

July 4, 2009

Jing Yu
Science Editor
World Journal of Gastroenterology

Title: Vanishing Bile Duct Syndrome in Hodgkin's Lymphoma: A Case Report and Literature Review

Manuscript ID: 26782

Dear Editor Yu:

Thank you for your consideration of our revised manuscript entitled "Vanishing Bile Duct Syndrome in Hodgkin's Lymphoma: A Case Report and Literature Review" for publication in *World Journal of Gastroenterology*. We are grateful to the editors and reviewers for the valuable feedback that has strengthened the manuscript. We have made the recommended changes in the text which we believe fully address the comments raised in peer review, and hope these will be found satisfactory by the editor.

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 26782

Title: Vanishing Bile Duct Syndrome in Hodgkin's Lymphoma: A Case Report and Literature Review

Reviewer's code: 03251862

Reviewer's country: United States

Science editor: Jing Yu

Date sent for review: 2016-04-26 16:33

Date reviewed: 2016-05-14 19:57

COMMENTS TO AUTHORS

In the manuscript entitled "Vanishing Bile Duct Syndrome in Hodgkin's Lymphoma: A Case Report and Literature Review", Bakhit et al., report a case and provide a thorough review of the literature. The manuscript is well written; the literature review is comprehensive and highly informative. I only have a few comments: Major point 1: The statement in the abstract "Precise pathophysiology remains unclear with multiple potential triggers of biliary duct apoptosis postulated" should (a) be reworded, and (b) indicates that the paper includes a discussion of the pathophysiological association of Hodgkin's Lymphoma and VBDS. The authors should consider adding a section in the discussion or remove this sentence. Major point 2: While the paper focuses on the association of VBDS and Hodgkin's Lymphoma, the Introduction statement: "VBDS has been associated with potential infectious etiologies, ischemia, autoimmune diseases, adverse drug reactions, and humoral factors associated with malignancy" – should be slightly expanded and list a more comprehensive, and grouped, list of etiologies/associations. Minor point: The authors should specify the contents of the "extended genetic panel sequencing" and how this was done (NGS? Sanger? Single-gene?).

Author Response: *We thank the reviewer for highlighting these important recommendation and suggestions. We have addressed all major points. Specifically, we have removed the sentence to clarify that the manuscript does not discuss pathophysiology. Additionally, we have made subtle changes to the sentence regarding multiple etiologies and most notably attached a new table that highlights the potential etiologies from previously published case reports. Lastly, regarding genetic panel testing, the manuscript was revised to state next-generation whole exome sequencing was utilized. We feel these edits have significant strengthened the manuscript and will be more relevant to a larger readership.*

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 26782

Title: Vanishing Bile Duct Syndrome in Hodgkin's Lymphoma: A Case Report and Literature Review

Reviewer's code: 03636431

Reviewer's country: Japan

Science editor: Jing Yu

Date sent for review: 2016-04-26 16:33

Date reviewed: 2016-06-06 13:55

COMMENTS TO AUTHORS

Bakhit et al. report a case of vanishing bile duct syndrome in Hodgkin's lymphoma, and review previous report concisely. Although the manuscript is well written, it needs some minor modifications. Minor point 1: Authors should unify the writing of "Hodgkin's Lymphoma". The word "Hodgkin Lymphoma" exists on line 10 of abstract. Minor point 2: Abstract section, line 11, "a 25 year-old" should be "a 25-year-old". The word also exists on line one of "case presentation" section. Minor point 3: Abstract section, line 13, "this an underlying cause" should be "this underlying cause". Minor point 4: Case presentation section, 3rd paragraph, line 9, "ischemia versus drug/toxin effect versus an entroinvasive infection" seems to be a colloquial expression. It might be better to express as "ischemia, drug/toxin effect, or an entroinvasive infection". Minor point 5: Case presentation section, 5th paragraph, line 4, "stage IIb" should be "stage IIB", if "b" means a presence of B symptoms. If it means a presence of bulky disease, it should be stage IIX or stage II with bulky lesion. And what pathological type was the patient's HL? If possible, please describe the pathological type of HL. Minor point 6: Case presentation section, 6th paragraph, the authors should refer which genes were tested, and how the examination performed. Minor point 7: Discussion section, 4th paragraph, line 10, "mustargen" and "oncovin" are trade names. It should be changed to mechlorethamine and vincristine, respectively. Minor point 8: Discussion section, 5th paragraph, line 11, Although authors described a positive outcomes of rituximab against VBDS caused by HL through immunological effect, the recovered liver function of a patient in reference No.48 doesn't seem to be an effect of rituximab (It seems to be an result of remission of HL). Minor point 9: Discussion section, 5th paragraph, line 4-5, what does "cholestasis secondary to VBDS is this most common presenting symptom HL" mean? I could not understand. Minor point 10: Table 1, reports of Gagnon (2013, ref No.18), Foramiti (2013, ref No.17), and Gill (2010, ref No.19) are not cases of HL. They are cases of non-Hodgkin lymphoma. Minor point 11: Table 1, what does "IC" stand for? May be Idiopathic cholestasis? Authors should use an abbreviation after spelling out.

Author Response: *We thank the reviewer for highlighting these important suggestions. We have*

addressed all major and minor points. We have standardized the use of Hodgkin's lymphoma (HL), staging of disease, elimination of trade names, and provided changes to the table as suggested. We appreciate these valuable recommendations and thank the reviewer for the feedback.