Gastrointestinal Stromal Tumour Associated with Neurofibromatosis Presenting as Multiple Intra-Abdominal Masses: A Case Report

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ABSTRACT

Gastrointestinal stromal tumours (GISTs) exhibit uncontrolled growth in the digestive system's stromal tissue, posing diagnostic challenges due to diverse symptoms. Often stemming from KIT or PDGFRA gene mutations, the spindle cell type is predominant among GISTs. A 51-year female presented with numerous small intestinal masses, histologically identified as spindle cell type GISTs. The patient had also numerous neurofibromas throughout her body. Immunohistochemical staining revealed positive results for CD117 and DOG-1 markers, crucial for GIST confirmation. This combination of genetic mutations, spindle cell histology, and positive staining aligns with typical GIST characteristics. The unique feature of the case was its occurrence in a case of neurofibromatosis type 1 (NF1). Management typically involves surgical resection and, if needed, targeted therapies like imatinib, contingent on individual case factors.

Key Words: *Neurofibromatosis, Gastrointestinal stromal tumours, Sarcoma.*

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INTRODUCTION

The clinical presentation of gastrointestinal stromal tumours (GISTs) varies widely, manifesting as abdominal discomfort, pain, or gastrointestinal (GI) bleeding. This heterogeneity in symptomatology can complicate early detection and diagnosis. Adding another layer of complexity, GISTs have been found to occur more frequently in individuals with neurofibromatosis type 1 (NF1), a rare genetic disorder characterised by neurofibromas and cafe-au-lait spots.[1] GIST with NF1 syndrome accounts for 1-3% of all GI malignancies, and 10-15 cases/million/year are reported worldwide occurring most commonly in the fifth to eighth decade of life with a median age of 60 years. These tumours are associated with a KIT gene mutation in 85% of the cases. GISTs occur most commonly in the stomach (66%) and less commonly in the jejunum and ileum (30%), and duodenum (5%). Gastric GISTs have comparatively low malignant potential than the tumours occurring elsewhere in the GI tract. Three main histological types are spindle cell type (70%), epithelioid cell type (20%), and mixed cell type (10%). GISTs affecting the stomach and appearing as an intra-abdominal tumour are uncommon in NF1. Our case highlights and raises awareness of the association of multiple GISTs in the setting of NF-1 mutation and provides a pertinent literature review.

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CASE REPORT

A 51-year woman presented to the Outpatient Department, reporting upper abdominal heaviness and a noticeable 7 kg weight loss over six months. There were no other complaints or family history of such conditions. Abdominal examination revealed multiple skin lesions (neurofibromas) (Figure 1) and a palpable, 20×15 cm, soft, cystic mass in the left hypochondrium, extending into the left lumbar, umbilical and epigastric regions. Other examination findings were unremarkable.

CT scan (Figure 2) reported this lesion as a large, intraperitoneal thick-walled cystic lesion extending from L1 to L5 vertebral level abutting the body and tail of the pancreas suspicious for intraperitoneal abscess or mucinous neoplasm. Surgical intervention was done. Intraoperative findings showed a 15×15cm mass with multiple cystic components arising from the distal jejunum (Figure 3). Multiple deposits of the same lesion were noted in the 1st and 3rd parts of the duodenum and mesentery of the jejunum (Figure 4).

All lesions were resected successfully with end-to-end entero-enteric anastomosis. Postoperative recovery was uneventful and she was discharged on the 7th day. Histopathology (Figure 5) showed GIST of spindle cell type with mitotic rate >5/50 HPFs. Immunohistochemical stains showed positivity for CD117 and DOG-1.

DISCUSSION

GIST is the most frequent mesenchymal tumour of the GI tract, that arises from the interstitial cells of Cajal. NF-1 is a neurocuta-

neous disease characterised by the mutation in the *NF1* gene that encodes GTPase activating neurofibromin. Neurofibromin mutation results in the development of neurofibromas all across the body.[1] Around 35% of GI tract cancers including GISTs are related to neurofibromatosis. This is because the loss of RAS protein in NF1 is linked to GISTs.[2] GISTs occur in 10-15 cases per million yearly. The patient in question had neurofibromatosis, highlighting the GIST-NF connection.[3]

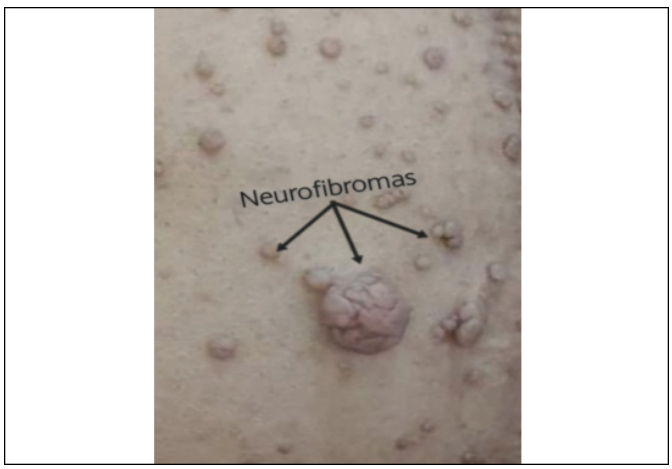

Figure 1: Multiple cutaneous neurofibromas.

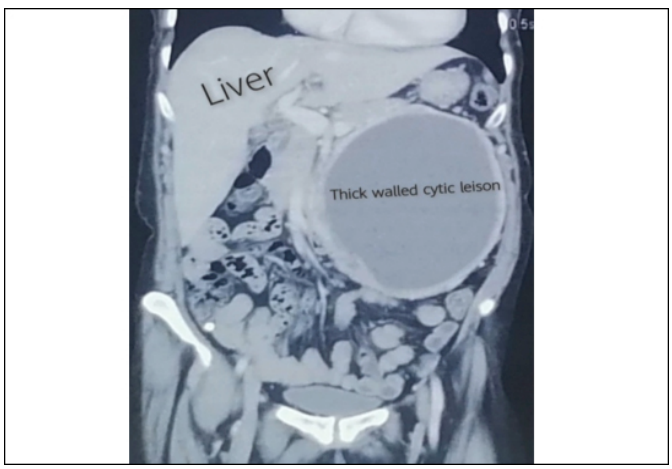

Figure 2: CT scan: Large thick-walled cystic lesion in the abdomen.

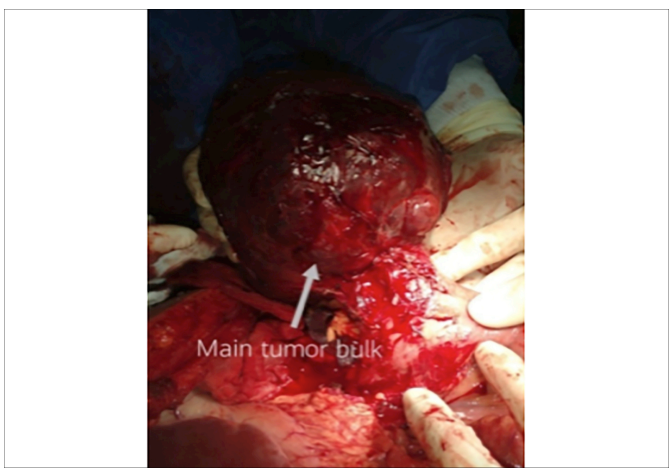

Figure 3: The cystic mass arising from the distal jejunum.

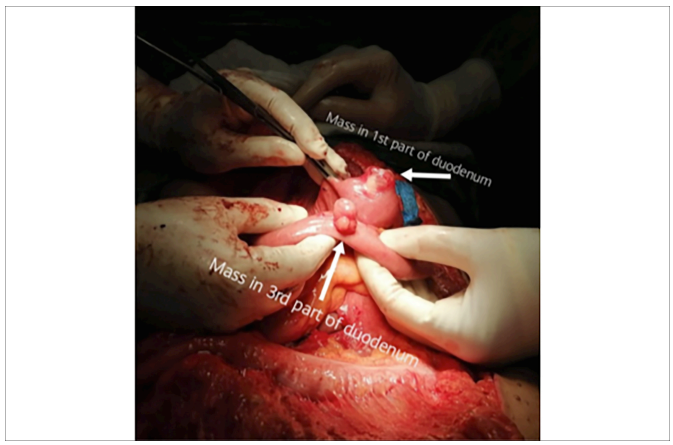

Figure 4: Deposits of tumour in the first and third parts of the duodenum.

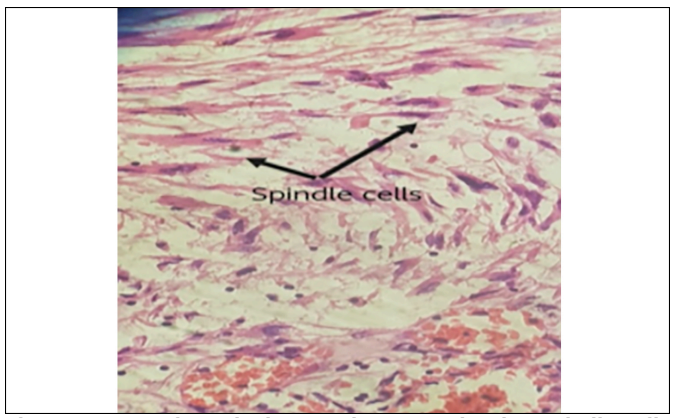

Figure 5: Gastrointestinal stromal tumour showing spindle cells (HE, ×400).

CT scan with contrast is needed to stage the GIST. Ghanem et al. classified the GISTs based on the size of the lesion on CT scan into: Small, <5 cm, intermediate, 5-10 cm, and large, >10 cm.[4] Additional diagnostic methods like MRI, ultrasonography, and barium series are beneficial. Molecular analysis of excised tissue confirms CD117 and DOG1 mutations, as reported in prior studies.[5]

Radiological and endoscopic examinations have diagnostic limitations for GIST. CD117-positive GIST patients generally have a favourable median five-year survival rate. Rarely, GIST is associated with NF 1 mutations.[6] Our study confirmed positive DOG-1 and CD117 markers, consistent with existing research. The patient, a 51-year woman, was slightly younger as compared with the usual age for GIST cases (around 60 years). GISTs are often seen in the stomach (60%) or small intestines (30%). The symptoms vary from case to case.[7] Differential diagnoses for GISTs include tumours like leiomyomas, leiomyosarcomas, angiosarcomas, and schwannomas, which typically lack CD117 expression. Prognostic factors in GIST include mitotic activity and tumour size. Our case showed spindle cell-type GIST, associated with a more favourable prognosis compared to other cell types.[8] Targeted therapy to rectify the pathogenic pathways is the key to GIST management, including tyrosine kinase inhibitors like imatinib mesylate.[9]

In conclusion, this case highlights and raises awareness of the association of multiple GISTs in the setting of NF-1 mutation. GISTs should be considered in the differential diagnoses of tumour-like masses in patients with neurofibromatosis.

PATIENT'S CONSENT:
Patient's explicit consent has been obtained to publish this case.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
NFH: Manuscript writing
TN: Analysis and revision.
AA: Analysis and drafting.
AJ: Revision and approval.
All authors approved the final version of the manuscript to be published.

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