

Dear Editor,

We are very grateful for your excellent and thoughtful review of the manuscript. Please see below with the detailed changes made to the manuscript in response to the comments.

Response to Editor's Comments

Overall, a great review that has the potential to serve as an excellent reference/resource for the readers. Although there are some revision requests, I do believe if this manuscript is revised according to the following requests, it will be very educational for the readers.

We thank the Editor for the kind comments. We have now addressed all the concerns and revised where advised.

1. Although some of the following sentences are common sense to some readers, it is still essential to provide appropriate evidence:

[Introduction] GISTs can arise anywhere in the GI tract, most commonly from the stomach and small intestine.

[Introduction] The majority of GISTs occur as a result of activating mutations in two receptor protein tyrosine kinases: KIT and/or platelet-derived growth factor receptor- α (PDGFRA).

[Introduction] Surgical resection is the preferred management for small GISTs, while tyrosine kinase inhibitors – imatinib mesylate and sunitinib malate – serve as crucial targeted therapies for locally advanced and metastatic GISTs.

[Pathology and Molecular Cytogenetics] In the pediatric population, GISTs typically do not have KIT or PDGFRA mutations, and generally demonstrate the epithelioid subtype and express CD117.

Response to comment 1:

Thank you for highlighting that. We added references for each of the above statements.

2. The following sentences seem to contain contradictions with each other. Please revise them into appropriate expressions to avoid misunderstandings.

[Clinical Features] Metastases are uncommon (10-20% of cases), but can occur via local or hematogenous spread

[Computed tomography] Metastases are present in approximately 50% of patients and often involve the liver and mesentery

Response to comment 2:

Thank you for highlighting that. We revised each of the above sentences as advised.

“Metastases are uncommon (10-20% of cases); however, when they do occur, they can occur via local or hematogenous spread.”

“Metastases are present in approximately 50% of patients, and metastases often involve the liver and mesentery; they demonstrate similar imaging features as primary GISTs [24,27].”

3. [Magnetic resonance imaging] “The presence of intratumoral cystic change with low apparent diffusion coefficient (ADC) values are predictors of high malignant potential.” As more specific evidence has been provided in the past regarding this statement (described below), it should be revised or added accordingly. - (PMID: 25341135) There was a negative linear correlation between the ADC values and the malignancy risk of GISTs ($r = -0.670$, $p < 0.05$).

Response to comment 3:

Thank you for sharing this. We added a statement about this including its reference.

“The presence of intratumoral cystic change with low apparent diffusion coefficient (ADC) values are predictors of high malignant potential [33]. A negative correlation between mean ADC values and malignancy risk of GISTs has been demonstrated [33].”

4. [Positron emission tomography-computed tomography] Please clarify the type of the radioactive tracer (I assume the authors are describing regarding 2-deoxy-2-[fluorine-18]fluoro-D-glucose (18F-FDG))

Response to comment 4:

Thank you for highlighting that. Yes, we added clarification that we are referring to 18F-FDG.

5. [Management and Surveillance] With the recent advances in molecular targeted therapy, many drug-specific and characteristic adverse effects have become known. Please add a description of this point. The followings are some important examples:

- o imatinib-associated intratumoral hemorrhage (PMID: 16549611)
- o sunitinib- and sorafenib-associated pancreatitis (PMID: 32302358)
- o imatinib- and sunitinib-associated pancreatic volume changes may indicate a worse prognosis in patients with GIST (PMID: 33281059, 27643769)

Response to comment 5:

Thank you for highlighting that. We added a paragraph under the “Management and Surveillance” section describing several drug-specific adverse effects, including the important examples.

“With the advancement of these molecular-targeted therapies, multiple associated adverse effects have been demonstrated, and some of these may be identified on follow-up imaging. Fluid retention is commonly seen with imatinib mesylate and can manifest with pleural effusions, pericardial effusion, ascites, or extensive subcutaneous edema [27]. Imatinib mesylate can be associated with intratumoral hemorrhage, especially in patients with large bulky tumors [1,27]. Tyrosine kinase inhibitors are associated with pancreatic findings. For instance, imatinib mesylate is associated with

asymptomatic pancreatic swelling; a $\geq 22\%$ increase in pancreatic volume has been shown to be a poor prognostic indicator ^[41]. Conversely, sunitinib malate is associated with pancreatic atrophy, and this finding is associated with poor prognosis ^[42]. Moreover, there are several case reports of pancreatitis associated with sunitinib malate and sorafenib therapy ^[43]. It is important to identify these adverse effects on imaging, which would allow for dose reduction, dose interruption, or drug discontinuation in the appropriate setting.”

6. [Table 2] for MRI findings of primary and metastatic GISTs, negative linear correlation between the mean ADC values and the malignancy risk should be noted (PMID: 25341135)

Response to comment 6:

Thank you for highlighting that. We added this description in Table 2.

7. [Figure legend 2] A) Axial CT image -> Axial contrast-enhanced CT image

Response to comment 7:

Thank you for highlighting that. We revised that as advised.

8. [Figure legend 2] B) Axial fused PET CT image -> Axial fused 18F-FDG PET CT image

Response to comment 8:

Thank you for highlighting that. We revised that as advised.

9. [Figure legend 2] C) “marked FDG avid”: please provide the SUV max.

Response to comment 9:

Thank you for highlighting that. We provided the SUV max.

10. [Figure legend 3] E) “marked diffusion restriction”: please provide the ADC value.

Response to comment 10:

Thank you for highlighting that. We provided the ADC value.