

# Pancreatic Metastasis in a Child Suffering with Treated Stage 4 Neuroblastoma

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We present here a very rare case of metastatic relapse in the pancreas of a 4-year-old boy who had been treated for stage 4 neuroblastoma. Computed tomography showed multiple metastatic masses in the pancreas with secondary pancreatitis. To the best of our knowledge, this is the first case report of pancreatic metastasis in a child with neuroblastoma.

**N**euroblastoma is the most common extracranial solid tumor of childhood, and its metastasis to distant organs such as bone, bone marrow and liver is well documented (1, 2). However, pancreatic metastasis of neuroblastoma has not yet been reported in the medical literature. We report here on a 4-year-old boy who had a metastatic relapse in his pancreas, combined with pancreatitis, after remission of stage 4 neuroblastoma.

## Index terms:

Neuroblastoma  
Pancreas, metastasis  
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## CASE REPORT

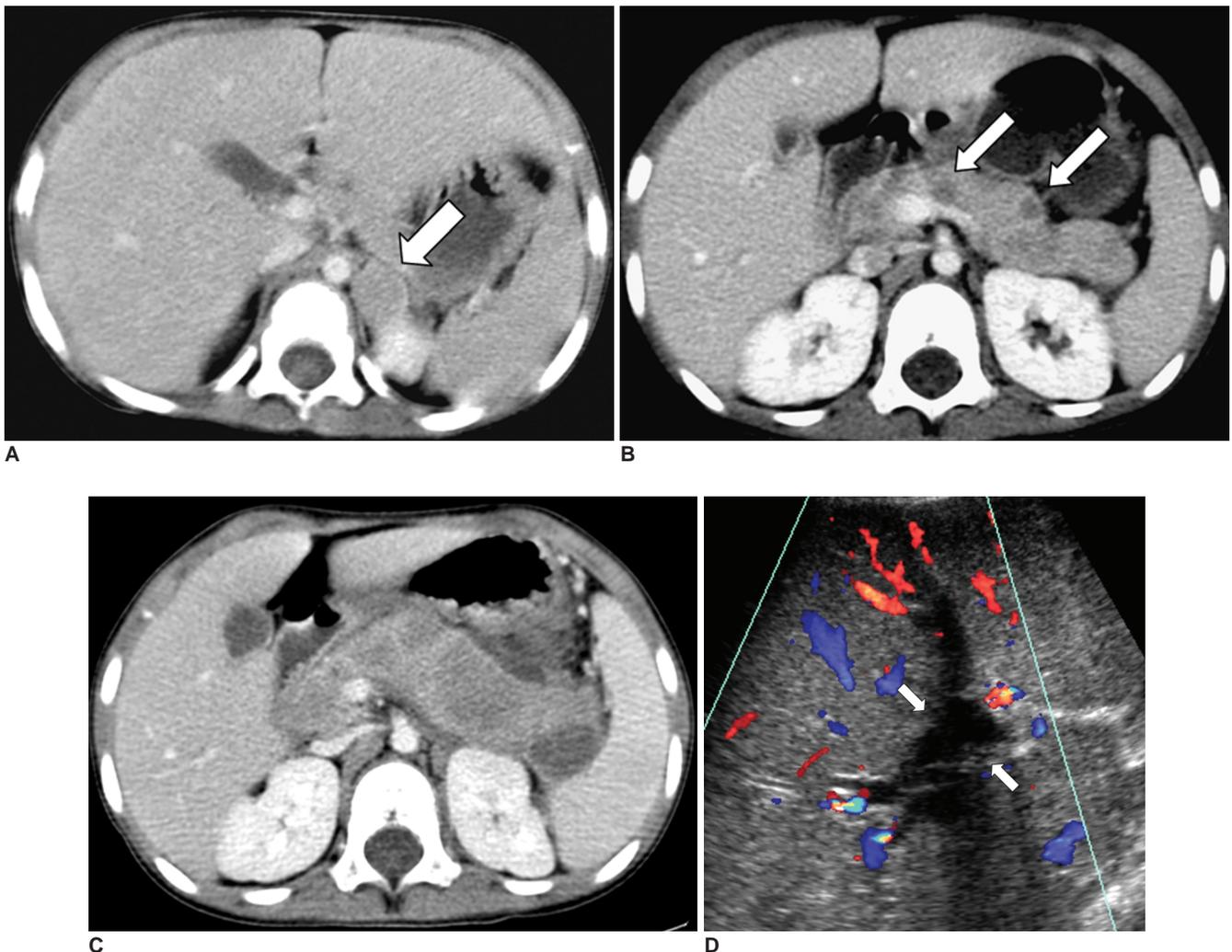
A 30-month-old boy initially presented with hip joint pain and fever, which failed to improve despite treatment that was given under the impression of a septic hip at a local hospital. One month later, he was admitted to another hospital due to progressed multifocal bone pain. The physical examination revealed right facial swelling and no palpable abdominal mass. The imaging work up, including bone scanning and MRI for the head, neck and pelvis, suggested multiple metastatic lesions in the skeleton and bone marrow. The abdominal sonography was unremarkable. He was referred to our hospital for further investigation. On admission, a 2.5 cm sized left adrenal mass was detected on the contrast-enhanced CT (Fig. 1A). On the laboratory studies, the serum neuron-specific enolase (NSE) and ferritin, and the urine vanillylmandelic acid (VMA) were elevated to 72 ng/ml, 1,245 ng/ml and 42 mg/day, respectively (normal ranges: 0–12 ng/ml, 22–322 ng/ml, and < 3 mg/day, respectively). Metaiodobenzylguanidine (MIBG) scintigraphy showed abnormal diffuse uptake in the whole skeletal system. Biopsy of the bone marrow revealed rosette formations of neuroblastoma cells. Therefore, the patient was diagnosed with stage 4 neuroblastoma of a left adrenal origin, according to the International Neuroblastoma Staging System. Subsequent chemotherapy was started, and this was followed by surgical resection of the residual adrenal lesion several months later. The pathologic diagnosis of the primary lesion was ganglioneuroblastoma with the large portion of the tumor being differentiated into ganglioneuroma, which was caused by the previous chemotherapy. After additional high dose chemotherapy followed by autologous peripheral blood stem cell transplantation, he was clinically considered to be in nearly complete clinical remission. The

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patient did well until recurrent abdominal pain developed at four years of age. At that time, contrast-enhanced CT scan of the abdomen demonstrated multiple small low attenuated nodular lesions in the pancreas (Fig. 1B). Three weeks later, the laboratory examinations revealed that the amylase and lipase were elevated to 538 U/L and 1,023 U/L, respectively (normal ranges: 13–100 U/L and 13–60 U/L, respectively). Contrast-enhanced abdominal CT showed diffuse swelling of the pancreas with an increase in the size of multiple pancreatic masses throughout the entire pancreas (Fig. 1C). Mild dilatation of the biliary tree was also noted. The chest CT that was performed for a palpable nodule in the sternal area also showed a destructive soft tissue mass of the sternum. MIBG scintigraphy

demonstrated newly appeared uptakes in the corresponding areas. The NSE was also elevated to 95 ng/ml (normal range: 0–12 ng/ml). After two weeks, progressive dilatation of the intrahepatic duct was noted on the follow up sonography; this was due to obstruction of the common bile duct by the pancreatic mass (Fig. 1D).

Based on these clinical and imaging findings, the diagnosis of multiple relapse of neuroblastoma in the pancreas and sternum was made. The patient's pancreatitis was presumed to be present secondary to pancreatic metastasis. Because the patient was in very poor general condition and he showed a rapid clinical decline with severe cholestasis, further chemotherapy could not be performed. The little boy was managed both conservatively and compassion-



**Fig. 1.** A 4-year-old boy with pancreatic metastasis who had been treated for stage 4 neuroblastoma.  
**A.** Contrast-enhanced CT scan shows a 2.5 cm sized mass (arrow) in the left adrenal gland. Surgery was performed after chemotherapy. The pathologic diagnosis was ganglioneuroblastoma.  
**B.** Contrast-enhanced CT scan demonstrates multiple small low attenuated nodular lesions in the pancreas (arrows).  
**C.** CT at three weeks after **B** shows marked diffuse swelling of the pancreas with an increase in size of multiple pancreatic masses throughout the entire pancreas. There are multifocal peripancreatic fluid collections caused by the combined pancreatitis.  
**D.** Abdominal sonography performed two weeks after **C** shows dilated intrahepatic ducts (arrows) due to obstruction by the pancreatic mass.

ately; sadly, he expired one month after the diagnosis of relapse.

## DISCUSSION

Neuroblastoma accounts for 8–10% of all malignancies in childhood and it occurs in the adrenal medulla and along the sympathetic nervous system by tumor arising from neuroblasts (1, 2). The prognosis depends on the age and stage at the time of diagnosis. Infants younger than one year or patients with localized tumor have a good prognosis, whereas approximately 70–80% of patients older than one year have metastatic disease at diagnosis and they have a poor prognosis with a high recurrence rate in spite of receiving the best current multimodality therapy (1, 2). Common sites of metastasis, via lymphatic and hematogenous routes, are the bone, bone marrow, lymph nodes, liver, dura and lung (1, 2).

Bone metastasis is common in children older than one year, and this often involves the long bones and orbit, which causes bone pain or proptosis. Massive hepatic involvement and skin metastasis are more frequent in infants (1). The unusual metastatic sites that were previously reported include the CNS, kidney, and the cardiac and skeletal muscles (3–5). To the best of our knowledge, there are no prior reports of pancreatic metastasis of neuroblastoma. Pancreatic metastasis is generally uncommon from any source, even if it has been reported that the colon, lung, and kidney are the most common sites of primary tumors that metastasize to the pancreas (6). Especially in children, pancreatic metastasis was reported in patients suffering with leukemia, lymphoma, Ewing sarcoma and rhabdomyosarcoma (7, 8). In the presented case, we were not certain at first that the multiple nodules found in the pancreas represented metastasis of neuroblastoma. However, as the pancreatic nodules increased in size, and this was associated with metastatic lesion in sternum and with the corresponding increased MIBG uptake and increased NSE value, then the diagnosis of pancreatic metastasis was made. Performing tissue diagnosis for the pancreatic lesion was difficult to achieve in this seriously ill little boy and it was simply not justified when the clinical, laboratory and imaging findings were sufficient to make the diagnosis of metastatic relapse. It's likely that there were residual tumor cells that became disseminated through the blood and lymphatic systems, and this caused early relapse at multiple sites, including the

pancreas.

As in our case, pancreatic metastasis may be complicated by biliary obstruction and pancreatitis. Metastasis-induced acute pancreatitis can occur as an initial manifestation of tumor or it can happen later during the course of disease (9, 10). Although the mechanisms to explain this phenomenon still remain controversial, it has been assumed that obstruction of the pancreatic duct by tumor, and the secretion of plasminogen activating enzymes that in turn activates trypsinogen-inducing autodigestion, may cause pancreatitis (9, 10). Whatever the mechanism is, metastasis induced pancreatitis may result in a very poor outcome as in our case; this is especially likely when it occurs together with extensive disease or severe pancreatitis (10).

In conclusion, we present here a very rare case of neuroblastoma that metastasized to the pancreas in a 4-year-old boy. Pancreatic metastasis should be taken into consideration for those patients who are found to have pancreatic nodules concurrent with neuroblastoma.

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