase (AST), alpha-fetoprotein (AFP), CA-125, serotonin and 5-hydroxyindoleacetic acid (5-HIAA) in urine were all normal.

Computed tomography (CT) and magnetic resonance imaging (MRI) demonstrated a large tumor of both left and right liver lobe with compression and displacement of portal vein leaving only segments 2 and 4 were free of tumor. Other lesions or primary tumors could not be found but there were enlarged lymph nodes of liver hilus and retroperitoneum (Fig. 1).

A percutaneous ultrasound-guided biopsy was taken and this showed a NET, evidenced by staining with synaptophysin. Upper and lower gastrointestinal endoscopy revealed no pathology. A somatostatin scan showed pathologic uptake only in the liver with moderate expression of serotonin receptors. Additional investigations such as bronchoscopy, head-MRI and the Double Contrast
Small Bowel Enema did not show any evidence of a primary lesion elsewhere. Because of the size of the tumor liver resection was not possible and the patient was placed on the waiting list for LT. Transarterial chemoembolization was carried out in two sessions before the liver transplantation. November 2000 the patient underwent living donor liver transplantation using right-lobe graft from his 70 years old mother with simultaneous appendectomy. The recovery after the operation was uneventful. Histology and immunohistochemistry of the liver tumor confirmed the findings of preoperative biopsy and showed a 23 cm large infiltrative neuroendocrine carcinoma (NEC) with Ki-67 proliferation index of 20%. Immunohistochemistry showed positive staining for synaptophysin and negative staining gastrin, serotonin, chromogranine, and neuron-specific enolase.

The histology of the appendix revealed fibrosis but no neoplasia. The investigated lymph nodes showed no malignancy. Initial immunosuppression with Tacrolimus was because of nephrotoxic and neurological side reactions replaced with Sandimmune and CellCept.

The patient remained disease free 7 years after the initial surgery, evidenced by serial CT and somatostatin scanning. During the follow up, the patient notified of disappearance of the initial clinical symptoms.

A follow up PET-CT scan in April 2008 revealed two nodular pulmonary lesions, one nodule was 8.8 mm in diameter in the right lower lobe, in posterior basal segment, subpleural (Fig. 3), and another nodule was 9.8 mm in diameter in the right lower lobe, central basal (Fig. 4) all without activity in PET. It was decided by an interdisciplinary panel to repeat CT scan in 6 months and the next CT scan in October 2008 showed progression of the pulmonary lesions but again no activity on PET scan.

According to the past medical history and progression of pulmonary lesions in follow up CT scans we decided to remove these nodules to assess their dignity. The preoperative lung function tests and extended laboratory tests were normal. Endoscopic surgery was inappropriate, because the lesion in the right lower lobe central basal was too deep to be thoracoscopically resected. Therefore, a right thorakotomy was performed and the both pulmonary lesions

Figs. 1 and 2. CT scans showing a hypo- (Fig. 1), partly hyper-dense liver (Fig. 2) mass involving both liver lobes. 

Figs. 3 and 4. CT image showing the subpleural lung lesion in the lower lobe (left) – histopathologically metastasis of neuroendocrine carcinoma (Fig. 3) and CT image showing the lung lesion localized in the middle of the right lower lobe (right) (Fig. 4).
were by wedge resection in toto removed. Subsequently a lymphadenectomy was performed.

A histopathologic examination revealed a metastasis of NEC for superficial localized lung lesion. The histology of the second nodule localized in the depth of the lower right lobe showed moderate chronic lung emphysema with chronic peribronchitis. There were no lymph node metastases. Immunohistochemical staining for AFP, CD56, and chromogranin was negative. The fraction of Ki-67-positive tumor cells was 20%. After surgery, the patient had an uneventful recovery without complications. To date, no recurrent or metastatic disease has been identified. The patient and his mother remains symptom free and in good health.

3. Discussion

An extrahepatic primary tumor must be excluded to confirm the diagnosis of PHCT. This requires extended preoperative diagnostic. Finally, a pathological confirmation of preoperative diagnosis and long follow-up are necessary to differentiate this uncommon type of tumors from other NET. There are no certain standards for the therapy of PHCT, presumably because the existence of this entity is still controversial. Surgery is only curative option for treatment of primary and secondary hepatic NET.13 Liver transplantation (LT) is considered potentially curative treatment for the patients with irresectable multiple, bilateral primary and secondary neuroendocrine liver malignancies.14–16 Unfortunately, there are no randomized control studies concerning this topic and only a small number of publications, because of rareness of this type of tumors. There are only few case reports regarding LT for patients with PHCT. Colleges from of St. James’s University Hospital in the UK, reported two patients transplanted for PHCT within the period from 1994 to 2002, in the same interval six patients with PHTC underwent liver resection. This is one of the largest series of patients with PHCT reported in European literature.17

We use the same principles for therapy of primary and secondary NET of the liver, because of the difficulties with diagnosis and unclear behavior of PHCT. With our case report, we want to emphasize a role of Living Donor Living Transplantation (LDLT) for treatment of irresectable neuroendocrine liver malignancies as curative approach.

We achieved a remarkable long-term survival of patient who underwent LDLT using right-lobe graft from his 70 years old mother, for irresectable liver-NEC with high mitotic activity (Ki-67 > 20%). This confirms that LDLT from elderly living donors for irresectable neuroendocrine liver malignancies can be safe and feasible. Living liver donation from elderly donors becomes more important therapy option for the patients with liver NET, because of the increasing shortage of donor organs. LT can be a potentially curative treatment in selected patients with irresectable primary and secondary neuroendocrine hepatic tumors. In case of PHTC, LT can bring cure, even for the Patients with high proliferative index of tumor cells.

4. Conclusion

Living liver donation from elderly donors for the patients with irresectable neuroendocrine liver malignancies can be as safe as deceased donation or liver donation from young donors (age < 50). Living donation from elderly donors might significantly expand the donor pool for patients with liver NET and potentially reduce waiting list mortality. Especially young patients with irresectable NET can benefit from option. However, case–control studies are needed to verify the advantage of LDLT for the patients with irresectable liver NET and to define selection criteria for these patients.

Conflict of interest

None.

Funding

None.

Ethical approval

All patients in our Department of Transplant Surgery are informed that medical data can be used for scientific purposes. The patient we report about is consent with publication of his data in this case report.

Author contributions

Aleksseev Denis is the Author and Armin Goralczyk, Thomas Lorf, Giuliano Ramadori, Aiman Obed are involved in the data collection.

References