Ms. Ref. No.: 52726

February, 2020

Dear Editor

We wish to express our gratitude to you and the reviewers for the careful review of our manuscript entitled "**Acute myeloid leukemia with t(11;19)(q23;p13.1) in a patient with a GIST undergoing imatinib therapy: A case report**". We have tried to revise our manuscript based on the reviewers' comments.

Here we have addressed the concerns of the reviewers on separate pages, as well as our responses to specific comments. I hope that you and reviewers will find these alterations satisfactory. We look forward to having our manuscript published in "***World Journal of Clinical Cases***".

Best wishes,

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REVIEWER 1 EVALUATION

Suggestions:

The manuscript deals with the acute myeloid leukemia (AML) in a patient already affected by metastatic GIST who was receiving pharmacologic treatment with imatinib mesylate. The development of AML after imatinib therapy has already been reported in the literature as stated by the Authors themselves, although only in a few cases. However, the KMT2A gene rearrangement was not reported in the previous studies. Despite this limited advance in the knowleadge, in my opinion, the manuscript do not add new interesting information to the current literature to be worthy of publication.

- ➔ The case reports of leukemia occurred in patients with GIST during IM treatment are very rare, with only four cases, including the present case. Moreover, it was the first time the KMT2A gene rearrangement was found.

  It is true that most physicians do not give much consideration to the risk of developing hematologic malignancy during IM treatment of GIST patients. In addition, we hope that this case report results in further studies identifying the off-target effects of tyrosine kinase inhibitors in association with the mechanisms of therapy-related myeloid neoplasms.

Furthermore, a language editing would be suggested.

- ➔ We revised the manuscript as your considerate recommendation. We submitted the certificate of language editing.

REVIEWER 2 EVALUATION

Suggestions:

I have the following concerns for the authors:

1. The time interval from the initiation of imatinib until the AML diagnosis is less than 4 years. Usually, it takes more years for a therapy-related AML to develop after any chemotherapy. It could have been the imatinib, but it also could have been predisposing gene mutations for AML, like an IDH mutation for example or a combination between imatinib and genes. This has to be emphatically stated in the discussion.

- ➔ As your considerate comments, we revised the manuscript as follows.
- ➔ Page 8 line 211
- ➔ Since the pathogenesis is not yet elucidated, it is impossible to clearly demonstrate that AML occurred due to IM administration even in the present case. The risk of leukemia may be increased with IM treatment alone, but may not be increased without a combination of IM and some predisposing genetic abnormalities, such as an isocitrate dehydrogenase (IDH) mutation.

2. Are there any publications with other inhibitors such as dasatinib, nilotinib and or ponatinib causing AML or MDS? Please report that to the discussion.

- ➔ As your thankful suggestion, we added some reports as follows
- ➔ Page 7 line 188
- ➔ Subsequent AML or MDS after treatment with second generation Bcr-Abl tyrosine kinase inhibitors including dasatinib, nilotinib, and ponatinib for CML was also reported.

3. What was the status of the genes: NPM1, FLT3-ITD, AND CEBPA at diagnosis?

- ➔ Although the screening for *NPM1*, *FLT3*, and *CEBPA* gene mutations are

required at the diagnosis, the cost of those mutation tests is high for some of our hospital patients. Unfortunately, this patient didn't agree to do any mutation studies because of the economic burden of an expensive cost.

4. Please correct the few grammatical/syntactical errors existing in the paper.

➔ We revised the manuscript as your considerate recommendation. We submitted the certificate of language editing.

REVIEWER 3 EVALUATION

Suggestions:

There does not seem to be much of review of literature in this case report. In this context, the wordings " and review of literature" may be deleted from the title.

➔ We revised the title as your considerate recommendation. The revised title is "Title: Acute myeloid leukemia with t(11;19)(q23;p13.1) in a patient with a GIST undergoing imatinib therapy: A case report"

Ms. Ref. No.: 52726

March, 2020

Dear Editor

We wish to express our gratitude to you and the reviewers for the careful review of our manuscript entitled "**Acute myeloid leukemia with t(11;19)(q23;p13.1) in a patient with a GIST undergoing imatinib therapy: A case report**". We have tried to revise our manuscript based on the reviewers' comments.

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Best wishes,

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REVIEWER 1 EVALUATION

Suggestions: I have no further corrections.

➔ Thank you for your considerate comment.

REVIEWER 2 EVALUATION

Suggestions: I appreciate the improvement the Authors made to the manuscript, following the suggestion of the reviewers (improving the quality of the work and performing the language editing). Unfortunately, I still convinced that the manuscript do not add new interesting information to the current literature to be worthy of publication.

➔ Currently, imatinib is recommended for the unresectable, recurrent, or metastatic GIST patients. These patients should receive Imatinib for long time until the progression of disease or unacceptable toxicities, like an acute leukemia as in our case. Maybe it is not an interesting case, but oncologist should be aware of developing acute myeloid leukemia when treating the GIST patients. Unfortunately, there are no further reliable studies after Miettinen *et al.* published the data about a nonrandom association between gastrointestinal tumors and myeloid leukemia. In that study, they reported only 5 patients who developed AML subsequent to a GIST. Because the standard care for those GIST patients is not changed, the problem is still ongoing. So, we would like to emphasize the association between acute myeloid leukemia and GIST patients with our case report.