Answering Reviewers

Dear Editor at World Journal of Gastroenterology,

Thank you for the review and good evaluation of our manuscript called "Multi-organ IgG4-Related Disease continues to mislead clinicians: a case report and literature review". We greatly appreciate the reviewers' time and have carefully considered their comments. We are also thankful for the offered possibility to publish our manuscript in the World Journal of Clinical Cases. We have revised the manuscript accordingly and are now submitting the revised version.

There is our detailed response to each point raised by the reviewers below.

ANSWER TO REVIEWER

Reviewer #1 (ID 04009274):

Dear Reviewer,
Thank you for your thoughtful and profound comments. We agree with them and have supplemented our clinical case accordingly. Please find below our explanations about changes in the manuscript as a response to your remarks.

Remark 1. History of past illness page 6, line 10 - GCs drops – please explain abbreviation.

Answer:

Thank you for pointing this out. It was the abbreviation for glucocorticosteroid eye drops. We now edited this sentence in full words. The abbreviation for GC is explained later in the text (page 6, line 12, page 14, line 9)

Remark 2. History of past illness page 6, line 23 – do you have data about T2 relaxation time on MRI which parameter is good marker of Graves' orbitopathy' activity?

Answer:

This is a really interesting point. However, we do not have data about T2 relaxation time on MRI.

Remark 3. History of past illness, page 6, line 23 – "antibodies against TTH" - do you mean TSH receptor antibody (TRAb)?

Answer:

Yes, we meant TSH receptor antibody (TRAb). We clarified this point in our manuscript and supplemented this part with laboratory testing values and also added that an anti-thyroid peroxidase (anti-TPO) antibodies were also within a normal range (page 6, line 31).

Remark 4. History of past illness, page 7, line 5 – Usage of retrobulbar GCs injection is not part of the therapic protocol/recommendation of Graves' orbitopathy. See reference: Bartalena L, Baldeschi L, Boboridis K, Eckstein A, Kahaly GJ, Marcocci C, Perros P, Salvi M, Wiersinga WM; European Group on Graves' Orbitopathy (EUGOGO). The 2016 European Thyroid Association/European Group on Graves' Orbitopathy Guidelines for the Management of Graves' Orbitopathy. Eur Thyroid J. 2016; 5(1):9-26. doi: 10.1159/000443828.

Answer:

Thank you very much for pointing out these important recommendations. We reached out to the endocrinologist, who treated this patient and clarified this part of treatment (page 7, line 12). It turned out that after unsuccessful treatment with intravenous methylprednisolone and radiotherapy endocrinologists started to doubt the diagnosis of Graves' orbitopathy and thought of idiopathic orbital inflammation, which can be treated with retrobulbar steroid injections. However, the patient refused this treatment after several injections and was out of reach for a year.

Remark 5. History of present illness, page 13, Figure 4, A, B - I think the numbers "8x13 mm and 2x21 mm" mean the sizes of dominant nodules in the right and left lobes of the thyroid. Did you perform fine-needle aspiration from the thyroid to exclude thyroid malignancy in the nodules? (or maybe prove Riedel thyroiditis/IgG4 related disease?)

Answer:

Yes, these are the sizes of dominant nodules in the right and left lobes of the thyroid. As the patient was treated at the Gastroenterology and hepatology department, the aspiration from the thyroid nodules was not performed. The material was taken only from salivary glands. After the multidisciplinary expert consultation, it was decided not to perform another biopsy.

Remark 6. Final diagnosis, page 15, line 3 – Why do you think that the prostate is also involved in IgG4 related disease in this case? Why are you sure that the patient's "asthma" is not pulmonary involvement of IgG4 related disease?

Answer:

Thank you for these insidious questions. In fact, those were the most debatable issues during the multidisciplinary expert consultation. We answered those questions in the "Multidisciplinary expert consultation" paragraph and further discussed in the "Discussion" section: "Diagnostic challenges of the presented case"(page 13, line 11 and page 19, line 20). It was discussed whether the patient's asthma is a pulmonary involvement of IgG4-RD. As it started in childhood and was in remission, it was decided that bronchial asthma is a co-morbid atopic disorder. The origin of the patient's urination problems remained questionable, but the majority of consultants voted for chronic IgG4-related prostatitis. In the course of the treatment, the urination problems regressed, and that confirmed our initial diagnosis.

Remark 7. Outcome and follow-up page 15, What about exophthalmos? Did you detect improvement also in eye symptom?

Answer:

Exophthalmos also improved over time. However, diplopia, vision disturbance and strabismus remained. The recession of the left inferior rectus muscle was recently performed to correct the high-level strabismus (page 14, line 14).

Remark 8. Discussion, page 16, line 10 – (50-0 years), please correct the numbers

Answer:

Thank you, this must have been the typing and editing mistake. The correct numbers are 50 - 60 years.

Remark 9. Discussion, page 17, it is interesting that you don't have the typical histological findings to make the diagnosis. Maybe it would be possible to do another biopsy from another involved organ...

Answer:

Thank you for this consideration. The need to perform an additional biopsy from another involved organ was also intensely debated during the multidisciplinary expert consultation. A decision was made, that there were enough criteria to establish the IgG4-RD diagnosis (multiple organ involvement, high IgG4 levels at 6.87 g/l, MRI showing autoimmune pancreatits and orbital myositis, salivary gland enlargement and histologically confirmed sialadenitis), and the biopsy result would not affect the treatment. Therefore, there was no urgent need for another biopsy.

At the moment, the biopsy can not be performed due to several reasons:

1. *The pandemic situation ;*
2. *It would be unethical to perform invasive procedure just for the record with no benefit for the patient. The patient is now in remission, and the biopsy will not make any changes for his course of treatment.*
3. *According to the newest ACR/EULAR criteria, the biopsy is not obligatory for establishing the diagnosis of IgG4-RD. Our patient met all ACR/EULAR criteria and gained 31 points.*