

March 18, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 8943-review.doc).



Title: Imaging findings of primary gastric plasmacytoma: A case report

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 8943

The manuscript has been improved according to the suggestions of reviewers:

1 The language has revised.

2 we have added the "Highlighted contents".

3 Format has been updated

3 Revision has been made according to the suggestions of the reviewer

Thank you again for publishing our manuscript in the World Journal of Gastroenterology.

Sincerely yours,

A handwritten signature in black ink that reads 'Bo Yin Wang'.

Boyin Wang, MD

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Reviewer #1:

This case report described the imaging findings of a rare case of primary gastric plasmacytoma. Few literature described the imaging findings of this disease. It is good report, but there are also some problems.

Response: We appreciate the thoughtful comments and suggestions of the reviewer for our paper and we are fortunate for meeting a kindness reviewer.

1. The language needs a major revision. Find someone whose native language is English to revise the language for you.

Response: The language in our manuscript has been polished. Please, check it over.

2. Use of abbreviations: When using abbreviations in the text, you should give the full phrase at the first time using the abbreviations, later, you can always use the abbreviation. For example, when using primary gastric plasmacytoma (GP), give GP in the brackets following the full phrase, and later you can always use the abbreviation to indicate the full phrase. However, the authors did not abide by this rule all the time. In the abstract, if the full phrase is used only once, do not give the abbreviation. Even if you used some abbreviations in the abstract, you should also give both the full phrase and the abbreviation in the text when first using them. In this article, the authors used abbreviations in the abstract, but did not give the full phrase in the text. Correct this problem in the text. Give the full phrase of CT, MRI, ADC, DWI, GP etc. in the text when first using them.

Response: We thank reviewer for instructing us to revise the abbreviations in detail and we have revised it. Please check it.

Instruction:

GP, CT, and MRI were revised as: **gastric plasmacytoma (GP)**, **computed tomography (CT)**, and **magnetic resonance imaging (MRI)**, respectively, when these abbreviations were firstly used.

Case report:

HU, T2WI, T1WI, DWI, ADC, and HE were revised as: **Hounsfield units (HU)**, **T2-weighted images (T2WI)**, **T1-weighted images (T1WI)**, **diffusion-weighted imaging (DWI)**, **apparent diffusion coefficient (ADC)**, and **Haematoxylin-eosin (HE)**, respectively, when these abbreviations were firstly used.

Discussion:

“PET” revised as **positron emission tomography (PET)**.

3. Use of citations: When citing others' work, use the last name of the author followed by et al if there are more than one authors. For example, “Avcu S et al [10] evaluated gastric tumors by using ADC-----” in the forth passage in the DISCUSSION, “Avcu S et al” should be “Avcu et al”.

Response: We have revised “Stasi R et al” and “Avcu S et al” to “**Stasi et al**”, “**Avcu et al**”.

4. References: Although there are quite a few papers regarding case reports of primary gastric plasmacytoma, there are really few case reports describing the imaging findings. In this case, this manuscript is quite good. However, some new references were not cited by the authors. Please check the PUBMED and cite some new case reports.

Response: Focusing on the imaging features of primary GP, we did not cite the references which the reviewer mentioned. We have reviewed the references carefully after the reviewer's reminding and find that *Helicobacter pylori* organisms in these cases are not identified so we have added these references and PET findings about primary GP.

“**although this organism was not detected in several published cases**”^[5,6]

Tan et al.^[5] reported two cases of gastric plasmacytoma following definitive radiotherapy and suggested that PET and CT imaging provided little or no value for estimating the extent of disease in the stomach but was valuable for excluding dissemination beyond the stomach.

5 Tan J, Lade S, Harrison S, Opat S, Mac Manus MP. Complete remission of localised gastric plasmacytomas following definitive radiotherapy. J Med Imaging Radiat Oncol 2012;56:328-31 [PMID:22697332 DOI: 10.1111/j.1754-9485.2012.02369]

6 Kanzawa M, Hirai C, Morinaga Y, Kawakami F, Hara S, Matsuoka H, Itoh T. Primary submucosal nodular plasmacytoma of the stomach: a poorly recognized variant of gastric lymphoma. Diagn Pathol

Reviewer #2:

This manuscript describes the CT, MR, endoscopic and endoscopic US findings of a case of primary gastric plasmacytoma.

Response: We appreciate the comments and suggestions of the reviewer for our paper and reviewer's questions are very helpful for us to further understand primary GP.

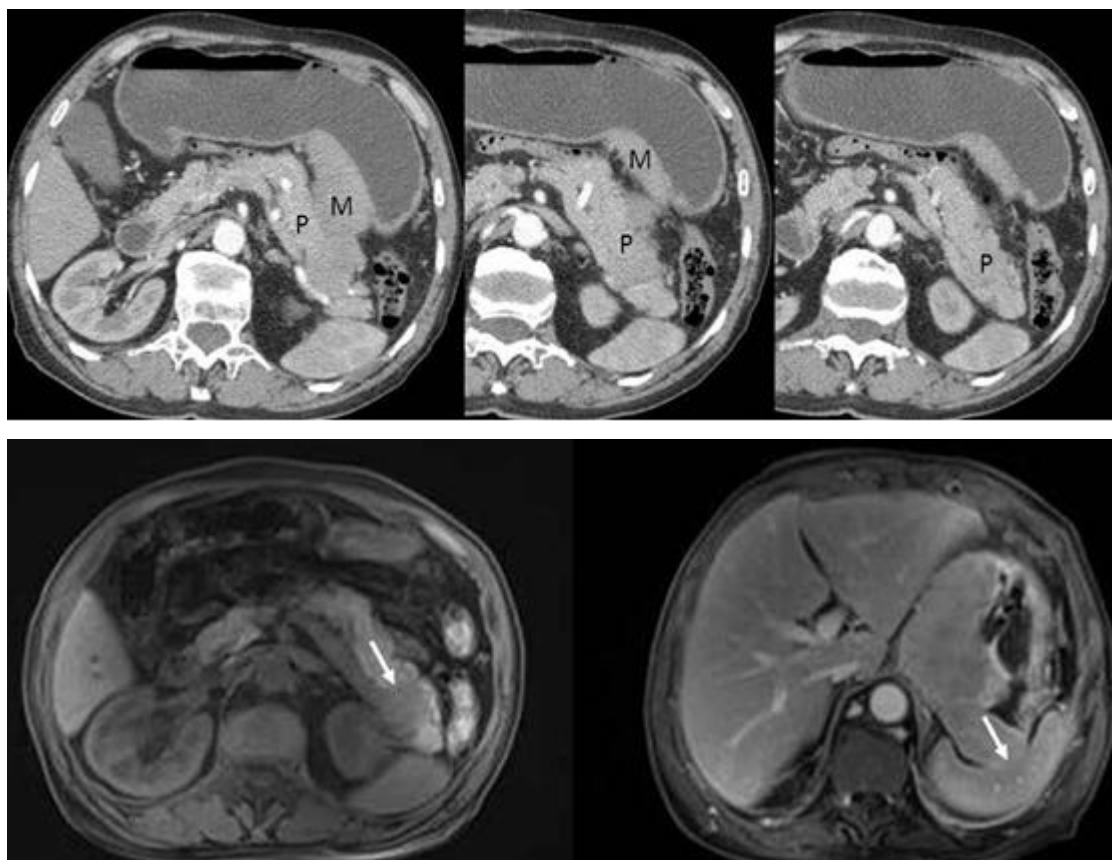
Case report:

1. Can the authors clarify what "..... symptoms of epigastric pain and repeated catch after eating" means?

Response: Sorry, it is our mistake. The sentence means that: A 79-year-old male was admitted to our hospital **after presenting with epigastric pain and a choking feeling after eating, which had lasted for approximately one month.**

2. From the CT and MR images provided, one cannot be confident that the mass is not arising from the pancreas and infiltrating into the stomach despite the authors conflicting comments that "The adjacent pancreas was compressed and displaced" and later said "The lesion infiltrated the adjacent pancreas and spleen." Also, the finding that the mass was submucosal does not help to determine if tumor was arising from the stomach wall or infiltrating from adjacent viscera. From the CT and MR images, the mass did not appear to infiltrate into the spleen. Perhaps a curved multiplanar reconstructed image of the pancreas showing the relationship of the tumor to pancreas and spleen would be helpful.

Response: Yes, images provided may be difficult to identify the mass is not arising from the pancreas, because this case of primary GP is a very special case that the lesion appeared as extraluminal mass and we are perplexed to ensure all provided images must have uniformity and few numbers of pictures as far as possible, furthermore, in this case report, we mainly emphasize more characteristic and different imaging features from former reported cases. We will provide some images to help to identify origin organs of the mass and whether, the mass infiltrated the adjacent pancreas and spleen.



It seems conflicting comments that "The adjacent pancreas was compressed and displaced" and later

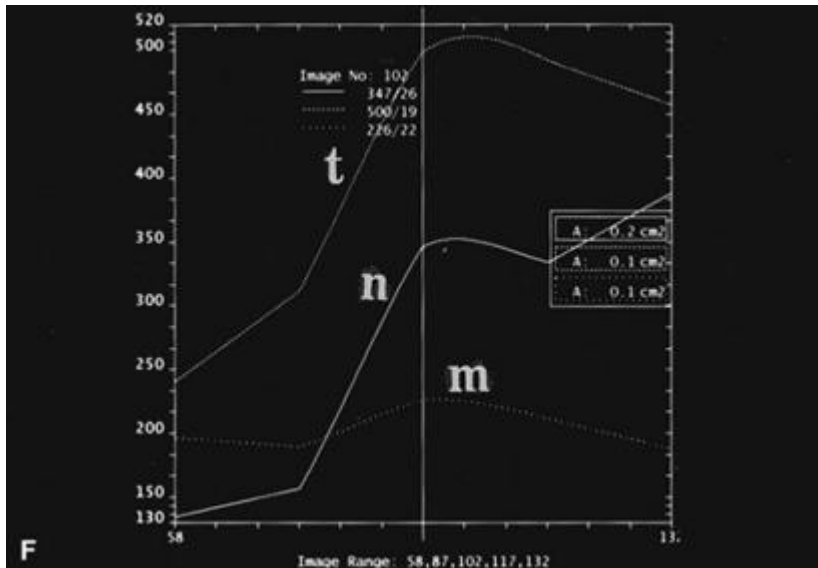
said “The lesion infiltrated the adjacent pancreas and spleen.” However, it reflects the fact that MRI has perfect soft tissue resolution: we are not sure the mass infiltrated the pancreas, only identify compress it on CT images, but we confidently identify that the mass infiltrated the adjacent pancreas and spleen on MRI images just as displayed MR images.

3. Authors should reconsider the comment that a change in CT attenuation from 40.4HU to 84HU as moderate enhancement. It is mild enhancement.

Response: Radiologists usually consider 10-20HU, 20-40HU, more than 40HU or 50HU as mild, moderate and marked or strong enhancement, respectively. We prudently believe that CT attenuation from 40.4HU to 84HU is moderate enhancement. Although, we do not find the definite criterion about different enhancement degree, but we provide two articles that mentioned the enhancement degree. [Cited from: (Liu Z, Lv X, Wang W, An J, Duan F, Feng X, Chen X, Ouyang B, Li S, Singh S, Qiu S. Imaging characteristics of primary intracranial teratoma. *Acta Radiol.* 2013 8. PMID: 24103916), (Line 7-9, page 2, Material and Methods- Image analysis part)]; [Cited from: (CT Features of Adrenal Pheochromocytoma: Evaluation with Clinical and Pathological Correlation. http://www.sirirajmedj.com/content.php?content_id=2513).(Line 14-17, the third paragraph, MATERIALS AND METHODS part)].

4. Authors should reconsider comment that the lesion is submucosal on MR as this is impossible to determine on the provided images.

Response: In MR study, the normal wall showed a two-layered structure; these two layers corresponded to the inner mucosal layer showing rapid and marked enhancement and the outer low-signal-intensity submucosal and muscular layers with delayed enhancement. [Cited from: (Kang BC, Kim JH, Kim KW, Lee DY, Baek SY, Lee SW, Jung WH. Value of the dynamic and delayed MR sequence with Gd-DTPA in the T-staging of stomach cancer: correlation with the histopathology. *Abdom Imaging* 2000;25(1):14-24. PMID:10652915); (line 21, page 21, in Discussion part)]. The undermentioned figure shows the different enhancement patterns between mucosal layer and muscle layer in some cases. (cited from Fig 6, the same referenced article)

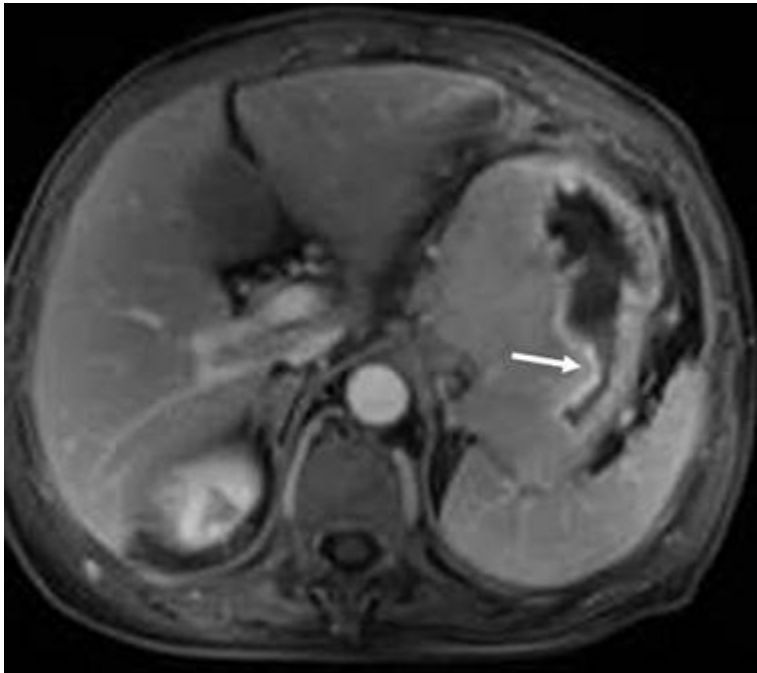


tumor is invading the duodenal cap through the pylorus. **F** Time-intensity curve demonstrates that the cancerous wall (*t*) is more rapidly enhanced (peak enhancing point is 60–90 s after Gd-DTPA intravenous injection) than the normal mucosal wall (*n*) and back muscle (*m*). **G** Photomicrograph

At contrast-enhanced CT, the normal GI wall also may demonstrate layered enhancement: an inner mucosal layer with marked enhancement, a middle submucosal layer with lower attenuation, and an outer muscular-serosal layer with moderate enhancement. [cited from: (Lee NK, Kim S, Kim GH, Jeon TY, Kim DH, Jang HJ, Park do Y. Hypervascular Subepithelial Gastrointestinal Masses: CT-Pathologic

Correlation. Radiographics. 2010;30(7):1915-34. doi: 10.1148/rg.307105028. PMID:21057127). (The part of "Determination of mass origin in the GI wall with CT", page 1916 to 1917)]

May be the resolution of MR images we submitted is not high enough, that make the reviewer dose not identify the marked enhancement mucosal layer confidently. Once, we submitted high resolution pictures resulted in large volume of file and could not download by the editors. Finally, our manuscript was withdrawn. We provide another picture which may be helpful to identify the enhancement mucosal layer.



5. Can the authors comment if the gastric mucosa overlying the mass was ulcerated at endoscopy?

Response: There were several superficial mucosa erosions overlying the mass. We have added the content about this issue.

An upper endoscopy revealed irregular bulging from the fundus to the posterior side of midbody, as well as several superficial mucosal erosions overlying the mass (Fig. 3A, B),

6. Can the authors comment how the biopsy specimen was obtained? Was it a blind biopsy at endoscopy, using endoscopic US or percutaneous CT/US guided?

Response: The biopsy specimen was obtained from blind biopsy at endoscopy. We have revised the sentence as "Analysis of the biopsy specimen obtained from endoscopy indicated primary GP"

7. Can the authors comment if serum and urine electrophoresis were performed?

Response: As we have mentioned in the manuscript, the laboratory data including IgM, IgG, IgA, and β 2 microglobulin were within normal limits.

8. Can the authors comment if other more sensitive imaging techniques, such as PET/CT or 99mTc Sestamibi scintigraphy, were performed to detect other sites of disease?

Response: It is regret that the patient did not performed PET/CT or 99mTc Sestamibi scintigraphy, but he was performed ECT and whole body 3.0T MRI and chest CT, and so on. All these examinations could not find related lesions.

9. Can the authors discuss if histopathologic evaluation of the surgical specimen enabled determination of the organ of origin of the tumor, and if it was early or advanced stage primary gastric plasmacytoma?

Response: In manuscript, we have described that One 10.1×15.0×16.0 cm mass was identified in the gastric

fundus and midbody.

We have added the stage of this primary GP. “The mass had infiltrated the lamina propria, pancreas, and spleen and was classified at an advanced stage.”

10. Can the authors comment if H pylori was present in the biopsy specimen?

Response: In the biopsy specimen, pathologists did not found H pylori. We have added this issue.

“... indicated primary GP and *Helicobacter pylori* was not detected.”

11. Discussion: Authors should consider changing “gastroenterography” to “upper gastrointestinal series”.

Response: Yes, upper gastrointestinal series is better than gastroenterography. We have changed it.

“... including upper gastrointestinal series, CT, MRI, positron emission tomography (PET), ...”.

12. Authors should change “Homogenous” to “homogeneous” throughout the manuscript.

Response: We have revised “homogenous” to “homogeneous”.

Line 6 in Abstract; line 4 in instruction; line 8, 18, 25 in case report; line 16, 27, 29, 47, 50, 53, 56, 65, 67 in discussion; line 2, 5, 9 in Figure legends.

13. I am not confident that the contrast enhancement characteristics allow differentiation of gastric plasmacytoma from gastric lymphoma, as suggested by the authors. Furthermore, the difference in ADC values between gastric lymphoma and plasmacytoma is insufficient to allow definitive differentiation based on ADC values alone, and the authors should emphasize this.

Response: we understand reviewer’s opinion. At first, we also diagnosed this case as gastric lymphoma. After we analyzed this case carefully, we found: (1) this primary GP appeared as a well-circumscribed extraluminal mass was different from most gastrointestinal lymphoma appeared as homogeneous concentric gastric wall thickening; (2) a gradual enhancement pattern was observed, since most gastrointestinal lymphoma indicates mild enhancement; (3) ADC value is a quantity index, it is more accurate to show the water molecular movement among mass. Rare article reported the ADC value of gastrointestinal lymphoma, let alone, that of primary GP. We compared the ADC value of this case of primary GP with that of reported gastrointestinal lymphoma and found the ADC value of primary GP and gastric lymphoma was $0.863 \times 10^{-3} \text{ mm}^2/\text{sec}$ and $1.09 \pm 0.08 \times 10^{-3} \text{ mm}^2/\text{s}$, respectively.

All these imaging features of this primary GP were never reported in English literatures. We proposed these imaging features may be helpful for differentiating primary GP from gastrointestinal lymphoma, but, just as we mentioned in manuscript, “However, additional cases are needed to analyse the ability of CT and MRI findings to differentiate primary GP from lymphoma.”

14. Authors should comment on the prognosis of gastric plasmacytoma, and provide any data on the follow-up of their case.

Response: we have added the data on the follow-up of this case.

Abdominal and pelvic CT analysis performed eight months after the operation indicated no recurrence or metastasis in any abdominal organs, and the laboratory results were within normal limits.

15. Figures and legend: Fig 3 legend: Authors should consider deleting "raw" from the legend.

Response: We have deleted the "raw" from the legend.

Fig. 3. and endosonography indicates the effacement of the normal structure

16. Annotations in the figures should be a suitable size relative to the image.

Response: Yes, we also believe the figures of CT attenuation with a suitable size are perfect. We could not measure CT attenuation on CT workstation since workstation computer automatically delete the patient data for certain months. Now, we have contacted the CT engineer to help us transport the patient’s raw image data from PACS back to workstation. We will try our best to resolve this problem.

17. References: Authors should consider including: Tan J, Lade S, Harrison S, Opat S, MacManus MP. Complete remission of localised gastric plasmacytomas following definitive radiotherapy. J Med Imaging Radiat Oncol 2012;56:328-331

Response: we have cited the reference suggested by reviewer.

Tan et al^[5] reported two cases of gastric plasmacytomas following definitive radiotherapy with PET findings and suggested PET and CT imaging was little or no value for estimating the extent of disease in the stomach but was valuable for excluding dissemination beyond the stomach.

5 Tan J, Lade S, Harrison S, Opat S, Mac Manus MP. Complete remission of localised gastric plasmacytomas following definitive radiotherapy. J Med Imaging Radiat Oncol 2012;56:328-31 [PMID:22697332 DOI: 10.1111/j.1754-9485.2012.02369]