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CASE REPORT

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Liver Transplantation for a Metastatic Pancreatic Solid-Pseudopapillary Tumor (Frantz Tumor): A Case Report

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

BCDEF 1 Michał Wójciak
ACDEF 1 Jolanta Gozdowska
D 2 Marek Pacholczyk
D 2 Wojciech Lisik
D 2 Maciej Kosieradzki
D 3 Andrzej Cichocki
D 1 Olga Tronina
E 1 Magdalena Durlik

1 Department of Transplantation Medicine, Nephrology and Internal Diseases, Institute of Transplantology, Medical University of Warsaw, Warsaw, Poland
2 Department of General and Transplantation Surgery, Institute of Transplantology, Medical University of Warsaw, Warsaw, Poland
3 Department of Surgical Oncology and Neuroendocrine Tumors, Centre of Oncology, Warsaw, Poland

Corresponding Author: Jolanta Gozdowska, e-mail: jola-md@go2.pl
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Background: Solid-pseudopapillary neoplasms (SPN) of the pancreas, first described by Frantz in 1959, are a very rare entity and account for 0.13–2.7% of all pancreatic neoplasms. They are seen predominantly in young women in their second and third decade of life.

Case Report: We report a case of a 51-year-old female first diagnosed with a pancreatic tumor in 2010 following a computed tomography (CT) scan of the abdomen. The lesion was originally thought to be a neuroendocrine tumor subsequently treated with chemotherapy, which delayed the appropriate treatment. The tumor was rediagnosed as a SPN only after pancreatectomy was performed. Due to the fact that the neoplasm metastasized to the liver, the patient underwent an orthotopic cadaveric liver transplantation (OLTx) in 2013. During the postoperative period lymph node metastases were identified in the abdomen. The patient received surgical treatment and palliative radiotherapy. Presently no signs of recurrence are found either in the bed of pancreatic resection or in the transplanted liver. The function of the transplant organ has demonstrated no abnormalities over the 4-year follow-up.

Conclusions: SPN of the pancreas is a rare disease associated with heterogeneous clinical course ranging from benign to metastatic. Choosing appropriate treatment requires individual clinical assessment of the disease's spread. Partial living donor liver transplantation or cadaveric liver transplantation might prove an effective therapeutic option for patients with multiple SPN metastases in the liver. It ought to be remembered, however, that the experience in this area is quite limited.

MeSH Keywords: **Liver Transplantation • Neuroendocrine Tumors • Pancreatic Neoplasms**

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Background

Solid-pseudopapillary neoplasms (SPN) of the pancreas described by Frantz in 1959 are a very rare entity and are said to account for 0.13–2.7% of all pancreatic neoplasms [1]. The clinical picture is dominated by nonspecific pain, dyspepsia, vomiting and nausea. About 20% of patients are asymptomatic. Even though at the time of diagnosis the neoplasm diameter is usually 5–10 cm, some patients present with lesions of 20–25 cm in size. The disease is encountered predominantly in young women in their second and third decade of life [2]. SPNs tend to be single, well-defined encapsulated pancreatic tumors with lobular composition, light brown in color, often with foci of hemorrhage. Calcifications and cystic lesions may be present as well [3]. The 1996 the World Health Organization classification distinguishes between solid-pseudopapillary tumor (SPT) with borderline malignancy potential and solid-pseudopapillary carcinomas [4]. Acidophils do not generally exhibit signs of cellular atypia. The tumor tissue rarely infiltrates blood vessels. Cellular origin of the tumor remains unclear as its cells do not resemble any of the pancreatic cells – neither the ones present during the prenatal period, nor those which develop after birth. Because of the β-catenin gene mutation, it has been suggested that SPN might originate in the cells identified within the pancreatic ducts. This matter, however, requires further investigation [5]. As differential diagnosis of SPN and neuroendocrine tumors of the pancreas may be very difficult, immunohistochemical staining for β-catenin, synaptophysin, and chromogranin should be performed [6].

The clinical course of the disease is generally asymptomatic, although some patients complain of pain. No abnormalities tend to be observed in the laboratory test results, while pancreatic and liver enzyme levels remain at normal levels as well. Usually there is also no evidence of extrahepatic cholestasis. The levels of tumor markers (Ca19-9, CEA, and alpha-fetoprotein) remain within their reference ranges [7]. SPN progresses slowly and is associated with good survival rate, although in about 15% of patients the tumor metastasizes to the liver, which, if the lesions are multiple, poses a considerable therapeutic challenge and may require orthotopic liver transplantation. Such a procedure was first performed in Japan in a 14-year-old female patient presenting with hepatic metastases 4 months after distal pancreatectomy and splenectomy were performed [8]. Moreover, in 2008 a successful liver transplantation in a 31-year-old female patient with hepatic SPN metastases was carried out at the Transplantology Institute of the Medical University of Warsaw. Presently, 9 years post-transplantation, the patient has no signs of recurrent neoplastic disease [9].

The objective of this paper was to report another case of a female patient who received a liver transplantation due to multiple hepatic metastases.

Case Report

A 51-year-old female with a tumor in the body of the pancreas identified during an abdominal computed tomography (CT) scan qualified for pancreatectomy in March 2010. The surgery was subsequently performed at the district hospital. During intraoperative examination, the lesion was deemed unresectable and specimens were obtained for pathologic evaluation. The tumor was reported to be a neuroendocrine cancer of the pancreas composed of cancer nests. Immunohistochemical staining was positive for synaptophysin, CK was negative, the Ki-67 proliferation index was about 15% and no somatostatin receptor expression was observed. Considering the aforementioned findings, the proposed course of treatment involved palliative chemotherapy. The patient was administered 6 cycles of 5-fluoroacil, leucovorin, and dacarbazine at adjusted doses; the last cycle was given on September 26, 2010. As a result, the disease stabilized. In March 2011, the patient was referred for a consultation at the Oncology Centre in Warsaw to be considered for another surgical treatment. Distal subtotal pancreatectomy was performed leaving the head and the uncinate process of the organ attached. This was followed by a splenectomy. No abdominal metastases were identified during the procedure. Following postoperative pathologic examination performed at the Pathomorphology Unit of the Oncology Centre, the primary diagnosis (a neuroendocrine tumor) was reevaluated and the disease was rediagnosed as a solid-pseudopapillary carcinoma of pancreas. A CT scan performed in October 2011 revealed multiple metastatic lesions in the liver. As metastasectomy was deemed not feasible, the patient was placed under outpatient observation. Two years later, in 2013, in the absence of disease progression in other organs, a decision was made to qualify the patient for a liver transplantation from a deceased donor (OLTx). On September 6, 2013 at the Department of General and Transplant Surgery of the Medical University of Warsaw the patient underwent cadaveric liver transplantation by piggy-back technique with end-to-end reconstruction of the common bile duct. The patient was discharged home more than 10 days after the procedure with good liver function: aspartate aminotransferase was 43 U/L, alanine aminotransferase was 52 U/L, alkaline phosphatase was 277 U/L, total bilirubin was 0.9 mg/dL, direct bilirubin was 0.7 mg/dL, creatinine was 1.1 mg/dL. During the post-transplantation period a few endoscopic retrograde cholangiopancreatography (ERCP) procedures involving insertion of bile duct stents were carried out to relieve narrowing of the ducts. In August 2014 a follow-up CT scan identified enlarged abdominal lymph nodes without other abnormalities observed in other organs. In view of the aforementioned finding, positron emission tomography (PET)-CT images were acquired, which demonstrated signs of an active neoplastic process in the lymph nodes in the coeliac trunk area (33×29 mm, SUV max. 16.1), in the area of lesser curvature of stomach and to the front of the head of the pancreas

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(the largest lymph node measured 16×11 mm, SUV max. 12.2) as well as in the greater omentum by the anterior abdominal wall (23×31 mm, SUV max. 13.2). Local recurrence was not visualized in the bed of pancreatic resection, which was indicative of the successful outcome of this definitive procedure. A decision was made to perform a surgical biopsy of lymph nodes; however, due to the occurrence of lesions with features of pyoderma gangrenosum on the skin in the patient's abdominal area which required treatment with orally administered prednisone, the procedure took place only in November 2014. Pathologic examination confirmed the spread of the pancreatic SPN to lymph nodes. Focal extracapsular extension of the neoplasm was identified with the tumor invading soft tissues surrounding the lymph nodes. Considering the indolent clinical course of the neoplastic disease and the lack of alternative treatment options, in March 2015 the metastatic lesions in the lymph nodes were resected. No complications occurred during the postoperative period. Pathologic examination confirmed that the lesion was a metastasis of SPN. The course of immunosuppression therapy following the procedure was changed and the calcineurin inhibitor (tacrolimus) displaying minor carcinogenic potential was replaced with a signal transduction inhibitor, mTOR inhibitor (everolimus) which exhibits anti-tumor effect. Unfortunately, in July 2015 a follow-up CT scan revealed another recurrence of SNP in the abdomen within the coeliac trunk lymph nodes, the lymph nodes between the coeliac trunk and the superior mesenteric artery as well as in those in the periaortic area. Since the patient did not qualify for chemotherapy, in February 2016 she underwent another laparotomy with partial resection of the metastatic lymph nodes located in the area of the superior mesenteric artery. The procedure was performed due to increased pain experienced by the patient. Following a radiotherapeutic consultation, definitive radiotherapy with a 6 MV x-ray photon beam was used to treat the remaining recurrent neoplastic metastases in the lymph nodes and the lymphatic drainage of the pancreas. In March 2016 the patient was given a total weekly radiation dose of 2700 cGy using 180 cGy fractions. The treatment was complicated by a significant (15 kg/month) weight loss in the course of increased anorexia. In a follow-up CT performed in July 2016 a solid lesion of 23×20×21 mm in size located in the bed of pancreatic head resection was still visible (most likely a metastatic lymph node). A scan performed on September 5, 2017 revealed a slight reduction of the lesion's size, which was then 18×16 mm. No other enlarged lymph nodes or focal lesions were visualized in abdominal cavity organs. The patient is in good general condition and remains under continuous observation.

Discussion

SPN is a rare type of pancreatic tumors. In 1995–2016, Lubezky et al. carried out 1320 pancreatic resections. SPN was diagnosed in 32 patients (2.46%) at the mean age of 28.4±12.2 years including 29 women (90.6%) and 3 men (9.4%). SPN presented predominantly in women under 40 years of age (72.4%). The most common symptom of the disease was abdominal pain (48%); no patient presented with jaundice. In 2 patients, multiple metastases were identified in the liver (n=1) and adjacent organs; features of vascular invasion were observed as well (n=1). The recurrence of the disease in the form of metastatic lymph nodes in the retroperitoneal space occurred 7 years after the resection (n=1). Liver metastases (n=2) were identified after 1 year and then 5 years after resection; 5- and 10-year disease-free survival rate was 96.5% and 89.6% respectively [10]. Similarly, Antoniou et al. described 5 cases of females with Franz tumor treated with radical pancreatectomy who continue to be under observation and do not present with symptoms of locally recurrent disease [11].

Beltrame et al. diagnosed SPT in 18 among 451 patients (3.7%) with cystic pancreatic neoplasms. In all of these cases, ultrasound examinations, CT scans, and tumor marker tests (CEA and Ca 19-9) were performed prior to the surgical procedures. SPT was diagnosed in 2 men and 16 women. Ca 19-9 was slightly elevated in only 1 patient. Two patients were diagnosed with neuroendocrine tumors during the preoperative period, in another 2 cases mucinous tumors were found, while the remaining number were diagnosed with SPT (n=14). All patients underwent pancreatectomy associated with portal vein (n=1) or liver metastases (n=1) resection. One patient died of metastatic disease (77 months post-surgery) and 17 (n=17) survived disease-free for the median time of 81.5 months (range 36–228 months) [12]. The patient whose case is reported in this paper was also initially diagnosed with neuroendocrine neoplasm; administration of chemotherapy resulted only in disease stabilization, and diagnosis was reassessed only after pancreatectomy was carried out.

Lee et al. reported a case of a 61-year-old female presenting with multiple metastases observed in the course of disease; 24 years earlier the woman was diagnosed with SPN and treated surgically. After 9 years, a CT scan visualized metastases in her liver and peritoneum. The lesions were subsequently resected. The patient underwent a total of 8 metastasectomies involving different organs, including the lungs [13].

It appears that also in the case reported in this paper the disease was indolent and benign despite its recurrent character.

The treatment of SPT in a majority of cases involves the resection of the tumor and its possible metastases. It should be emphasized that neither chemotherapy nor radiotherapy yield sufficient results [2]. It is also worth noting that in the case of the patient treated at our center, despite the initial lack of response to chemotherapeutic treatment, radiotherapy aimed at the bed

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of pancreatic resection and the lymphatic drainage of this organ was successfully used to treat the locally recurrent disease.

Medical literature reports only single examples of liver transplantations carried out due to the occurrence of multiple metastases of Franz tumor to this organ. Therefore, the experience in the use of this procedure is still quite limited. Kocman et al. described a case of a 21-year-old female who underwent distal pancreatectomy and splenectomy following a diagnosis with SPT. After 3 years of observation, a routine follow-up ultrasound revealed multiple focal lesions in her liver. In consequence, the patient underwent hepatectomy and a partial living donor liver transplantation. During the observation period lasting 24 months disease recurrence was not identified [14]. Sumida et al. reported a case of a 14-year-old patient with SPT in her pancreas, who presented with non-resectable hepatic metastases. A partial liver transplantation was successfully carried out after obtaining the fragment of the organ from a living donor. Disease recurrence was not observed during an observation period lasting 2 years [8]. Dovigo et al. described a case of a 44-year-old female with non-resectable metastases in her liver, who also underwent a liver transplantation. In this case, disease recurrence was observed 4 years after the surgery. It was the first liver transplantation performed in Spain in a patient with metastatic SPN [16].

Conclusions

Solid-pseudopapillary neoplasm (SPN) of the pancreas is a rare disease associated with heterogeneous clinical course ranging from benign to metastatic. Choosing appropriate treatment requires individual clinical assessment of the disease's spread. Partial living donor liver transplantation or cadaveric liver transplant might prove an effective therapeutic option for patients with multiple SPN metastases in the liver. It ought to be remembered, however, that the experience in this area is quite limited.

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