A RARE CASE OF EXTRA-GASTROINTESTINAL STROMAL TUMOR WITH LIVER METASTASIS

KP Fidel, JC Bocobo

Institute of Digestive and Liver Diseases, St. Luke's Medical Center Quezon City

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Significance: Gastrointestinal stromal tumors (GIST) are the most common mesenchymal tumors of the gastrointestinal tract, occurring most frequently in the stomach, jejunum and ileum. A small number may originate from outside the gastrointestinal tract such as the mesentery, omentum and peritoneum and are designated as Extra-Gastrointestinal Stromal Tumors (E-GIST). Clinicopathological features and prognosis of E-GISTs are limited due to the extremely rare incidence, much more when it presents as a metastatic disease. Hence, reporting a case of metastatic E-GIST would be valuable in extending our knowledge on this kind of rare entity.

Clinical Presentation: A 56 year-old male with a history omental mass eight years prior now presents with intermittent abdominal pain, diagnosed to have multiple hepatic lesions. Underwent liver biopsy which revealed spindle cell neoplasm, with positive immunostaining: (+) CK 117, (+) CD 34, (-) DOG-1. However, mutational analysis was not done. Patient was then started on Imatinib therapy.

Discussion: Most cases of Omental GISTs reported do not have metastasis on presentation. Also, due to the rarity of omental E-GISTs, there are no specific treatment data from clinical trials and surgical resection is the only effective modality. Literature regarding treatment of liver metastasis from GISTs are limited to hepatic resection, use of Tyrosine-Kinase inhibitors (TKI), or both. Doing mutational analysis is recommended prior to starting Imatinib therapy.

Recommendation: Our existing data on metastatic E-GIST is not sufficient to conclude as to the proper management of these cases. But Imatinib therapy following complete resection of the tumor may prolong overall survival.

Keywords: case report, extra-gastrointestinal stromal tumor, liver metastasis, imatinib therapy

INTRODUCTION

GISTs are the most common mesenchymal tumors of the gastrointestinal tract originating primarily from interstitial cells of Cajal or related stem cell-like precursors of the gastrointestinal tract wall characterized by the expression of the receptor tyrosine kinase Kit.[1] It is a disease entity predominantly of people older than 50 years of age, with adults less than 40 years of age accounting for 5% to 20%.[2] Accordingly, they occur most frequently in the stomach (60%), jejunum and ileum (30%), and less frequently in the duodenum (5%), colorectal (<5%), in the esophagus and appendix (<1%).[1] More than 95% of GIST express the KIT protein (CD117), a transmembrane tyrosine kinase receptor for stem cell factor and recently DOG-1 has also been suggested as a useful diagnostic marker.[3]

A small number may originate from outside the gastrointestinal tract and these are designated extra-GISTs (EGISTs). These kinds of tumors arise from pacemaker cells outside of the GI tract or if mesenchymal cells have the ability to recapitulate the phenotype. Another string advocated that tumor might come from pluripotent stem cells located outside the GIT. Another hypothesis is an extramural extension of a stromal tumor within the GIT.[3] Though uncertain, their histological appearance and immunophenotype are identical to those of classical GISTs. EGISTs arising from the omentum are very rarely reported, with only 57 previous cases in literature.[4] Clinicopathological features and prognosis of E-GISTs are limited due to its incidence, much more when it presents as a metastatic disease. Here we report a rare case of Omental GIST with liver metastasis which initially presented as an abdominal mass, which later presented with abdominal pain 8 years later.

CASE

Our case is a 56 year old male, non-hypertensive, diabetic, who initially presented in 2011 with right lower quadrant pain, diagnosed to have a 40 x 24 x 15cm multilobulated mass with solid and cystic components. He underwent diagnostic laparoscopy with excision of omental mass and the pathology report was consistent with a spindle cell neoplasm hence advised Imatinib therapy. However, was lost to follow-up. Interim was unremarkable.

In 2019, 8 years after the initial diagnosis, he came back with a 5-day history of epigastric pain, crampy, intermittent, non-radiating and unrelated to food intake. On consult, he had stable vital signs, was comfortable with no icterisia or jaundice, no pallor, with no signs of chronic liver disease. Abdomen was flabby with noted post-surgical scar, normoactive bowel sounds, soft with direct tenderness on the epigastric area but no rebound tenderness. An abdominal ultrasound was done showing multiple solid to cystic hepatic masses at the right lobe, the largest of which measures 9.4cm x 9.2cm x 8.3cm. To further characterize these lesions, a Dynamic CT scan of the liver was requested which showed hepatomegaly with multiple arterial enhancing lesions

with varying enhancement pattern in the venous and delayed phases. The largest lesion was seen at spanning segments V and VI measuring 9.9cm x 6.6cm x 9.5cm and showed peripheral arterial enhancement with more fill-in in the venous phase but with decreased enhancement in the delayed phases (Figure 1). AFP was normal.

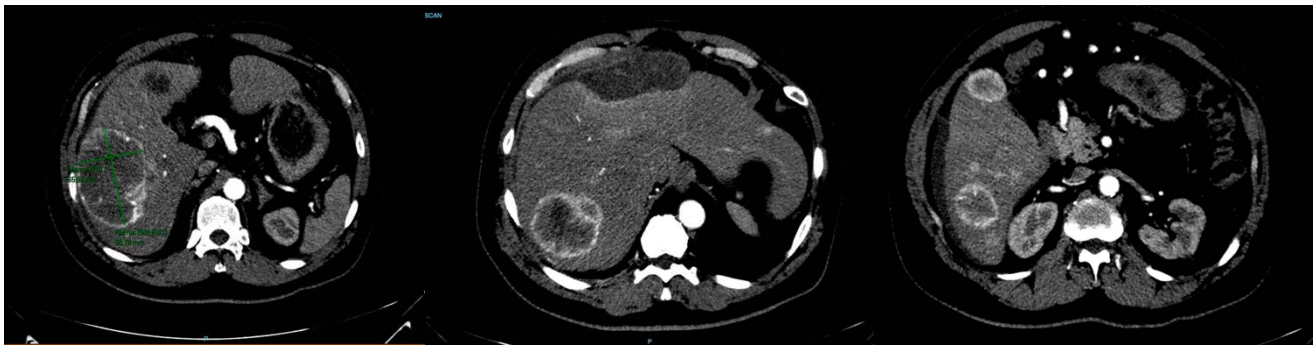

Figure 1. Multiple arterial enhancing lesions with varying enhancement pattern

Hence a liver biopsy was performed which showed atypical spindle cells arranged in loose clusters and scattered singly. The atypical cells have elongated to ovoid, moderately pleomorphic, hyperchromatic nuclei and scant cytoplasm with indistinct cytoplasmic borders (Figure 2). Findings were consistent with a spindle cell neoplasm. Immunohistochemical studies were performed and showed that cells of interest are positive for Vimentin, CD117 and CD34. It was equivocally reactive with Desmin, however, the cells did not show immunoreactivity for Pancytokeratin, S100 and DOG1 (Figure 3). Since the omental mass was already excised 8 years prior, Imatinib therapy was then started and he is on his second cycle at present.

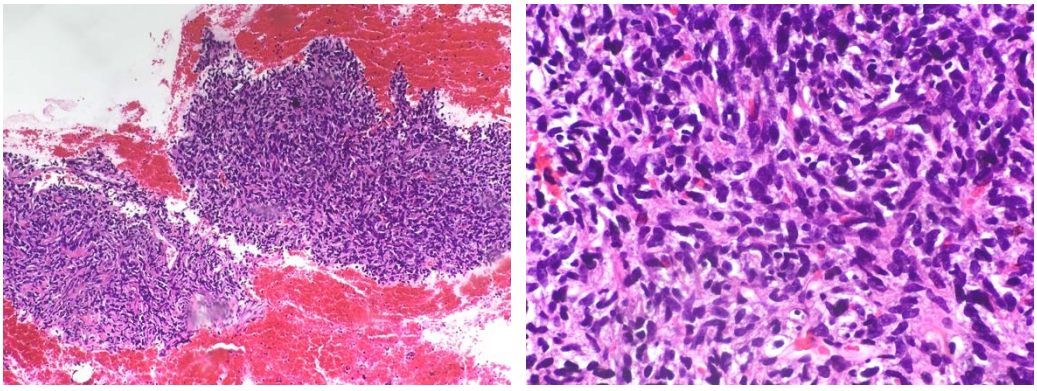

Figure 2. Atypical spindle cells in LPO (left) and HPO (right)

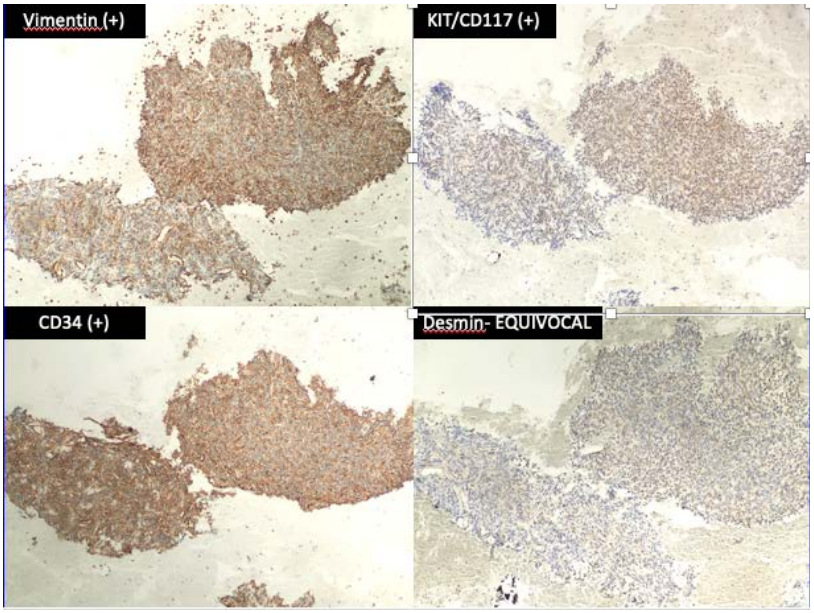

Figure 3. Immunohistochemical studies

DISCUSSION

Clinical manifestations of GISTs are highly variable and it depends on tumor size and location. Omental GISTs can remain silent despite their size. Thus, early diagnosis of omental GISTs is very difficult. Once it reaches a significant size, symptoms will appear. The most common symptom was abdominal pain (49%), followed by abdominal mass (20%%) and abdominal distension.[5] Our case presented with abdominal mass same as most of the cases reported.[1,2,3] However, all of those cases have no evidence of metastasis. In one study, tumor size ranges from 11-20cm[3] with a mean diameter of 15.35cm.[2] Our patient presented with an omental mass with a widest diameter of 40cm.

Computer tomography (CT) is the primary modality of choice for the diagnosis. Usually tumor size exceeds 10 cm, have irregular margins, heterogeneous and calcifications characteristics among others. Histopathologically, microscopic features are site-dependent and more than 85% appears as spindle cell tumors[1] such as in our case, whereas a minority is epithelioid or mixed phenotypes.[3] This is consistent with one study wherein 48% patients diagnosed with omental GIST displayed spindle cell morphology, 33% patients displayed epithelioid morphology and 20% displayed mixed morphology.[5] More than 95% of GIST express the KIT protein (CD117), and recently DOG-1 has also been suggested as a useful diagnostic marker. In the study of Feng et al., CD117 positivity was detected in 85% of patients, whereas CD34 positivity and DOG-1 positivity were detected in 84% and 18% of patients respectively.[5] Both CD117 and CD34 tested positive in our case. In contrast, in a case series by Alves et al., CD117 positivity was not seen in all four cases and only CD34 was positive in all tumors.[3]

Hepatic resection was once the only possible therapy for GIST patients with liver metastases, but this was associated with a high recurrence rate.[8] The emergence of tyrosine kinase inhibitors, such as imatinib mesylate, has radically altered the

outcome of metastatic GIST patients, with an 80% response rate and a median survival time which has increased to 5 years.[6] In the treatment of advanced stage disease, Imatinib remains the mainstay treatment for metastatic and unresectable GIST[7] but mutation testing is recommended prior to therapy according to the European Society of Medical Oncology since approximately 10% of patients with metastatic GIST have Imatinib resistance, Exon 9 mutation of the KIT gene requires a higher dose of Imatinib and some mutations are not responsive to Imatinib therapy.[9] Unfortunately, this was not done in our case. A study by Shi et al. compared the OS of those GIST patients with liver metastasis who received TKI therapy alone from those who received imatinib therapy postoperatively. The median overall survival for patients with TKI only therapy was 53 months. In contrast, patients who received surgery combined with TKIs had a tendency to have an improved median overall survival of 89 months.[6] Hence, Imatinib therapy as an adjuvant to complete resection has been carried out safely and may prevent relapse to prolong long-term survival. In our case, Imatinib therapy was only given since the multiple hepatic masses were unresectable.

CONCLUSION

Primary Omental GIST with liver metastasis is a rare disease and our existing data is not sufficient to conclude as to the proper management of these cases, but surgical resection combined with TKIs seems to constitute the most efficient treatment. Also, doing mutational analysis prior to TKI therapy is of utmost importance for a more tailored therapy.

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