

ESMO Clinical Unit Visit Report

Institut Català d'Oncologia - Hospital Duran i Reynals
Barcelona, Spain

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Allogenic hematopoietic stem cell transplantation observership

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Introduction: My home institution, the University of Debrecen has an autologous stem cell transplant unit and initiated allogenic transplantation last year (2016). Therefore, there is a pressing need for experience that covers all aspects of allogenic transplantation. The relevance of the Clinical Unit Visit Fellowship was for me to spend sufficient time at the Hematology Department and Hematopoietic Stem Cell Transplant Programme, Institut Català d'Oncologia (ICO) - Hospital Duran i Reynals in Barcelona, Spain to understand and learn the critical aspects of the successful operation of the unit, by shadowing allogenic transplant patients, observing treatment and outcomes.

The ICO in Barcelona is a leading and internationally recognized center for hematopoietic stem cell transplantation. The institution does 20-31 allogenic transplantations annually. They have also done 33 haploidentical transplantation so far in case when patients don't have a HLA identical sibling or a 10/10 matched unrelated donor. The center is responsible for 1/3 of allogenic stem cell transplants in Catalonia with a population of 7.5 million inhabitants.

Main part: At my arrival I was accompanied through the whole department. There are 28 inpatient beds at the hematology ward, of which there are 8 transplant beds. There are 3 groups treating the inpatient service: transplant, lymphoma-myeloma and the general hematology team. One team consists of a senior and a junior doctor. There are also 40 outpatient infusion chairs, which serves 3 patients a day, therefore the outpatient treatment of a total of 120 patients is covered daily. The ward is served by the Intensive Care Unit (ICU) of Hospital Bellvitge, placed opposite side of the road. There are 36 ICU beds; all of them are separated in boxes with independent air condition systems. In case of clinical instability (hypotension, septic shock or respiratory insufficiency), the ICU team takes over the patients soon. In case of emergency, a resuscitation team arrives immediately to the patient.

The chemotherapy is ordered in a computer system called ESPOQQ, which automatically calculates doses, appropriate hydration and required prophylaxis. The system is in direct connection with the pharmacy, which is a cutting edge, state of the art facility for preparing chemotherapy and even oral daily medications without human intervention. The nurses also use a computer system to record physiological data.

Central lines are carried out by a radiology team, patients receive predominantly subclavian central lines. In case of a permanent vein access with stable peripheral veins a peripherally inserted central catheter is used. They have equivalent results compared to tunnelled catheters in terms of infections but easier implantation. Transplant physicians carry out bone marrow samples, biopsies and lumbar punctures.

An infectious disease team also serves the hematology ward. They visit patients on a regular manner, review antimicrobial treatment and consult with the attending hematologist physician. There is also a social worker, a nutritionist, who frequently visits patients.

The local Blood Bank in Bellvitge is in charge of stem cell collection and photopheresis therapy. The latter is carried out as second line treatment of graft versus host disease or as treatment of cutaneous lymphomas. The aphaeresis equipment is similar to ours. Patients have a central line that is also carried out by the radiology team on an outpatient manner. Mobilization is usually carried out with granulocyte colony stimulating factors over a 5 days period, because it can be easier planned, than chemo-mobilizations. Nevertheless chemo-mobilizations have the advantage of giving the next cycle of chemotherapy without significant delay. Basically, the system is planned much more to the outpatients setting compared to ours.

The central Blood Bank in Barcelona is in charge of organizing the supply of Catalonia with blood products. It is also organizing the human leukocyte antigen (HLA) typing of patients; their relatives and possibly identifying unrelated donors. There are 450 hematopoietic stem cell transplantations in Catalonia annually. There is also some initiating effort being done towards chimera antigen receptor T-cell therapy, in which the Blood Bank also takes part. HLA typing is done by next generation sequencing method since 2016. The Blood Bank generates reports, but eventually the treating transplant physician decides, which donor to choose. Hapidentical transplantations are running without *ex-vivo* manipulation. If needed, CD34+ selection can be carried out.

One day I also visited the local radio-oncology department, who carries out total body irradiation (TBI). Patients usually receive 4x 3.25 Gys (total dose of 13 Gys) of irradiation with a linear accelerator. As conditioning therapy, TBI is usually included in case of acute myeloid leukemia or similar diagnosis.

I visited several outpatient clinics. Namely, the lymphoma/myeloma, transplant, and long-term outcome outpatient clinics.

During my stay I saw 2 haploidentical transplantations in full length. A 58 year-old-man diagnosed with chronic myelomonocytic leukemia and a 56 year-old-woman diagnosed with acute myeloid leukaemia. Conditioning of both patients consisted of fludarabin, cyclophosphamide and busulfan. For graft versus host (GVH) prophylaxis patients received post-transplantation cyclophosphamide, cyclosporine A and mycophenolat mofetil. Antimicrobial prophylaxis was pentamidin, aciclovir and posaconazol. Stem cell source was unmanipulated peripheral stem cells, the man received graft from his daughter, the woman received graft from her son. Treatment of both patients went without major complications. The woman was observed at the ICU for hemodinamical instability due to sepsis caused by cholecystitis. Nevertheless, there was no need for either circulatory or respiratory support. The treatment of the man was complicated by hemorrhagic cystitis from day +30, BK virus was identified in his urine with 41,602 copies/mL, which received extensive fluid therapy for.

I observed allogenic transplants with matched sibling or unrelated donors also. The rest of the patients were hospitalized due to post transplant lymphoproliferative disease, pulmonary and hepatic GVH disease.

A 67-year-old man was admitted due to fever with no focal origin. Previously, he received haploidentical stem cell transplantation in April 2017 from his daughter after several relapses of follicular T-cell lymphoma. Post-transplant period was complicated by cytomegaly virus reactivation and skin GVH disease. The latter, he received corticosteroids and extracorporeal photopheresis for. During his work-up, he had progressively increasing number of Epstein-Barr virus copies along with enlarged lymph nodes, confirmed by PET/CT. As pre-emptive therapy of the probable post-transplant lymphoproliferative disease the patient received 375 mg/m² rituximab on a weekly manner for 4 consecutive weeks. For this treatment, his EBV copy number decreased and lymphadenomegaly disappeared.

A 56-year-old woman was admitted due to progressive dyspnoea. Previously, after receiving induction and consolidation therapy due to be diagnosed with intermediate risk acute myeloid leukaemia M₀, she underwent allogeneic stem cell transplantation with a 10/10 matched unrelated donor 7 months before. At her admission, after ruling out infection or cardiac failure, her symptoms were compatible with lung chronic GVH disease. Despite her stable cardiopulmonary condition, supporting with O₂, inhalative steroids, leukotrien antagonist, macrolid antibiotics, she remained refractory to systemic corticosteroids and tacrolimus, therefore second line treatment of GVH disease was initiated with second generation tyrosine kinase inhibitor dasatinib. For this treatment, she responded well, and she could have been discharged home.

A 62-year-old man was admitted with a weak graft causing pancytopenia, initially diagnosed with myelodysplastic syndrome and underwent a haploidentical transplant in July 2017. However, donor chimerism was found to be 100%. Nevertheless, increasing jaundice was observed, caused by a hepatic GVH disease, confirmed by transjugular hepatic biopsy. After improving his jaundice with increasing doses of corticosteroids followed by sirolimus and tacrolimus, his haploidentical donor son was organised to provide a CD34+ selected “boost” to improve his pancytopenia. Severe and durable neutropenia contributed to a small subcutaneous abscess at the interdigital commissure of the leg.

During my stay, I attended the European Society for Bone and Marrow Transplantation International Training Course on 8-10 September, where I presented a case, the “Advances in the diagnosis and treatment of lymphoid neoplasm’s: multidisciplinary and practical approach” on 2-3 November, and the Tutorial in lymphomas and stem cell transplantation on 15-17 November, 2017, the latter two organized by the ICO faculty.

Conclusion: The opportunity to study in an environment that cultivates both the treatment and research aspects of the specialty was highly pertinent to my current professional endeavours mark an enduring effect on my career. Hopefully, this visit would be the basis of a long-term collaboration.

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