CASE REPORT

Pancreatic gastrointestinal stromal tumour with liver metastasis five years after Whipple's procedure: A rare case with management challenges

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Abstract

Pancreatic gastrointestinal tumour is an unusual primary tumour of the pancreas. A 31-year-old male came to the clinic with jaundice and weight loss. Cross-sectional imaging showed a mass in the pancreatic uncinate process. Image-guided biopsy revealed gastrointestinal stromal tumour, so pancreaticoduodenectomy was performed, followed by adjuvant Imatinib. The patient had oligo-metastasis in the liver five years post-surgery and underwent liver resection. This is an unusual case where a pancreatic GIST presented with metastasis while on adjuvant treatment. Hepatectomy and multimodal therapy increases the survival if the disease is confined to the liver.

Keywords: Pancreas, Gastrointestinal stromal tumour, Whipple's procedure.

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Introduction

Gastrointestinal stromal tumours (GISTs) are uncommon tumours, originating from the gastrointestinal tract (GIT). The most commonly involved organ is the stomach, followed by other parts of the GIT.[1] Stromal tumours located outside GIT are called extra-gastrointestinal stromal tumours (EGISTs), and are seen at unusual sites.[2] Pancreatic EGIST is very uncommon and only 45 cases have yet been reported.[3] We describe the case of a young male, who had Whipple's procedure performed for pancreatic head GIST at our institution, developed liver metastasis after five years and underwent liver resection.

Case

A 31-year-old male presented to the outpatient surgical clinic of Aga Khan University Hospital, Karachi on February 3, 2012, with three-months history of jaundice, pruritis, and weight loss. Physical examination revealed jaundice and a palpable gallbladder. Laboratory investigations showed normal baseline laboratory tests, but liver functions were abnormal with a bilirubin of 12.1 mg/dl, alkaline phosphatase of 435, IU/L, and serum CA 19-9 level of 217U/ml. Ultrasound of the abdomen showed a large mass in the pancreatic head with biliary dilatation. Pancreatic protocol computerised tomography scan (CT) revealed a 53x49 mm enhancing mass in the pancreatic uncinate process with compression on the duodenum and common bile duct with resultant biliary dilatation (Figure-1). Considering the imaging features atypical for a primary pancreatic adenocarcinoma, CT-guided biopsy was performed. Histopathology showed spindle cells with

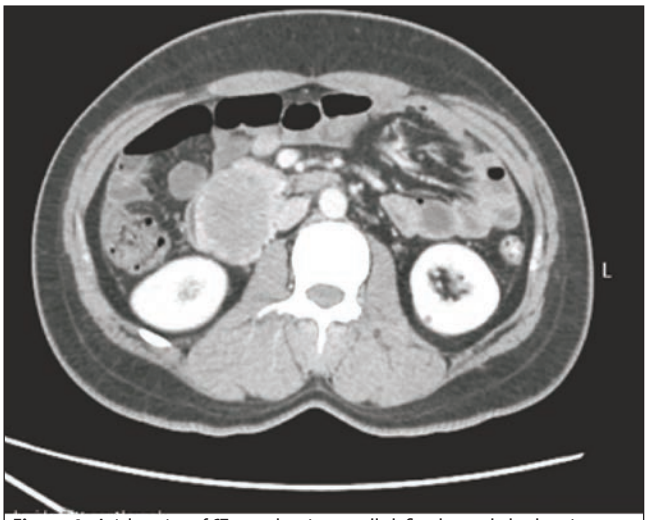

Figure-1: Axial section of CT scan showing a well-defined, rounded enhancing lesion in the uncinate process of pancreas measuring 53x49 mm.

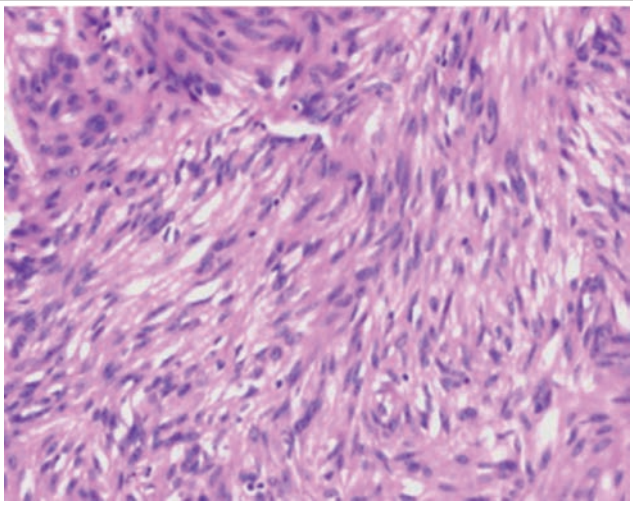

Figure-2: Spindle shaped cells arranged in a nested pattern with hyalinised areas with elongated and oval nuclei.

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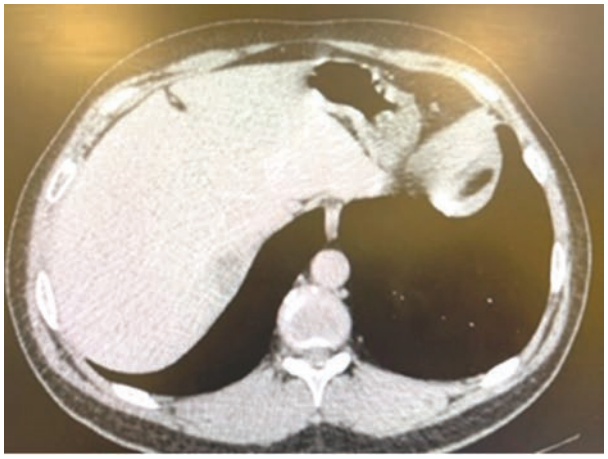

Figure-3: Axial section of CT scan showing metasatic GIST in segment VII of liver.

eosinophilic cytoplasm and hyperchromatic nuclei strongly reactive for CD117 and CD 34 confirming GIST. The patient underwent a standard Whipple's procedure. Final histopathology revealed pancreatic GIST with high-risk features, including size of 6.5x6x5cm and mitotic index of 43/50 on high power fields (HPF) (Figure-2). All tumour margins were negative. The patient had smooth postoperative course and on the eighth postoperative day he was discharged and referred to the oncology clinic for adjuvant treatment due to high-risk features on final histopathology. The patient was started on Imatinib and had regular follow-ups including surveillance CT scans. The CT scan performed at five-year follow-up showed a lesion in segment VII of the liver, which was biopsied, and histopathology was consistent with metastatic GIST (Figure-3). The case was discussed in the institutional tumour board meeting and resection was advised. The patient underwent segment VII hepatectomy and final histopathology confirmed negative margin resection of metastatic GIST. The patient was discharged on the fifth postoperative day on adjuvant Imatinib. He is asymptomatic with no disease three years after the second surgery and his last follow-up was in October 2020.

Discussion

Extra-intestinal GISTs account for 5% to 10% of all GISTs. EGISTs arising from pancreas only constitute 5% of all EGISTs.[4] The concept of GIST was introduced, due to the improvement in immunohistochemical analyses. The tumour cells are believed to stem from the pacemaker cells of GIT called interstitial cells of Cajal. These cells have many characteristics similar to EGISTs, including CD117 and CD34 expression. The immunohistochemical marker unique for EGISTs is tyrosine kinase (CD117 antigen) and is present in about 95% of GISTs which differentiate it from other smooth muscle tumours.[5,6] Furthermore, GISTs are positive for CD34 in 40 to 70% cases. These may also show positivity to other mesenchymal markers, such as vimentin, myoid, and neural markers.[7]

Origin of extra-intestinal GISTs still stays debatable. One hypothesis is the minimal or complete loss of contact with the muscularis propria due to mural GISTs ingrowth.[8] The other school of thought is that GISTs may arise from precursor cell similar to smooth muscle, which justifies existence away from GIT. Popescu et al proposed the presence of Cajal cells in the human exocrine pancreas, similar to the enteric interstitial cells.[9] The precise function of these cells is questionable, the presence of exocrine pancreatic Cajal cells supports EGISTs arising from the pancreas.

EGISTs presents clinically in variable patterns depending on the location and size of tumour in the pancreas. Preoperative diagnosis of EGIST is a challenge as the diagnostic accuracy of CT scan is not very high. Fifty percent of the reported cases in literature showed heterogeneous mass with necrotic areas or solid cum cystic appearance that could raise the possibility of cystic neoplasm of pancreas.[10,11] Tissue diagnosis is the only way to diagnose EGIST in preoperative setting, which can be either done with endoscopic ultrasound or percutaneous image-guided biopsy. Our patient had CT-guided percutaneous biopsy and the histopathology confirmed EGIST with strong immunohistochemical positivity to CD117 and CD 34.

First line of treatment for resectable EGIST is negative margin resection; the procedure depends on the location and extent of the disease.[12] Our patient underwent a standard Whipple's procedure because of the location of the tumour. Lymphadenectomy is not indicated due to the rare regional lymph node metastases.[13] Clinical behaviour of EGISTs is variable with stable disease for years to metastatic disease on presentation. National Institute of Health consensus criteria categorise risk stratified tumour behaviour into very low to high risk of metastasis, depending upon its size and mitotic activity. A tumour of more than 10cm in size with greater than 10 mitoses per 50 HPF is at high risk for aggressive behaviour.[14] Our patient's final histopathology revealed pancreatic EGIST with high risk features, with tumour size of 6.5x6x5 cm with mitotic index of 43/50 HPF.

Imatinib, a tyrosine kinase activity inhibitor of C-Kit, has been recommended for the treatment of EGISTs with high-risk features.[15] The administration of Imatinib is recommended in patients with high-risk features only by a trial which compared the R0/R1 resection with and without Imatinib.[16] Considering the high risk features on final histopathology, our patient received adjuvant Imatinib

400mg. There is no consensus on the duration of the use of Imatinib for these patients. One phase II trial studying five-year Imatinib therapy for high-risk patients showed five-year recurrence free survival rate of 90% and overall survival rate of 95%.[17] Most recurrence of GIST occurred in either liver or peritoneum within 24 months after resection as reported by DeMattero et al.[15] Reith et al reported that due to aggressive tumour biology, 39% patients either develop metastatic disease or die of EGISTs.[18]

Our patient presented five years after surgery for EGIST with liver oligo-metastasis and underwent a second major resection. Management of patients with liver metastasis after resection is multimodal. A study by Shi Y. N. et al showed combination therapy with tyrosine kinase inhibitors and hepatic resection had better outcomes with increased median survival when compared with those who only received Imatinib indicating better prognosis in patients with combined therapy.[19] Our patient remains symptom free three years after the second resection.

Conclusion

Pancreatic EGIST involving uncinate process is an unusual tumour. Negative margin resection is the foremost treatment for resectable tumours followed by adjuvant Imatinib. Disease free and overall survival is prolonged by metastetectomy of the liver lesions amenable to resection and multimodal therapy.

Disclaimer: None.

Conflict of Interest: The head of department who has signed the IRB letter is also one of the co-authors.

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Consent: All authors declare that informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

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