Author's response to reviews

Title: Suspected metastatic Adrenocortical Carcinoma revealing as Pulmonary Kaposi Sarcoma in Adrenal Cushing’s syndrome

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Author's response to reviews: see over
Dear Ms. Cruz,

Please find attached the revised version of our manuscript:

**Suspected metastatic Adrenocortical Carcinoma revealing as Pulmonary Kaposi Sarcoma in Adrenal Cushing’s syndrome**

We are grateful for the positive and constructive comments of the reviewers and believe that they certainly helped us to improve the manuscript. We have provided detailed responses to the reviewer’s queries and comments and have also revised the manuscript accordingly. The changes are highlighted in the manuscript. We sincerely hope that the changes we now have incorporated into the revised version of the manuscript will allow acceptance of our manuscript for publication in the BMC Endocrine Disorders.

Sincerely,

Margarita Bala, MD

**Reviewer #1:**

Bala et al. described an interesting case of cortisol-secreting adrenocortical tumor associated to a Kaposi Syndrome, which go into remission after cure of hypercortisolism. The case is well written and point out the effect of cortisol on immune system, although the mechanism is not fully explained in the literature. It would be of interest (if it’s feasible) to have more details on the patient’s immune systems (before and after the adrenalectomy), as the complete blood count, eventually the CD4/CD8 ratio, the immunoglobulins.

Level of interest: An article of outstanding merit and interest in its field

We thank the referee for the positive evaluation of our manuscript.

The patient presented in our clinic for further evaluation of suspected metastatic adrenal carcinoma. Therefore we did not initially perform any specific preoperative examination of the patient’s immune system. The differential white blood cell count before the adrenalectomy revealed relative lymphopenia which was normalised 8 weeks after adrenalectomy (Table 1). Shortly after making the diagnosis of Kaposi Sarcoma, precisely eight weeks after adrenalectomy, specific testing of the immune status showed normal CD4 cell counts (1014 cells/mm$^3$; normal range: 410-1590 cells/mm$^3$) and normal CD4/CD8 ratio (1.18; normal range: 0.8-4.2). Immunoglobulins have not been measured. We now have added this aspect in the manuscript (lines 129-132; 171-178 and Table 1)

**Reviewer #2:**

Level of interest: An article of importance in its field

We thank the reviewer for the positive evaluation of our manuscript.
1- Minor Essential Revisions:

a- Legends of figures vary between the manuscript (1 and 2), the legends (A, B, C) and the figures (from 1 to 3, from i to iii)

There are 2 Figures in the manuscript divided in figure 1A, 1B, 1C and figure 2A, 2B. Moreover figures 1A, 1B, 2A and 2B are subdivided in i. to iii (e.g. 1B(i), 1B(ii), 1B(iii)). That is specified in the Text and in the legends.

b- The proposition of fifth type of Kaposi Sarcoma should be discussed in discussion and not only mentioned in conclusion.

We now have added this aspect to the discussion and not in conclusion (lines 196-199).

2- Discretionary Revisions

a- As Cushing syndrome, it could be interesting to precise the incidence of Kaposi Sarcoma in introduction.

We now have added this aspect to the introduction (lines 71-72)

b- Can you precise the type of adrenalectomy (partial, limited, extended)? Its approach (laparoscopic, open, transperitoneal, retroperitoneal)?

The patient underwent a laparoscopic unilateral adrenalectomy. It has been added accordingly in the manuscript (line 117).

c- Pathological figures have some limited interest. It should be interesting to develop their legends with explicative arrows.

A detailed description of the staining has been added to the figure legends (lines 258-261). As specific staining can be seen, we believe that additional arrows are not needed.

d- Table 2 should be cited in introduction and discussion when the four types are described. Tables are not usually cited in conclusion.

Table 2 is cited in the discussion.

e- There are too references for a case report.

We agree with the referee, but we tried to provide a detailed overview of the literature, to point out the effect of cortisol on immune system and also emphasize the need of careful evaluation of patients with adrenal lesions. This would not be possible with fewer references (current 28 references). We, therefore, would prefer to leave the references as cited in the current version.
Editor’s Additional Request:

(1) **Requesting for Email-add**
It has been added accordingly in the manuscript.

(2) **Requesting for Line Numbering**
It has been added accordingly in the manuscript.

(3) **Please put the consent section after the Conclusion section.**
It has been changed accordingly in the manuscript.