Author's response to reviews

Title: Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss Syndrome) Presenting as Diffuse Myositis

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Author's response to reviews: see over
AUTHOR’S RESPONSE TO REVIEWS

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Version: 3 (21 Oct 2014)

Reviewer's report (Referee #1)
Title: Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss Syndrome) Presenting as Diffuse Myositis
Version: 2 Date: 18 August 2014
Reviewer: Amarjit Anand
Reviewer's report:
This is an interesting case report of an atypical presentation of EGPA.
The topic is introduced well.
Appropriate reference to previous studies have been made.
The case presentation itself describes the clinical scenario and sequence of events that led to the diagnosis.
Relevant negative and positive findings are mentioned.
The authors discuss the histological findings, although have not provided images.
The authors provide an explanation for the histology findings.
There are a few grammatical errors throughout the paper – lines 26, 27, 40, 53, 56, 58, 69, 83, 84, 119
The authors state written consent was obtained.
Overall, this is an interesting case report of an atypical presentation of EGPA.
The authors describe the unusual clinical presentation, diagnostic challenges and provide an explanation of their findings. I would consider publication of this case report following some grammatical amendments.

1) Spelling/grammar has been reviewed and corrected in several areas.

Reviewer's report (Referee #2)
Title: Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss Syndrome) Presenting as Diffuse Myositis
Version: 2 Date: 12 September 2014
Reviewer: Shigong Guo
Reviewer's report:
This is an interesting and rare case of Churg Strauss Syndrome with myositis with histological features of primary inflammatory myopathy.
The case report is well structured with a clear objective and is also written in clear, precise, scientific English.
However the educational merit of this case report needs some further exploration before this manuscript is ready for consideration for publication.

My questions for the authors are:

Line 84:
The authors mention that in the current literature, patients who have Churg Strauss with myositis underwent histological biopsies that revealed only vasculitis rather than the 'usual features of primary inflammatory myopathy that would be expected in a true “myositis”’ – and this is what makes their report stand out in that there were histological features of myositis.

1. Why is it that these other published cases, “true myositis”/primary inflammatory myopathy features cannot be found on biopsy?
   Either because they didn’t look for specific histologic features or used immunohistochemistry or simply because of phenotypic variability. As it is the case in most multi-organ autoimmune diseases, specific end-organ involvement in EGPA can vary for reasons difficult to establish and may target blood vessels alone in certain patients and muscle fibers as well in others. Comments to that effect were added in paragraph starting on line 188.

2. What is so different/special about this case, that these histological findings were able to be elicited?
   As written in paragraph starting on line 188, ours is the first case to stress and show evidence of primary myositis in EGPA with specific biopsy features that help distinguish it from vasculitic/ischemic myopathy. These features are now stressed in both the introduction and the conclusion. Why is it that our case had myositis is difficult to answer as explained above.

3. Line 138 the authors state the muscle biopsy was taken from the “biceps” - please clarify if this is biceps brachialis or biceps femoris?
   The biopsy site is biceps brachialis (now stated in the text as well as reason why).

4. The Uehara paper that the authors cited [ref 10] as an example that “true myositis” features was not found on biopsy, Uehara et al took the biopsy from the quads femoris, whereas in this case the authors took the biopsy from the biceps. Do you think that the site of the biopsy could have made a difference in the differing histological findings? And why?
   Biopsy sites in systemic rheumatologic disease are generally chosen based on intermediate involvement so as to get neither "end stage" nor "minimally pathologic" muscle since the goal is to collect informative findings. It is hard to vouch for why others picked a muscle and not another but indeed we can't rule out that perhaps in those other cases another muscle may have shown true myositis. Unless future experience with a larger number of cases tells us otherwise, we currently see no reason why there should be an anatomic specificity for the biceps brachialis in its predisposition for myositis.
5. What do the authors suggest should be the diagnostic criteria for Churg-Strauss with myositis – i.e. do you need to have features of primary inflammatory myopathy on biopsy in order to make this diagnosis? If not, do the authors think the previously published cases of myositis are really “myositis”?

We think that a definite diagnosis of EGPA with myositis should be substantiated by biopsy findings that demonstrate myositis in addition to vasculitis. It is precisely lack of such unequivocal demonstration that makes us reconsider whether the previously published cases of myositis really were. A comment on line 181 already addressed this issue and we added a sentence with a recommendation at the end of the manuscript.

**Other changes included in the latest version:**

1) The authors order was updated. The second and third authors were switched, following reconsideration of their respective roles and mutual agreement. "Author contributions" section was also updated.
2) Reference citation formatting was updated.
3) An "Acknowledgements" section was added.
4) Sources of funding are disclosed on the first page of the manuscript as well as in the "Acknowledgements" section.
5) A higher quality version of Figure 1 will be uploaded with this updated version of the manuscript. This image will be named 'High Quality' and is meant to replace 'Low Quality'.

Thank you,

Marc-Etienne Parent M.D.