Reviewer’s report

Title: Acquired platelet dysfunction due to chronic myelogenous leukemia leading to massive hemorrhage: Improvement of platelet dysfunction following treatment with imatinib

Version: 2 Date: 21 October 2010

Reviewer: Fani Athanassiadou

Which of the following best describes what type of case report this is?: Findings that shed new light on the possible pathogenesis of a disease or an adverse effect

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: Yes

Does the case report have explanatory value?: Yes

Does the case report have diagnostic value?: Yes

Will the case report make a difference to clinical practice?: Yes

Is the anonymity of the patient protected?: Yes

Comments to authors:

Conducted clinical trials have clearly demonstrated the efficacy of imatinib in the remission of ph+CML. On the other hand, the observed resolution of bone marrow fibrosis and the reappearance of normal megakaryocytes after imatinib therapy needs further future investigation.

of a Ph translocation happens prior to the differentiation of the pluripotent stem cell into different myeloid lineages.

In vitro studies (Int J Hematol. 2002 Jul;76(1):35-43) have also showed that enforced Bcr-Abl expression was sufficient to increase the number of both multilineage progenitors and myeloid progenitors.

Furthermore, Thiele et al. (Leukemia & Lymphoma 2004;45:1627-31) found that the atypical microkaryocytes that are prevalent in Ph+ CML are significantly reduced after imatinib therapy with a further reappearance of normal sized megakaryocytes. According to these results this reappearance could also serve as a morphologic hallmark to monitor efficacy of this molecular target therapy.

A very interesting study (Buet D, Raslova H, Geay JF, et al. p210(BCR-ABL) reprograms transformed and normal human megakaryocytic progenitor cells into erythroid cells and suppresses FLI-1 transcription. Leukemia. 2007;21(5):917-25.) reported that ectopic expression of p210(BCR-ABL) in the megakaryoblastic Mo7e cell line and in primary human CD34(+) progenitors trigger erythroid differentiation at the expense of megakaryocyte (MK) differentiation demonstrating that alteration of signal transduction via p210(BCR-ABL) reprograms Megakaryocyte cells into erythroid cells by a downregulation of a transcription factor FLI-1. This suggests that BCR-ABL represents a "molecular switch" for the decision for growth and differentiation in hematopoietic stem cells in general.

I strongly recommend that these points should be mentioned in the discussion section to strengthen your hypothesis of platelet function improvement after imatinib therapy.

Specific comments:

1. In your abstract section you recommend to monitor platelet function in future studies using imatinib in CML, but bearing in mind that your data are based only in one case report it should be wiser to suggest this monitoring and not to recommend (recommendations and guidelines should only be based on prospective and large studies and not on case reports and case series). You should also emphasize the need of further research to ensure your clinical observation. You could also suggest the monitoring of platelet function in CML patients receiving 2nd generation tyrosine kinase inhibitors (such as dasatinib) maybe in your discussion section, since they are also used in refractory Ph+CML patients.

2. You could mention which was the first chemotherapy protocol that the patient received initially.

3. Have you done any laboratory examinations for the concurrent existence of any other pathological situations that may affect blood clotting (MTHFR mutations for example) in your patient? (you should clarify this point).

Quality of written English: Acceptable

Declaration of competing interests:
I declare that I have no competing interests