Treatment of Posttransplant Lymphomas

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Jacobson and LaCasce have provided a thorough review of post-transplant lymphoproliferative disorders (PTLDs), but the authors did not completely cover the field. While the article describes the development of lymphoid tumors related to Epstein-Barr virus (EBV) in patients who have received an organ transplant, it did not consider PTLDs developing after hematopoietic stem cell transplant, a condition also related to EBV but which is more aggressive. Not all PTLD cases are related to EBV, however, and as in patients with HIV (human immunodeficiency virus) infection or hereditary immune deficiency, other lymphoma subtypes may be observed, including T-cell lymphomas[1] (anaplastic large cell lymphoma,[2,3] hepatosplenic lymphoma[4]), indolent lymphomas[5]; and also Hodgkin lymphoma,[6,7] multiple myeloma,[8] or lymphoproliferative disorders associated with human herpes virus 8 infection.[9]

Some of these lymphoproliferative disorders are associated with EBV infection, but not all. They are rare compared with the classical diffuse large B-cell lymphoma (DLBCL) or Burkitt lymphoma PTLDs. PTLDs not related to EBV usually occur later than EBV-positive tumors and may represent up to 20% of lymphoid proliferations occurring in transplanted patients.[10] No large series exist describing the outcome of these specific lymphomas. As they usually occur late after the transplant, often longer than 3 years later, decreasing the immunosuppression has no effect on the PTLD. Rituximab (Rituxan) alone is not the solution, as some of these cases are CD20-negative. The recommended treatment is the one applied for these different lymphomas in nontransplant patients.

**The Three Main Settings of PTLD**

PTLD is not a simple disease but a complicated situation with three main settings, as described by Drs. Jacobson and LaCasce: (1) pleiomorphic lymphoid proliferation related to EBV reactivation, usually occurring during the weeks or months following the transplant; (2) monomorphic lymphoid proliferation related to EBV reactivation, with the aggressiveness of DLBCL or Burkitt lymphoma; and (3) late DLBCL, for which the relationship to EBV is less certain. In the first two cases, EBV is detected in the tissues by in situ hybridization for EBV-encoded RNA (EBER) or by immunohistochemistry for latent membrane protein-1 (LMP-1). These cases are susceptible to respond to a decrease in immunosuppression. Without good treatment allowing patients to reach a complete response (CR), however, those with monomorphic PTLD and late PTLD will die from the lymphoma. Jacobson and LaCasce reviewed the different therapeutic possibilities, but they did not propose any practical decision tree. As they said in their article, there are not any internationally accepted recommendations.

I usually recommend the following: For patients with polymorphic proliferation, reducing the immunosuppression is the first step. If the symptoms do not abate after a few days, rituximab treatment must follow. Antiviral therapy can be added but this is usually sufficient to obtain a CR. Patients with early monomorphic proliferation have a more aggressive lymphoma, and a CR must be obtained before one can expect a long survival. Reducing the immunosuppression is rarely sufficient, and rituximab must be added systemically. If the symptoms do not abate in a few days (or a maximum of 1 week), or in case of worsening, chemotherapy is the solution. The standard R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen is then...
recommended and is usually sufficient. There is a debate in the literature regarding the combined use of chemotherapy and rituximab because of the possible increase in risk of infection.[11,12] Such a risk does not exist for R-CHOP in DLBCL patients outside the transplant setting.[13] As the patient will die in a few months if a CR is not reached, I prefer to use R-CHOP in patients with aggressive CD20+ B-cell lymphomas.

Patients with late PTLD usually do not respond to immunosuppression, and the outcome of the lymphoma resembles what is observed in non–post-transplant lymphomas.[10,14] Here, too, we have anecdotal cases and short series to elaborate on the best regimen. Frail patients can receive rituximab first, then R-CHOP if there is no response, but for other patients CR must be the primary objective of the treatment; R-CHOP is the best option for B-cell PTLD, CHOP alone is best for CD20-negative PTLD, and ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine) is appropriate in Hodgkin lymphoma.

Finally, for patients progressing after a partial or complete response, classical salvage regimens can be used, followed by high-dose therapy and autotransplant.

In summary, the development of PTLD in a transplant patient may jeopardize his or her survival, and everything has to be done to reach a CR. As in other aggressive lymphomas, the first treatment must be the good one, and very few patients can be salvaged.

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**References**


28. Choquet S, Oertel S, Anagnostopoulos I, et al. Results of the largest study on


34. Study of HQK-1004 and ganciclovir/valganciclovir to treat Epstein-Barr virus (EBV)-positive lymphoid malignancies or lymphoproliferative disorders. National Institutes of Health clinical trial ID NCT00992732.


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