CASE REPORT

Pancreatic Metastasis from Nephroblastoma: An Unusual Entity

Safi Dokmak[1], Carmen Cabral[1], Anne Couvelard[2], Beatrice Aussilhou[1], Jacques Belghiti[1], Alain Sauvanet[1]

Departments of [1]Hepatobiliary and Pancreatic Surgery and [2]Pathology, AP-HP, Beaujon Hospital, University Paris VII. Clichy, France

ABSTRACT

Context Pancreatic metastasis from renal cell carcinoma is a well-known entity. When metastatic disease is limited to the pancreas, pancreatic resection is the optimal treatment**.** A nephroblastoma is a frequent childhood cancer but can also occur in adults. A metastatic nephroblastoma mainly affects the lung and the liver. Pancreatic metastases from a nephroblastoma are very rare. **Case report** We report an extremely rare case of pancreatic metastases in a 20-year-old man who had a right nephroblastoma resected at 9 years of age and liver metastases treated by right hepatectomy at 18 years of age. Pancreatic metastasis was revealed by acute pancreatitis. Imaging studies revealed one 2 cm nodule in the pancreatic head with upstream dilatation of the Wirsung duct. Imaging studies revealed no other localization except a 1.5 cm liver nodule. Surgical resection was performed without preoperative chemotherapy because the patient was symptomatic and had already received numerous chemotherapy protocols. The patient underwent pancreaticoduodenectomy and limited liver resection with an uneventful postoperative course. Pathological examination confirmed pancreatic and liver metastases from a nephroblastoma composed of blastematous cells mixed with embryonic tubular structures without lymph node metastases. After resection, the patient received adjuvant high dose chemotherapy with autologous hematopoietic stem-cell support. After a 21-month follow-up, the patient was in good general condition but had liver recurrence without intra-pancreatic recurrence. **Conclusion** This is probably the first case of pancreatic metastasis from a nephroblastoma reported in a living patient. A nephroblastoma, like clear cell renal carcinoma, can be considered a possible etiology of pancreatic metastasis from a primary renal tumor.

INTRODUCTION

Pancreatic metastasis from renal cell carcinoma is a well-known entity [1, 2]. When metastatic disease is limited to the pancreas, pancreatic resection is the optimal treatment with up to 60% of patients surviving 2 years after resection [2]. Nephroblastoma is a frequent childhood cancer but can also occur in adults [3]. Metastases from a nephroblastoma mainly affect the lung, the liver and the central nervous system [4, 5, 6, 7]. Pancreatic metastasis from a nephroblastoma was not cited in a recent study which included an analysis of a surgical and autoptic database and a review of the literature [1]. This case report presents a very rare metachronous pancreatic metastasis from a nephroblastoma treated by a pancreaticoduodenectomy.

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Key words Neoplasm Metastasis; Pancreaticoduodenectomy; Wilms Tumor; Pancreas

Correspondence Alain Sauvanet
Department of Hepatobiliary and Pancreatic Surgery, AP-HP, Beaujon Hospital, University Paris VII, 100 Boulevard du Général Leclerc, 92100, Clichy, France
Phone: +33-1.4087.5222; Fax: +33-1.4087.0926
E-mail: alain.sauvanet@bjn.aphp.fr

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CASE REPORT

In March 2007, a 20-year-old man with a previous history of a right nephroblastoma with liver metastases treated by surgery and chemotherapy presented with acute epigastric pain. Biochemical tests confirmed the diagnosis of acute pancreatitis with a serum lipase level of 400 IU/L (reference range: 80 IU/L). There was no jaundice.

He had been treated for a nephroblastoma at 9 years of age using neoadjuvant chemotherapy according to the protocol of the SIOP 93-01 Wilms' tumor study (vincristin, actinomycin D and epirubicin) followed by a radical right nephrectomy. Pathologic examination revealed a nephroblastoma having a predominantly epithelial component without anaplastic features classified as intermediate according to the SIOP study; there was no capsular involvement, hilar vascular invasion or lymph node metastasis. The tumor was classified as stage II N0. Adjuvant chemotherapy was given postoperatively according to the same protocol. Nine years later, the patient developed a single 10 cm right liver metastasis treated by chemotherapy (ifosfamide, etoposide and carboplatin) followed by right hepatectomy. At this time, there were no pancreatic abnormalities at imaging or intraoperatively. Hepatic surgery was followed by adjuvant radiotherapy

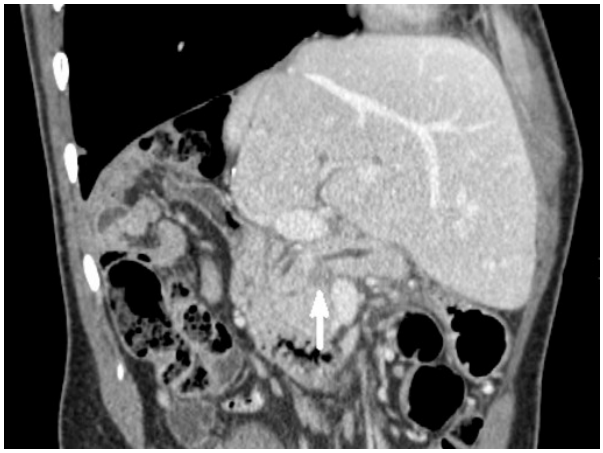

Figure 1. Preoperative CT scan with oblique reconstruction: hypodense nodule (arrow) in the pancreatic head with upstream dilatation of the main duct. The morphology of the liver is related to a previous right hepatectomy.

(40 grays on the liver and the right kidney bed). After a hepatectomy, routine follow-up included a CT-scan every 4 months.

An episode of acute pancreatitis was treated by analgesics and nil per orally for 4 days. On CT scan, there were no findings suggestive of necrosis. A 2 cm hypodense nodule with upstream dilatation of the main pancreatic duct was discovered in the pancreatic head (Figure 1). A CT scan also revealed another hypodense nodule of 1.5 cm in the left hepatic lobe. A complete metastatic work-up revealed no other sites of metastasis. Magnetic resonance cholangiopancreatography confirmed the presence of main duct stenosis in the pancreatic head with upstream dilatation (Figure 2). The diagnosis of pancreatic and hepatic metastases from a nephroblastoma was suspected. Surgical resection was performed without previous chemotherapy because the patient was symptomatic and had already received radiotherapy and numerous chemotherapy protocols. A pancreaticoduodenectomy with a limited wedge resection of the liver lesion was

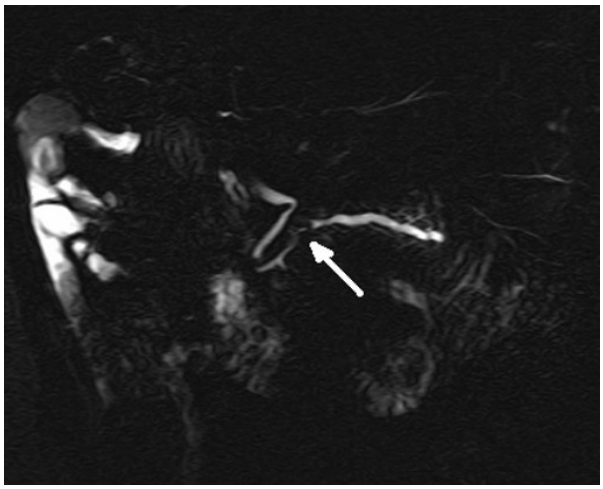

Figure 2. Magnetic resonance cholangiopancreatography: presence of main duct stenosis (arrow) in the pancreatic head with upstream dilatation.

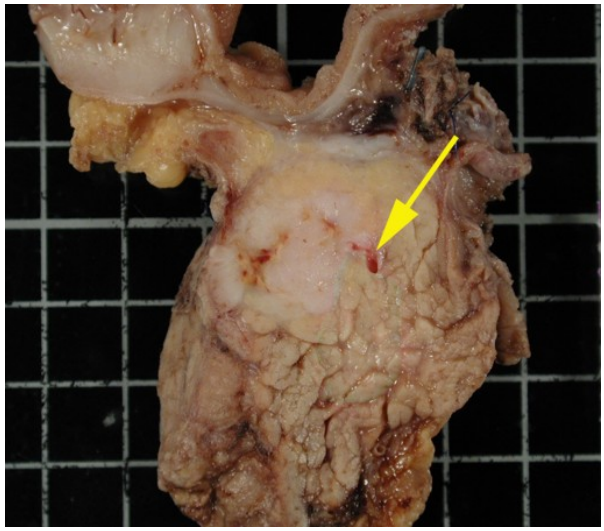

Figure 3. Gross appearance of the pancreatic metastasis. The lesion which measures 2 cm, is located in the head of the pancreas at its junction with the main pancreatic duct (arrow); its cut surface is solid and pale gray with a central area of hemorrhage.

performed in April 2007. The postoperative course was uneventful and the patient was discharged on day 14. Pathological examination confirmed that both the pancreatic and the liver nodules were metastases from a nephroblastoma. Grossly, the metastases were well circumscribed, rounded, and their cut sections were predominantly solid with areas of hemorrhage. In the pancreas, the 2 cm nodule was located close to the main pancreatic duct (Figure 3). Microscopically, the tumors in both sites were densely cellular and well-delineated from the surrounding parenchyma (Figure 4). They consisted of extensive small round areas of embryonic tubular structures with focal undifferentiated blastematous cells. There were no features of anaplasia. Histologically, the tumor was classified as a biphasic mixed type of intermediate risk (Figure 5). All 20 lymph nodes analyzed were negative. Postoperatively, the patient received two cycles of high

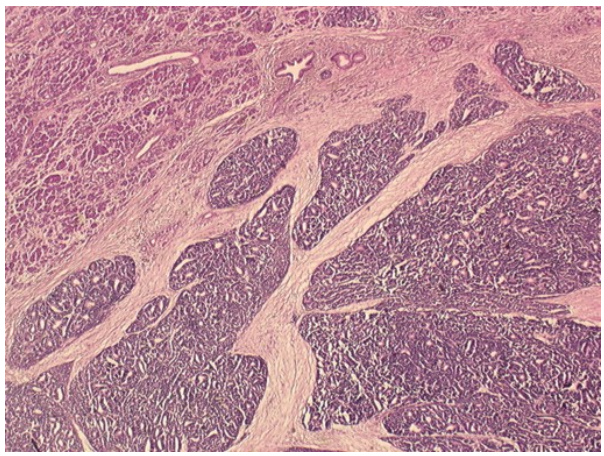

Figure 4. Microscopic appearance of the pancreatic metastasis. Low-power microscopic view showing a combination of blastema and immature tubular formations and the surrounding pancreatic parenchyma at the periphery.

dose chemotherapy and autologous hematopoietic stem-cell therapy in order to prevent occurrence of relapsing metastatic disease. After a 21-month follow-up, the patient was in good general condition but developed a liver recurrence; however, there were no other recurrences, either intra-pancreatic or at other sites.

DISCUSSION

The pancreatic gland is an unusual site of metastases. A recent study identified pancreatic metastases in 3.9% of 973 surgical specimens and 1.6% of 4,955 adult autoptic cases [1]. Pancreatic metastases are usually associated with a widespread metastatic disease so they are not usually amenable to surgical resection particularly when the primary neoplasia is lung carcinoma or melanoma [8, 9]. However, metachronous and isolated pancreatic metastases can be considered for surgery irrespective of the primary tumor site [10, 11]. Pancreatic metastases from renal cell carcinoma are a particular entity since they are solitary in 60% of cases, and the median time interval between the resection of the primary tumor and the diagnosis of pancreatic metastases is 7 to 9 years [2, 8, 12]. This favorable natural history presents a strong argument in favor of a resection with acceptable long-term survival. A recent survey of the literature showed that the average survival rate after resection was 80% with a 2-year follow-up [2]. In some series, the 5-year survival rate ranged from 40 to 50% [12, 13, 14].

Nephroblastoma (Wilm's tumor) represents 6% of all pediatric malignant diseases and 93% of renal cancers in childhood, respectively. This tumor is very rare in adult patients [3]. The most frequent distant metastases of a nephroblastoma are the lungs (10% of the patients with nephroblastomas), the liver (2%), and the central nervous system (1%) [3, 4, 5]. Other localizations are rare. To our knowledge, a pancreatic metastasis from a nephroblastoma has never been reported in a living patient. Our case is also of interest because the pancreatic metastasis was revealed by an onset of acute pancreatitis due to obstruction of the main pancreatic duct which is observed in 10 to 30% of patients with pancreatic metastases [8, 10, 12].

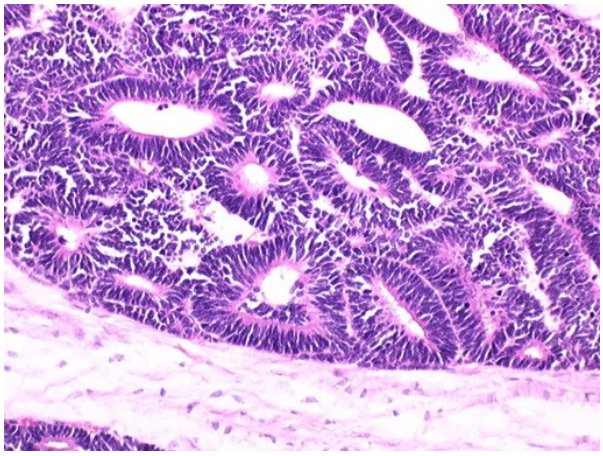

Figure 5. Microscopic appearance of the pancreatic metastasis. High-power view showing numerous immature tubular formations.

Treatment of metastases from a nephroblastoma usually relies on a combination of chemotherapy, surgery and radiotherapy. Lung metastases are most frequently synchronous and are treated by chemotherapy with or without low-dose irradiation. With this approach, the majority of lung metastases disappear completely and the 5 year-survival rate is close to 70% [4, 15]. Surgery for lung metastases is mainly indicated for recurrence after initial treatment [15]. Synchronous liver metastases are also treated initially by chemotherapy but, due to a lower response rate in this localization, surgical resection can be indicated and overall survival is lower than for lung metastases [6, 16]. Furthermore, recurrent disease has a less favorable prognosis justifying more aggressive chemotherapy [15, 17]. The treatment of metastases in the central nervous system is less standardized but symptomatic metastases are treated by surgery followed by chemotherapy and/or radiotherapy [7].

In our case, the diagnosis of pancreatic metastasis from a nephroblastoma was very probable due to the sequence of events: the normal appearance of the pancreas two years ago at the time of the first hepatectomy and the concomitant recurrence of liver metastases. Despite the initial favorable histology without anaplastic features, late metachronous metastases occurred 9 years after the first diagnosis, an event which seems more frequent in patients 2 years of age or older at first diagnosis [18]. Since the patient was young and symptomatic and there were only two metastatic sites at imaging, we decided to perform surgical resection as the first step of the treatment. Chemotherapy alone was incapable of eliminating the risk of another episode of acute pancreatitis. Radiotherapy was not possible due to previous irradiation in the right hypochondrium. After concomitant pancreatic and liver resection, the patient received adjuvant high-dose chemotherapy to prevent a recurrence of metastatic disease. Indeed, the patient presented with metastases in 2005 and then in 2007, although he already had received 2 lines of chemotherapy. Despite this additional treatment, he developed intra-hepatic recurrence suggesting the progressive appearance of chemoresistance.

In conclusion, our case highlights an extremely rare cause of pancreatic metastasis. Nephroblastoma, like clear cell renal carcinoma, can be considered a possible etiology of pancreatic metastasis from a primary renal tumor. Furthermore, pancreatic metastasis is also a rare cause of acute pancreatitis. Treatment of this unusual entity relies on a combination of surgery and chemotherapy.

Conflict of interest The authors have no potential conflicts of interest

References

1. Adsay NV, Andea A, Basturk O, Kilinc N, Nassar H, Cheng JD. Secondary tumors of the pancreas: an analysis of a surgical and autopsy database and review of the literature. Virchows Arch 2004; 444:527-35. [PMID 15057558]

2. Wente MN, Kleeff J, Esposito I, Hartel M, Müller MW, Fröhlich BE, et al. Renal cancer cell metastasis into the pancreas: a single-center experience and overview of the literature. Pancreas 2005; 30:218-22. [PMID 15782097]

3. Reinhard H, Aliani S, Ruebe C, Stöckle M, Leuschner I, Graf N. Wilms' tumor in adults: results of the Society of Pediatric Oncology (SIOP) 93-01/Society for Pediatric Oncology and Hematology (GPOH) Study. J Clin Oncol 2004; 22:4500-6. [PMID 15542800]

4. Ehrlich PF, Hamilton TE, Grundy P, Ritchey M, Haase G, Shamberger RC; et al. The value of surgery in directing therapy for patients with Wilms' tumor with pulmonary disease. A report from the National Wilms' Tumor Study Group (National Wilms' Tumor Study 5). J Pediatr Surg 2006; 41:162-7. [PMID 16410127]

5. Malogolowkin M, Cotton CA, Green DM, Breslow NE, Perlman E, Miser J, et al. Treatment of Wilms tumor relapsing after initial treatment with vincristine, actinomycin D, and doxorubicin. A report from the National Wilms Tumor Study Group. Pediatr Blood Cancer 2008; 50:236-41. [PMID 17539021]

6. Fuchs J, Szavay P, Luithle T, Furtwängler R, Graf N. Surgical implications for liver metastases in nephroblastoma--data from the SIOP/GPOH study. Surg Oncol 2008; 17:33-40. [PMID 17935976]

7. Lowis SP, Foot A, Gerrard MP, Charles A, Imeson J, Middleton H, et al. Central nervous system metastasis in Wilms' tumor: a review of three consecutive United Kingdom trials. Cancer 1998; 83:2023-9. [PMID 9806663]

8. Moussa A, Mitry E, Hammel P, Sauvanet A, Nassif T, Palazzo L, et al. Pancreatic metastases: a multicentric study of 22 patients. Gastroenterol Clin Biol 2004; 28:872-6. [PMID 15523224]

9. Z'graggen K, Fernández-del Castillo C, Rattner DW, Sigala H, Warshaw AL. Metastases to the pancreas and their surgical extirpation. Arch Surg 1998; 133:413-7. [PMID 9565122]

10. Mori N, Sawada T, Satoh H, Kawaguchi M, Hara H, Matsushita K. A resected case of solitary pancreatic metastasis from adenocarcinoma of the lung. JOP. J Pancreas (Online) 2008; 9:698-703. [PMID 18981550]

11. Nikfarjam M, Evans P, Christophi C. Pancreatic resection for metastatic melanoma. HPB (Oxford) 2003; 5:174-9. [PMID 18332980]

12. Reddy S, Edil BH, Cameron JL, Pawlik TM, Herman JM, Gilson MM, et al. Pancreatic resection of isolated metastases from nonpancreatic primary cancers. Ann Surg Oncol 2008; 15:3199-206. [PMID 18784960]

13. Bassi C, Butturini G, Falconi M, Sargenti M, Mantovani W, Pederzoli P. High recurrence rate after atypical resection for pancreatic metastases from renal cell carcinoma. Br J Surg 2003; 90:555-9. [PMID 12734861]

14. Thompson LD, Heffess CS. Renal cell carcinoma to the pancreas in surgical pathology material. A clinicopathologic study of 21 cases with a review of the literature. Cancer 2000; 89:1076-88. [PMID 10964338]

15. Kalapurakal JA, Dome JS, Perlman EJ, Malogolowkin M, Haase GM, Grundy P, Coppes MJ. Management of Wilms' tumour: current practice and future goals. Lancet Oncol 2004; 5:37-46. [PMID 14700607]

16. Varan A, Büyükpamukçu N, Cağlar M, Köksal Y, Yalçn B, Akyüz C, et al. Prognostic significance of metastatic site at diagnosis in Wilms' tumor: results from a single center. J Pediatr Hematol Oncol 2005; 27:188-91. [PMID 15838388]

17. Campbell AD, Cohn SL, Reynolds M, Seshadri R, Morgan E, Geissler G, et al. Treatment of relapsed Wilms' tumor with high-dose therapy and autologous hematopoietic stem-cell rescue: the experience at Children's Memorial Hospital. J Clin Oncol 2004; 22:2885-90. [PMID 15254057]

18. Larsen E, Perez-Atayde A, Green DM, Retik A, Clavell LA, Sallan SE. Surgery only for the treatment of patients with stage I (Cassady) Wilms' tumor. Cancer 1990; 66:264-6. [PMID 2164436]