A cerebral hemorrhagic complication following PBSC collection

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Abstract: Intensive treatments such as autologous stem cell transplantation are standard procedures for lymphoma and myeloma patients. The number of autologous and allogenic procedures available is continuously increasing. To perform these procedures, we need to harvest a sufficient number of circulating marrow stem cells by leukapheresis after stimulation with filgrastim. The collection of peripheral stem cells PBSC is generally a safe procedure, but some patients could present short-term or long term toxicity due to filgrastim stimulation, venous access or the procedure of leukapheresis. Here, we present the case of a lymphoma patient, in which the collection of PBSC was followed by a cerebral hemorrhagic event, possibly related to the procedure of apheresis.

Response to Reviewers: The changes requested by the reviewers and made by the authors:

1. Rituximab at 375mg/m² was associated to first as well as the second chemotherapy. We modified the texte

- ... and Prednisone) associated to Rituximab, resulting ...
- ...Methylprednisolone) also associated to Rituximab ...
- ...third cycle of ESHAP-Rituximab chemotherapy...

2. As suggested by reviewer 1: The patient was negative for recent head injury.

3. The name of chemotherapy was reviewed: ESHAP

4. Correction on platinum based-chemotherapy

5. As demanded by reviewer 1 the image of CT scan was omitted

6. ESHAP chemotherapy is frequently associated with grade 3-4 haematological toxicity, requiring blood or platelet transfusions. Prior to aphaeresis the patient was already been transfused on platelets. No hemorrhagic event was noticed. Before starting the aphaeresis procedure the patient underwent a platelets transfusion for thrombopenia at 19 Giga/L. After the third aphaeresis, at the moment at hospitalisation into emergency unit the platelet count was 43 Giga/L. We believe that, that the

hemorrhagic complication was due to: chemotherapy induced thrombopenia to the intense stimulation resulting into high levels of WBC and to the aphaeresis procedure.

***Conflict of interest**

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A cerebral hemorrhagic complication following PBSC collection

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Running Title: hemorrhagic complication, PBSC, lymphoma

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Dear Editor,

Intensive treatments such as autologous stem cell transplantation are standard procedures for lymphoma and myeloma patients. The number of autologous and allogenic procedures available is continuously increasing. To perform these procedures, we need to harvest a sufficient number of circulating marrow stem cells by leukapheresis after stimulation with filgrastim. The collection of peripheral stem cells PBSC is generally a safe procedure, but some patients could present short-term or long term toxicity due to filgrastim stimulation, venous access or the procedure of leukapheresis. Here, we present the case of a lymphoma patient, in which the collection of PBSC was followed by a cerebral hemorrhagic event, possibly related to the procedure of apheresis.

A 58 year-old patient was treated for a diffuse large B-cell lymphoma with anthracyclin-based chemotherapy (Vincristin, Cyclophosphamide, Doxorubicin and Prednisone) associated to Rituximab, resulting in partial remission. After 3 courses, the treatment was switched to a platinum-based rescue regimen (ESHAP – Etoposide, Cytarabin, Cisplatin and Methylprednisolone) also associated to Rituximab. This type of chemotherapy is frequently associated with grade 3-4 hematological toxicity, requiring blood or platelet transfusions. After the third cycle of ESHAP-Rituximab chemotherapy, the patient was stimulated with filgrastim for five consecutive days at a daily dose of approximately 10 µg/kg, in preparation for a peripheral stem cell harvest for an autologous transplantation. Apheresis was performed when the circulating level of CD34 cells was greater than 10 cells per 1 µL of blood. Because the blood count revealed a thrombopenia at 19 gigas/L, the patient underwent a platelet transfusion before starting aphaeresis. Three aphaeresis procedures in three consecutive days were necessary to obtain a sufficient graft. During apheresis, patient blood pressure was stable at 120 -140 mmHg and pulse was normal.

The evening following the last apheresis, the patient was hospitalized in the emergency unit for disorientation, aphasia, headache and vomiting. The patient was negative for recent head injury. Computed tomography found the presence of a subdural hematoma in the temporoparietal right region (Photo 1). Upon hematoma detection, the blood count results were as follows: Hemoglobin: 10.2 g/dL, Platelets: 43 gigas/L, WBC: 31 gigas/L. The coagulation test had the following results: TP 13.2 / 13.7 seconds; ratio 93%, TCA 34/30 seconds; ratio: 0.88. It was decided that surgery was not needed. A new computed tomography performed 36 hours later revealed amelioration of the hematoma, and the patient continued his therapeutic program.

Over the past decade, there has been an increasing number of autologous stem cell transplantations performed because these procedures became the standard therapeutic approach for myeloma and lymphoma (1,2). There are also an increasing number of allogenic procedures using peripheral stem cells (3). Leukapheresis procedures after intense cytokine stimulation are generally safe procedures (4). There are some studies, mainly in volunteer healthy donors, which described the adverse events of leukapheresis. Short-term toxicities occurred as local reactions due to filgrastim administration, complications associated with central venous catheterization, and/or problems with leukapheresis, including bleeding secondary to anticoagulation and hypocalcemia due to acid citrate dextrose use as well as hypotension (5). Long term toxicity, while extremely rare, could include toxic death or hematological malignancies (6).

For our patient, the intense stimulation, resulting in high levels of WBC associated with chemotherapy-induced thrombopenia, was complicated by a cerebral hemorrhage. In our experience, this case is the first reported cerebral hemorrhagic complication potentially due to

stem cell harvesting. This complication was rapidly regressive, and thus, the patient could continue his therapeutic program.

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