

RESPONSE TO REVIEWERS



July 7, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 11375-review.doc).

Title: Nodular lymphoid hyperplasia in the gastrointestinal tract in adult patients: a review.

Author: Andreia Albuquerque

Name of Journal: *World Journal of Gastrointestinal Endoscopy*

ESPS Manuscript NO: 11375

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

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewers

Reviewer #01489500 suggested that "I don't agree with the proposed systematic approach which basically suggests that we investigate everyone with NLH. I would probably suggest that only symptomatic patients should be investigated further for associated diseases. Therefore, I think the paragraphs follow-up and conclusion should be modified accordingly"

ANSWER TO THE REVIEWER: figure 3 that proposed a systematic approach to patients with Nodular Lymphoid Hyperplasia (NLH) was eliminated, as suggested, and follow-up and conclusion modified accordingly.

There are several diseases linked to NLH, such as, common variable immunodeficiency, selective IgA deficiency, or *Giardia* infection and, more rarely, human immunodeficiency virus infection, celiac disease, or *Helicobacter pylori* infection. These diseases should be suspected in patients diagnosed with NLH; whether or not all of them should be excluded in all patients with NLH is yet to be determined because there are no studies concerning this subject.

Reviewer #00504725 suggested that "Why recommend checking for celiac when you state the association of NLH with celiac is rare? Similarly, as you note the link between extraintestinal lymphoma is uncommon so why do surveillance?"

ANSWER TO THE REVIEWER: the recommendation of checking for celiac disease was eliminated and

substituted by the notion that celiac disease and NLH of the gastrointestinal tract may be associated and that celiac disease should be suspected in patients diagnosed with NLH.

Figure 3 that proposed a systematic approach to these patients that included celiac disease was removed.

Concerning surveillance, the recommendation stated in this manuscript is to perform surveillance for intestinal lymphoma, as recommended in the literature by some authors. Extra-intestinal lymphoma association with NLH is very rare, and there is no recommendation in the literature nor in this manuscript for this surveillance.

Reviewer # 02953383 suggested that:

1. Since terminal ileum is the most common location for NLH and easily accessible by colonoscopy, the authors may provide the typical endoscopy figures of NLH in the terminal ileum in addition to the two duodenal figures.

ANSWER: a typical endoscopic figure of NLH in the terminal ileum was added, as suggested.

2. Similarly, since barium study is also important in the diagnosis of NLH, may the authors provide typical figures for the reader's references.

ANSWER: currently, in my Department, these patients are submitted to small bowel capsule endoscopy, and, as such, a typical capsule endoscopy figure was added.

3. Typical figures of histology of NLH are also suggested.

ANSWER: a typical histological figure of NLH was also added.

4. The authors have kindly provided a proposed systemic approach for NLH. However, the figure 3 seems a little difficult to follow. A step-by-step flow chart would be more instructive. In addition, the abbreviation in the figure should be clarified in the legend.

ANSWER: due to the suggestion of the previous two reviewers figure 3 was eliminated.

5. Page 4, line 4, "38" should be delete.

ANSWER: deleted, as suggested.

6. Page 6, line 9 from below, "to access the disease extension in the small bowel." should be "to assess the disease extent ..." ?

ANSWER: correction was made.

7. Page 7, the section of "FOLLOW-UP" may change to "TREATMENT and FOLLOW-UP".

ANSWER: changed, as suggested.

8. Page 8, the section of "CONCLUSION" is more like "PERSPECTIVE".

ANSWER: changed, as suggested.

3 References and typesetting were corrected.

Thank you again for publishing my manuscript in the *World Journal of Gastrointestinal Endoscopy*.

Sincerely yours,

A handwritten signature in black ink, consisting of a stylized initial 'A' followed by a series of connected loops and a wavy line extending to the right.

Andreia Albuquerque

Gastroenterology Department, Centro Hospitalar São João, Porto

Alameda Professor Hernâni Monteiro

4200-319 Porto, Portugal

Tel. +351 225 512 100; Fax +351 225 025 766

a.albuquerque.dias@gmail.com