RESPONSES FOR COMMENTS

Dear Editors and Reviewers:

Thank you so much for your critical comments on our CASE REPORT entitled "***Gastric cancer with severe immune thrombocytopenia: Case report and literature review"*** (Manuscript ID 41600). We highly appreciate the reviewer's carefulness and broad knowledge, as they have provided us with a number of beneficial suggestions.

Based on the helpful and significant suggestions, we have carefully revised the manuscript. We are now sending the revised manuscript for your re-consideration for *World Journal of Clinical Cases*.

We hope the new manuscript will meet the standards of *World Journal of Clinical Cases*. Please check our point-by-point responses to all your and the reviewers' comments below.

Best wishes,

Dr. Jian-Chun Yu
Department of General Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Science and Peking Union Medical College.
yjcpumch@126.com

Comments and Responses for Reviewer #1

Comment: *This paper describe a case of advanced gastric cancer complicated with severe ITP, medically refractory from 10 years. The patient was treated with radical resection of the gastric cancer, associated to preoperative PLT transfusion and early EN. Simultaneous splenectomy seems to successfully obtain a stable increase in the platelet count after two years. The presentation of the case is good; the patient seems to be treated according to the modern guidelines and correctly managed; a review of the literature is also presented from which only five cases are obtained in the last two decades. I have not suggestions for the Authors. The only note is that this clinical case is a rare association of pathologies, without bringing important novelties in the treatment. The authors treated two concomitant pathologies, probably not related by cause relationships. Performing splenectomy, they followed one of the possible therapeutic approaches for ITP (see Kojouri K et al. Blood. 2004;104(9):2623-34). It*

is therefore not surprising that the patient has shown a durable improvement in the platelet count.

Response: We appreciate the reviewer's carefulness and suggestion. There are several novelties in these article. We report a rare case of gastric cancer complicated by severe and medically refractory ITP and a review of the related literature. In patients with a sever ITP, most patients may not achieve a long-term stable response to a splenectomy[1]. In this case, splenectomy was performed because of its high response rates in short-term postoperative time. Simultaneous splenectomy can reduce postoperative complication rates and bleeding risks for sever ITP patients with major surgery, which may lay a foundation for future clinical work. Early EN is also important in this case to implement as a way to accelerate rehabilitation of intestinal function and immune response.

Ref:

1. Rijcken E, Mees ST, Bisping G, et al. Laparoscopic splenectomy for medically refractory immune thrombocytopenia (ITP): a retrospective cohort study on longtime response predicting factors based on consensus criteria. Int J Surg 2014; 12: 1428-1433.

Comments and Responses for Reviewer #2

Comment: *This good case report might contribute to improving our understanding of the behavior and perioperative management of sever and medically ITP patients with gastric cancer.*

Response: We appreciate the reviewer's comments.

Comments and Responses for Reviewer #3

1. ***Comment:*** *More attention needed to be payed to the details. For example, the word "foundation" was misspelled in the "Supportive foundations", and there was a small error in the first sentence of the "CASE REPORT".*

Response: We appreciate the reviewer's comments and apologize for the typos. After a careful review, we changed some of the mistakes in the text.

2. ***Comment:*** *References were a bit outdated. There were 26 references in the text, of which only 5 references were published in the last 5 years, and no reference was published in the past 3 years.*

Response: Thanks for your suggestion. We replaced some outdated references in the article. There were 11 references were published in the last 5 years, of which 6 reference was published in the past 3 years.

3. ***Comment:*** *The case presentation was not detailed enough. The description of the personal history (occupation), family history and past history was not specific enough. The patient was diagnosed with immune thrombocytopenia 10 years ago and medications including steroids, immunoglobulins, androgen derivatives, cyclosporine A and thrombopoietin were administered respectively since the first diagnosis. However, there was no significant effect. This article didn't elaborate on the specific medication of the patient in the past 10 years, including the medication time, dose and changes in therapeutic effect. At the same time, the previous medical history and general condition were closely related to surgery and postoperative recovery, while there was no corresponding explanation in the text neither.*

Response: Thank you for your comments. We added personal history (occupation), family history, past history and general condition in the text. And a detailed description of medication for ITP was added in the manuscript including medication time, dose and changes in therapeutic effect. We hope that these changes will help the readers to have a better understanding of this patient's ITP treatment and perioperative general condition.

4. ***Comment:*** *The elaboration of the key concept was not specific enough. Some studies showed that the severity of ITP was related to the degree of thrombocytopenia; however, some researchers believed that the disease severity was based clinically on bleeding scores rather than a PLT count. Although the patient's symptoms of gastrointestinal bleeding, changes in HGB and PLT had been mentioned in the text, there was no detailed assessment of the bleeding scores and no clear definition for the severe and medically refractory ITP.*

Response: We appreciate the reviewer's suggestions. Definition for the severe and medically refractory ITP was added in the manuscript. We used Khellaf's bleeding score to assess the severity of ITP[1]. According to Khellaf's bleeding score, this patients presented with Gastrointestinal hemorrhage and acute anemia with a high bleeding score of 15, which indicated a severe ITP with high risk of life-threatening

hemorrhage. Khellaf's bleeding score is attached as follows and readers can found it from the reference.

Table 1. The bleeding score.

Age*	
Age over 65 years	2
Age over 75 years	5
Cutaneous bleeding*	
Localized petechial purpura (legs)	1
Localized ecchymotic purpura	2
Two locations of petechial purpura (e.g. legs + chest)	2
Generalized petechial purpura	3
Generalized ecchymotic purpura	4
Mucosal bleeding	
Unilateral epistaxis	2
Bilateral epistaxis	3
Hemorrhagic oral bullae, spontaneous gingival bleeding or both	5
Gastrointestinal bleeding*	
Gastrointestinal hemorrhage without anemia	4
Gastrointestinal hemorrhage with acute anemia (> 2g Hb decrease in 24h) and/or shock	15
Urinary bleeding*	
Macroscopic hematuria without anemia	4
Macroscopic hematuria with acute anemia	10
Genitourinary tract bleeding*	
Major meno/metrorrhagia without anemia	4
Major meno/metrorrhagia with acute anemia	10
Central nervous system bleeding	
Central nervous system bleeding and/or life-threatening hemorrhage	15

**For these items, only the highest value was taken into account.*

Ref:

1. Khellaf M, Michel M, Schaeffer A, Bierling P, Godeau B. Assessment of a therapeutic strategy for adults with severe autoimmune thrombocytopenic purpura based on a bleeding score rather than platelet count. *Haematologica* 2005; 90: 829-832.

5. ***Comment:*** *This study contributed to improving our perioperative management of sever and medically ITP patients with gastric cancer. And simultaneous splenectomy, preoperative PLT transfusion and early EN could reduce the risk of bleeding and improve the success rate of surgery. However, the reference significance of this case was affected due to the lack of detailed description of the preoperative general condition, preoperative medication and disease severity.*

Response: We appreciate the reviewer's comments. Aiming to lay a foundation for future clinical work, we report a first case of gastric cancer complicated by severe and medically refractory ITP treated with subtotal gastrectomy and splenectomy and a review of the related literature. We added detailed description of the preoperative general condition, preoperative medication

and disease severity in the manuscript and hope to increase the reference value of this case.

We hope that these revisions are satisfactory and that the revised version will be acceptable for publication.
Thank you very much for your work regarding our paper.

Wish you all the best!
Sincerely,

Dr. Jian-Chun Yu
Department of General Surgery
Peking Union Medical College Hospital
Peking Union Medical College and Chinese Academy of Medical Sciences
Beijing 100730, People's Republic of China
Email: yjcpumch@126.com