ALLOGENEIC STEM CELL TRANSPLANTATION IN HODGKIN'S DISEASE STAGE IV WITH RELAPSE AFTER AUTOLOGOUS STEM CELL TRANSPLANTATION

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Abstract: *We present the case of a young patient with Hodgkin disease who benefited from an allogeneic stem cell transplantation from a compatible sibling. 3 years prior the allogeneic transplant, the patient received an autologus hematopoietic stem cell transplant after which it relapsed. Upon admission in our clinic, he was in stage IVB with high fever, abdominal masses and adenopathies on both sides of the diaphragm. We administered 2 DHAP salvage courses with relatively good response, with the disappearance of the B symptoms and the decreasing of the volume of the adenopathies. Having in view the significant residual disease we decided to administer a miniBEAM protocol before the allogeneic transplantation. We present the evolution of the case, the complications and the results obtained.*

Cuvinte cheie: *boala Hodgkin, transplant alogen, celule stem*

Rezumat: *Prezentăm cazul unui bolnav tânăr cu boală Hodgkin cu scleroză nodulară stadiul IVB la care s-a efectuat un transplant alogen de celule stem hematopoietice de la un donator familial compatibil. Bolnavul a recăzut la 3 ani după un transplant autolog. La prezentarea în clinica noastră constatăm recăderea bolii, prezenţa ganglionilor mediastinali, laterocervicali, retroperitoneali, inghinali, bolnavul fiind în stadiul IVB. Am administrat două cure DHAP cu răspuns favorabil cu ameliorarea stării generale cu scăderea în volum a adenopatiilor dar, cu boală reziduală semnificativă. Bolnavul având o soră compatibilă, am considerat că are indicaţia de transplant alogen de celule stem hematopoietice. Având în vedere boala reziduală, am decis să administrăm înaintea transplantului o cură miniBEAM care să fie urmată de allotransplant. Prezentăm evoluţia, complicaţiile şi rezultatele obţinute.*

The aim of presenting a stg. IV B Hodgkin disease case which started in childhood and presented multiple relapses, the last one after the autologus stem cell transplantation is to demonstrate the possibility of the treatment with allogeneic transplantation even in cases which are impossible to treat without this method of treatment.

The other aim was to present a new way of debulking by using the miniBEAM protocol, which is followed, after the recovery of the blood count, by related or unrelated allogeneic stem cell transplantation. By this complex treatment, we can obtain the cure of these patients.(1,2)

The treatment methods used and presented in this paper are the autologus stem cell transplantation and the allogeneic transplant from a related HLA compatible donor. In the case of patients with Hodgkin's and non Hodgkin's lymphoma, the autologus transplant is a frequently used method of treatment in cases with chemosensitive multiple relapses.(3) In case relapse occurs after the autologus transplantation, the patients are given the so called „salvage" chemotherapy treatments followed by related or unrelated HLA compatible transplants.(4) A new method of debulking and treatment of the residual disease pre-transplant is the application of the miniBEAM protocol.

CASE REPORT

We present the case of a 24-year old male patient with Hodgkin's disease, nodular sclerosis histology type diagnosed in childhood at 14. Initially, he underwent 6 courses of BEACOPP, the last one in 2006. After the treatment, he was lost for follow up because he did not present for check up. The first relapse appeared in 2008 and manifested in pulmonary, retroperitoneal and inguinal adenopathies with compression followed by the lymphoedema of his right leg. Chemotherapy was started with partial response and complicated with the thrombosis of the right jugular vein.

In 2010, the patient was referred to our transplant centre for mobilization and collection of stem cells for autologus transplantation. The mobilizing treatment consisted of chemotherapy, the DHAP protocol followed by the administration of granulocyte growth factors (G-CSF). We obtained a number of 9.5 $X10^6$ /kg CD34+ cells.

For pre-transplant conditioning treatment, we used the standard BEAM protocol. (BCNU 300 mg/m^2 day -6, Etoposid 400-800 mg/m^2 days -5,-4,-3,-2, Ara-C 800-1600 mg/m^2 days -5,-4,-3,-2, Melphalan 140 mg/m^2 day -1).

In the period of aplasia, he had a urinary tract infection with Pseudomonas aeruginosa and a bronchopneumonia caused by E. Coli with good response to the antibiotic treatment. The evolution of the case was favourable. The engraftment for granulocytes appeared on day 14 post-transplant and for platelets on day 21.

The patient was in remission until April 2012, when he relapsed for the second time. The relapse manifested in the reappearance of B symptoms (fever, pruritus, perspiration, loss

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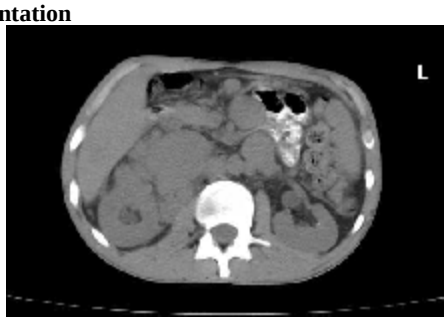
of weight), dyspnoea, generalized adenopathies and lymphoedema of the right leg.

On the CT scan, we can observe the presence of mediastinal adenopathies, pulmonary nodules in the left superior segment, masses of adenopathies in the abdomen and retroperitoneum with a size up to 12 cm.

Figure no. 1. CT scan at second relapse post-autologus transplantation



Chemotherapy was restarted and we applied the salvage treatment using the DHAP protocol. The response to the treatment was relatively favourable with the shrinking of the adenopathies. Due to the presence of a still considerable residual disease, we decided to use a new method of treatment recently introduced in the treatment of relapsed lymphomas. It consisted in chemotherapy using the protocol miniBEAM for debulking pre conditioning regimen for allogeneic transplantation.

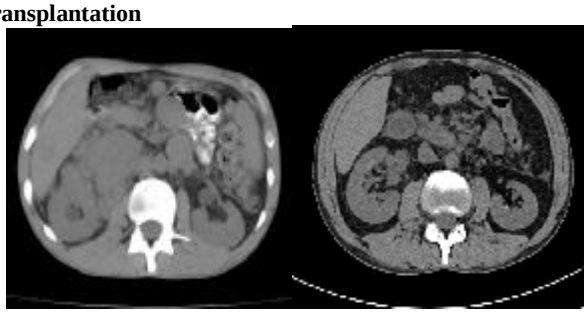
The MiniBEAM protocol contains the following doses: BCNU 60 mg/m^2 day 1, Etopozid 200 mg/m^2 days 2-6, ARA-C 100 mg/m^2 days 2-6, Melphalan 20 mg/m^2 day 7.

Considering the evolution of the case, the multiple relapses including the relapse post autologus transplantation, we decided to proceed to the allogeneic stem cell transplantation, the patient having an HLA compatible sister. The donor was not an ideal one being female and with 3 childbirths before donating but in lack of a better donor we collected stem cells obtaining 4.27 X10^6 /kg CD34+ cells and 417 X10^6 T cells.

The treatment of conditioning was the standard one, using the Bu-Cy protocol (Busulfan 16 mg/kg days -7, -6, -5, -4, Cyklofosfamid 60 mg/kg/day day -3,-2). Immunosupression consisted of the administration of short courses of methotrexate and tacrolimus.

The patient presented the following complications in the period of aplasia: grade 2 mucositis, oesophagitis with Candida albicans, sepsis caused by teicoplanin resistant MRSA, thrombosis of the left iliac vein. At present, the time of follow up is of 5 month. At the last check up we could notice the absence of subjective symptoms, good physical condition with the following blood count: WBC 8480, Hgb 14.6 g/dl, Plt 110.000/mm^3. Chimerism analyses showed that the patient is a full donor chimera. The CT scan showed the disappearance of the adenopathies.

Figure no. 2. CT scans pre and post allogeneic transplantation



Conclusions:

We consider this case being a success in spite of the multiple difficulties during the treatment, because of the childhood onset, 2 relapses, several serious infectious and thrombotic complications. The evolution of the case demonstrated the importance of the autologus and allogeneic stem cell transplants in cases in which such a treatment is the only way to cure these patients.

Autologus transplantation is a curative treatment in the case of chemosensitive lymphomas.(5) In case of relapse post-autologus transplants, the patients with Hodgkin's and non-Hodgkin lymphomas have the indication of allogeneic stem cell transplantation from related or unrelated HLA compatible donors. The new method we presented was the administration of the miniBEAM treatment for debulking and treatment of the residual disease, this being a recently new introduced treatment of lymphomas. This protocol has to be followed by an allogeneic stem cell transplantation in order to prevent a new relapse.(6,7)

Another conclusion is that in the case of patients with lymphomas with several relapses post-chemotherapy including relapse post-autologus transplantation, the allogeneic transplant preceded by miniBEAM treatment protocol for residual disease is a new and feasible method of treatment with curative intent, which in spite of its difficulties can lead to the cure of these extremely difficult cases.

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