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Associated commentary

Cancer risk associated to solid organ transplantation

Plaza López de Sabando D
Adjunct physician. Paediatric Haematology-Oncology and Stem Cell Transplantation Unit. Working Group on Central Nervous System and Liver Tumours of the Sociedad Española de Hematología y Oncología Pediátrica. Working Group on Lymphocyte Pathophysiology in Immunodeficiencies of IdiPaz. Hospital Universitario La Paz. Madrid. Spain.

Correspondence: Diego Plaza López de Sabando, diego_dea@yahoo.es

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Cancer risk associated to solid organ transplantation

Plaza López de Sabando D

Adjunct physician. Paediatric Haematology-Oncology and Stem Cell Transplantation Unit. Working Group on Central Nervous System and Liver Tumours of the Sociedad Española de Hematología y Oncología Pediátrica. Working Group on Lymphocyte Pathophysiology in Immunodeficiencies of IdiPaz. Hospital Universitario La Paz. Madrid. Spain.

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Congenital or acquired states of immunosuppression, which include solid organ transplants (SOTs), are a well-known predisposing factor for cancer development in childhood. The preparative regiments for SOT, as well as anti-rejection prophylaxis and treatment, impair the immune response and limit the immune system's capacity to recognise and eliminate cancer cells and to suppress the activity of oncogenic viruses. The 20-year cumulative cancer risk of SOT recipients is estimated at more than 50%, 5-10 times that of the general population, and is one of the leading causes of mortality in this group.[1]

As is the case in other situations in paediatric oncology, age is a determinant that leads to scenarios differing from those in the adult population. The probability of developing cancer in individuals aged less than 25 years is up to 50 times higher. The carcinogenic risk of immunosuppression is compounded by additional risks associated with exposure to various agents and by lifestyle factors in adulthood that now, due to the increases in survival that have been achieved, last longer, and can lead to the development of atypical events with longer latency periods.

The incidence of cancer differs from the incidence in adults. As described in the reviewed article,[2] the most frequent type of cancer in paediatric SOT recipients is lymphoma, usually in the context of post-transplant lymphoproliferative disorder (PTLD). The most prevalent among them is mature B-cell non-Hodgkin lymphoma (NHL) (diffuse large B-cell, Burkitt and Burkitt-like lymphoma, in decreasing order of frequency), the risk of which increases by a factor of nearly 500, while Hodgkin or T-cell lymphoma is more rare. Its development is associated with reactivation/infection (especially with primary infection) by Epstein-Barr virus (EBV) in 85%-90% of cases.

The risk factors described for the development of lymphoma in SOT recipients reflect two key issues: the intensity of immunosuppression (increased risk in transplants that require more intense immunosuppression: intestinal, multivisceral, heart and lung), and the probability of primary infection by EBV (increased risk in patients who are seronegative before transplant, in the first year post transplantation, and with age < 5 years). The risk associated with intestinal or multivisceral transplantation is particularly high for several reasons: the presence of large amounts of lymphoid tissue in the graft, with a high probability of EBV transmission and chronic immune stimulation by the allograft that may be associated with the extranodal site of disease in the transplanted organ.[3]

At present, there are no preventive measures of proven efficacy. Viral load monitoring seems to be one of the best strategies; in case of reactivation, it is recommended that the intensity of immunosuppression be reduced. There is insufficient evidence on the role of antiviral treatment or adoptive cellular therapy for prophylaxis or pre-emptive therapy. In patients with confirmed lymphoma, in addition to discontinuation of immunosuppression, treatment is based on the use of anti-CD20 monoclonal antibodies combined with chemotherapy of varying intensity.[4]

The incidence of other types of cancer is also high, but the risk factors described above have not been associated with their development, possibly because the interaction of immunosuppression and EBV is not as significant. In these other types, the pathogenesis involves defects in the immune surveillance of transformed cells, the direct effects of various drugs (alkylating agents, calcineurin inhibitors…) and the action of other carcinogenic viruses (hepatotropic viruses, human herpesvirus-8, human papillomavirus, polyomaviruses…); transmission of tumour cells in the graft is an infrequent phenomenon (0.2%). The most frequent cancers are those involving the skin (basal cell and squamous cell carcinomas), the transplanted organ, the thyroid, bladder or vulva, and other cancers that typically occur in childhood such as hepatoblastoma and nephroblastoma. Conversely to lymphomas, the risk of developing these other cancers increases with age; the reduction in SOT-related complications and improvements in survival are the main determinants, due to the reduction in competing factors, of the increasing incidence of these cancers. The latency periods are longer compared to NHL and to those in adult patients. The prognosis and treatment depend on the histology and spread of the malignancy. We ought to highlight that the incidence of other cancers that are common in the paediatric age group, such as central nervous system or bone tumours, is not increased in SOT recipients.[5]

Knowing and being able to quantify the risk of cancer development in these patients would be useful for the development of screening tests and protocols for its early diagnosis and treatment.

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