Author’s response to reviews

Title: Systemic amyloidosis with bilateral conjunctival involvement: a case report

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Author’s response to reviews: see over
Dear Editors,

I am pleased to send to you the revised version of our paper *Systemic amyloidosis with bilateral conjunctival involvement: a case report* to be considered for publication in *BMC Ophthalmology*.

We thank the reviewers for their constructive criticism which has certainly helped to improve the manuscript. We have attempted to address (in blue) all the points raised by them.

**Reviewer 1 (Andre Okanobo):**

“Major Compulsory Revisions: Considering the case report for systemic amyloidosis with bilateral conjunctival involvement, it is important to provide the picture of the esophagus and rectus mucosal biopsy with Congo red staining under polarizing microscopy that confirms the diagnosis of systemic amyloidosis.”

Unfortunately, we could not obtain histopathology pictures from the esophagus and rectus mucosal biopsies, as the gastroenterological evaluation and histopathological study of biopsies were performed in other medical institution. However, we count on their specialized expert report that contributed to make the diagnosis of systemic amyloidosis.

We have included the results of bone marrow biopsy and two pictures of it.

“Discretionary Revisions: Pag 79-80: The sentence would be better: Tear film sample was obtained to rule out infection by common antibiotic resistant bacteria or Chlamydia spp.”

We have followed the reviewers suggestion.

**Reviewer 2 (Merle Fernandes):**

“Conjunctival amyloidosis with systemic involvement is very rare however, it is recommended and is generally well known, that a thorough evaluation and investigation of patients with conjunctival amyloidosis has to be done. This case does not add much more to the existing literature.”

The existing literature on the subject is very scarce, as conjunctival amyloidosis is a very rare disease, and in most cases it is unilateral and isolated without systemic amyloidosis. In our paper we present an extremely infrequent case of a patient with **bilateral conjunctival amyloidosis associated with asymptomatic systemic amyloidosis**.

We strongly believe that our paper contributes importantly to the knowledge and medical awareness of this possible association and the importance of a prompt diagnosis of a possible underlying systemic amyloidosis. In fact, conjunctival amyloidosis presents generally as a chronic conjunctivitis and its diagnosis is usually overlooked, as is frequently the case of systemic amyloidosis that may become symptomatic in advanced and severe cases, compromising the patient’s life.

Reference 6 has not been cited in the manuscript.
It was an error of typing. Correction made.

Typographical errors ‘i’ to be replaced by ‘y’ at several places in the manuscript ex ‘polyclonal’ should be ‘polyclonal’, “hipergammaglobulinemy” should be “hypergammaglobulinemia”

**Corrections made.**

Abstract
Page 2 Para 1 Line 29 “She presented a....” should read as “She presented with...”

**Correction made.**

Page 2 Para 1 Line 32 “Mucosal biopsy....and rectus...” Was a rectal mucosal biopsy or rectus muscle biopsy done?

**The biopsy was obtained from the esophagus and rectus mucosa.**

Page 4 Para 3 Line 79 “Lachrymal samples...to discard...” Does this refer to a conjunctival swab? This could be rephrased to “A conjunctival swab was obtained to rule out ......”

**A correction was made in that sentence.**

Page 4 Para 3 Line 79 The authors should mention if follicles were present or not, since Chlamydial infection is associated with follicular reaction in the conjunctiva.

Yes, a follicular reaction was present in the lower fornix. A phrase was added in that line of the Case report section of the manuscript.

Page 5 Para 1 Line 89 Since systemic amyloidosis can affect several organs in the body, the authors should mention whether a complete review of systems was done as just liver and heart function evaluation do not suffice.

Although the patient was systemically asymptomatic, a complete systemic review that included hematology, genitourinary, gastrointestinal, cardiovascular and central nervous systems, was performed.

Page 5 Line 58 Change “Conclusions” to “Discussion”

**Changed.**

Page 5 Para 2 Line 93 “The patient...years” should read as “The patient was treated with topical lubrication and the ocular lesions of both eyes remained stable after a follow up of 3 years.”

**Modified.**

Page 5 Para 3 Line 105 (now line 108) The reference for Demirci et al is [4] and not [3].

**Changed.**

We have added a sentence in the Case report section of the Abstract:
“Immunohistochemistry of bone marrow biopsy showed an increased number of plasma cells and an over-expression of light chain kappa subunit.”

We have added a sentence in the third paragraph of the Case report section:
“In order to rule out multiple myeloma or plasma cells dyscrasia, bone marrow biopsy was obtained showing a positive expression of CD 138+, a well known marker for identification and quantification of plasma cells in bone marrow and other tissues, as well as an increased population of plasma cells with an over-expression of the subunit kappa (Figures 2 A and B).”

We have added a new picture (#2) with the following legends:
“Figure 2: Immunohistochemistry of bone marrow biopsy. (A) Staining with specific antibodies for CD 138 showing increased number of plasma cells (in brown; x400). (B) Over-expression of immunoglobulin light chain kappa subunit (in orange-brown; x400).”

Former figures A, B, C, and D are now grouped in Figure 1 (Figure 1A, 1B, 1C and 1D).

We have added a last sentence in the third paragraph of the Discussion section:
“In addition, immunohistochemical studies of bone marrow biopsies showed an increased population of plasma cells with the amyloidogenic over-expression of the subunit kappa.”

We have added a paragraph in the Aknowledgements section:
“The authors are grateful to Dr. Ana V. Sanchez and Dr. Ana B. de Diller from the Department of Pathology, Hospital Privado Centro Medico de Cordoba, Argentina, for their invaluable assistance concerning bone marrow biopsy analysis and imaging.”

We hope the revised manuscript will be found suitable for your kind consideration.

Yours sincerely,

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