

LETTER

Gastrointestinal Stromal Tumors of the Pancreas

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Dear Sir,

We read with great interest the case report published by Padhi *et al.* in the 2010 May issue of JOP. J Pancreas (Online) titled "Extragastrointestinal Stromal Tumor Arising in the Pancreas: A Case Report with a Review of the Literature" [1]. Extragastrointestinal stromal tumors arising in the pancreas are extremely rare. Only nine cases have been reported in the literature up to today including the one by Padhi *et al.* [1, 2, 3, 4, 5, 6, 7, 8, 9]. We here report another case, probably to be the 10th in medical literature of a pancreatic gastrointestinal stromal tumor (GIST) patient with an aggressive outcome.

Our patient is a 31-year-old male in his usual state of health until February 2009 when he began to experience abdominal pain and fatigue accompanied by a 4.5 kg weight loss. There was no history of pancreatitis or abdominal trauma. He had a small episode of hematemesis for which he had blood work performed including complete blood count that revealed hemoglobin of 4.6 g/dL (reference range: 14.0-18.0 g/dL). He was admitted to the hospital where received 5 units of packed red blood cells and he was subsequently evaluated with upper endoscopy. Upon the procedure a friable area of mucosa was identified on the duodenum of which no biopsy could be taken. After this finding he had a CT scan which showed a 5.1x4.2x5.6 cm hypervascular mass in the pancreatic head compressing the common bile duct with minimal dilatation. The mass was further characterized by MRI, in which a 5.0x4.3 soft tissue mass was invading the pancreatic head and duodenum, obstructing the common bile duct without pancreatic duct obstruction. On admission, his total bilirubin was 7.3 mg/dL

(reference range: 0-1.20 mg/dL), alkaline phosphatase was 686 U/L (reference range: 30-130 U/L), CA 19-9 was 11 U/mL (reference range: 0-37 U/mL), and CEA was 0.9 ng/mL (reference range: 0-3.0 ng/mL).

The patient underwent a pylorus-preserving pancreatoduodenectomy and the pathology confirmed a c-kit positive GIST of pancreas. The malignant gastrointestinal stromal tumor was 8.0 cm invading the pancreatic head, completely encircling the pancreatic duct and disrupting the ductal epithelium. Twelve peripancreatic lymph nodes were negative for malignancy, proximal and distal duodenal margins, as well as pancreatic resection margin, were all negative for tumor. The histological sections of the tumor showed a densely cellular spindle cell tumor with a high mitotic rate (24 mitotic figures per 25 high power fields counted). An immunohistochemical stain for c-kit was strongly positive within tumor cells.

His post-operative course included a spike in his white blood count to 17.1 x1,000/ μ L (reference range: 4.0-10.0 x1,000/ μ L) A CT scan at that time indicated a small amount of retroperitoneal fluid which was then drained by interventional radiologist with no sequel. After collecting blood and fluid collection, he was empirically started on amoxicillin. However, no organisms were found on culture and recovered fully. He was sent to see us in the medical oncology clinic to discuss role of adjuvant therapy.

Due to the tumor's large size, high mitotic rate and invasive behavior, this diagnosis was identified as a high risk malignant gastrointestinal stromal tumor. He was offered imatinib 400 mg orally once daily [10]. He tolerated therapy with imatinib with minimal toxicities including nausea and periorbital edema.

He was closely monitored for recurrent disease with PET scan and CT scan alternating every 3 months. A CT scan at the ninth month showed two lesions in right hepatic lobe suspicious for metastases. A PET scan confirmed the lesions.

Due to failure to imatinib, PCR-sequencing analysis of c-kit gene was performed. c-kit gene mutation involving exon 11, 13, 17 and 18 was not identified. A DNA polymorphism of L862L was present in exon 18 of c-kit gene [11].

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A fine needle aspiration was performed. The biopsy confirmed the metastatic GIST and imatinib was increased to 800 mg orally once a day [12]. Restaging MRI showed multiple arterial phase enhancing lesions in the liver as follows: a 2.5 cm mass in segment 6 was T2 hyperintense and T1 hypointense, and demonstrated peripheral and heterogeneous internal enhancement. This had increased in size (previously 2.0 cm). A transient hepatic intensity difference was noted associated with this lesion. A 1 cm peripheral lesion bordering segments 6/7 was T2 hyperintense and T1 hypointense and had also increased in size (previously 7 mm). A transient hepatic intensity difference was noted associated with this lesion. A lesion located posteriorly in segment 7 measured 1.5 cm. Multiple other subcentimeter arterial phase enhancing foci were stable. A 5 mm focus in segment 4A was new. There was no biliary ductal dilatation. The spleen, kidneys and adrenal glands were unremarkable. There was no free fluid or adenopathy. The hepatic and portal veins were patent. Therefore, he was switched to sunitinib malate 50 mg orally once daily for 28 days followed by 2 weeks off [13]. The patient currently has stable disease.

The clinicopathological features and treatment outcomes of previously described pancreatic GISTs have been well described by the authors [1]. The authors suggested, based on their case and review of the literature, that pancreatic stromal tumors may follow a benign course following definitive surgery as compared to extragastrintestinal stromal tumors arising from other sites. However, our patient has an aggressive outcome with development of liver metastases within 8 months of starting adjuvant imatinib and continued to progress on the higher dose. We agree with the authors that GISTs should be considered in the differential diagnosis of the more common cystic neoplasms of the pancreas.

Conflict of interest Dr. Saif received honorarium for speaker bureau on Novartis

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