Peer Review File

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Reviewer Comments

Fang and colleagues report a concurrent CMML and gastric adenocarcinoma case in a 75 yo female. While the study case is of interest, several aspects should be clarified.

Major comments:

1. CMML diagnosis criteria should refer to WHO 2022 (Khoury et al, Leukemia 2022) classification (notably, lowered absolute monocyte count to 0.5G/L).

Reply 1: Thank you so much for your good suggestion, we have updated the CMML diagnosis criteria in the revised manuscript.
Changes in the text: we have modified our text as advised (see Page 2, line 47)

2. CMML karyotype should be added (and discussed, mostly normal in CMML patients). Variant allelic fractions of somatic mutations (TET2, CBL) should also appear in the manucript. When describing flow cytometry, did the authors checked for the monocyte repartition (Selimoglu Buet et al Blood 2015) that helps discriminating between reactive/ inflammatory monocytosis and primary/CMML monocytosis?

Reply 1: Thank you so much for your good suggestions. We have added data on the karyotype and variant alleles of somatic mutations (TET2, CBL) in the revised manuscript. In terms of monocyte repartition, Selimoglu-Buet et al annotated the composition of monocyte subsets in patients with CMML. Utilizing flow cytometry to segregate monocyte subsets, the authors demonstrated that classical monocytes (CD14+/CD16-) were uniformly increased in CMML (cutoff value, 94.0%). Unfortunately, we did not check for the monocyte repartition in this patient's peripheral blood. Because the patient had been clinically diagnosed with CMML, this test was not performed on the patient in order to save costs. These patients will be routinely tested in the future according to the WHO 2022 CMML diagnostic criteria.
Changes in the text: we have added this data to our text as advised (see Page 3, line 89).

3. How was the C-reactive protein level at CMML diagnosis? Inflammation can increase the monocyte count in CMML patients. This point should be discussed.

Reply 1: Thank you so much for your good suggestions. The patient came to our hospital with a pulmonary infection and a mild elevation of C-reactive protein (CRP, 59mg/L, normal range: 0-10 mg/L). After antibiotic treatment, CT scan of lungs and CRP returned to normal, but the levels of white blood cells, monocytes and hemoglobin remained abnormal. Moreover, the peripheral blood smears of the patient showed significantly elevated monocytes, and bone marrow flow cytometry analysis suggested dysplastic myelocytes and granular megakaryocytes, and abnormal molecular

molecules in the bone marrow, which could be distinguished from reactive monocytosis.
Changes in the text: we have added this data and discussion to our text as advised (see Page 5, line 140).

4. Did the patient have any known risk factors for developing gastric carcinoma (HP infection, diet, overweight, alcohol or tobacco use..?)
Reply 1: Thank you so much for your good question. The patient had no risk factors related to gastric carcinoma.
Changes in the text: we added this data to our text (see Page 6, line 152).

5. Did the authors look for hemostasis disorders? CMML can be associated various acquired bleeding disorders, this should also be discussed.
Reply 1: Thank you so much for your good question and suggestion. The patient had no history of hemorrhagic diseases, such as liver disease, surgery, and use of anticoagulant and antiplatelet drugs.
Changes in the text: we have added this data to our text as advised (see Page 3, line 95).

6. The presence of clonal abnormalities (somatic mutations in TET2/CBL, karyotype ?) argue for the clonal nature of CMML and against a paraneoplastic origin.

Reply 1: Thank you so much for your good suggestions. We have added this in the discussion section of the revised manuscript.
Changes in the text: we have added this in the discussion section of the manuscript (Page 7, line 189).

Minor comments:
1. Genes names should be in italic

Reply 1: Thank you so much for your good suggestion. We have modified this in the manuscript.
Changes in the text: we have modified our text as advised (see Page 3, line 87).

2. Figure 1: arrows with cell legends should be added to specify the cell type (monoblasts, myelocytes..)

Reply 1: Thank you so much for your good suggestion. Since the abnormal cells in the original figure 1 were few and atypical, we added four more typical pictures (figure 1 in the revised revision) of the bone marrow smear results.
Changes in the text: we have modified our text as advised (see Page 4, line 125).

3. Figure 2B : Does the picture represent esophageal varices? If yes, this should be mentionned in the legend ◦

Reply 1: Thank you so much for your good question. Figures 2A and 2B showed tumor-like lesions

but no esophageal varices.
Changes in the text: Nothing changed in terms of this.

4. 2% bone marrow blasts does not represent an increase of blasts (>=5%)

Reply 1: Thank you so much for your good suggestion. We have changed the expression in the text.
Changes in the text: we have modified our text (see Page 3, line 85).