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EDITORIAL

Viral etiology in pediatric hematological neoplasms



Etiología viral en neoplasias hematológicas pediátricas

In recent years, a group of infectious agents, mostly viral in nature, have been associated with the development of malignant diseases. The first human oncogenic virus, the Epstein-Barr virus (EBV), was described 51 years ago, which was isolated from pediatric patients with Burkitt's lymphoma who resided in Equatorial Africa. This discovery established the basis for viral oncology, which today recognizes eight viral agents directly or indirectly associated with human cancer.

EBV is a member of the herpesviruses family and together with Kaposi's sarcoma-associated herpesvirus are the prototypical representatives of the subfamily of the gammaherpesviruses. These viruses are characterized by their ability to significantly induce lymphomas and sarcomas in immunocompromised individuals. Similarly, members of the subfamily of the betaherpesviruses, such as the cytomegalovirus (CMV), human herpesvirus type 6 and human herpesvirus type 7, are being recognized as important agents associated with human neoplasms that favor tumor aggressiveness. CMV together with EBV are viral agents of great significance for immunocompromised individuals, particularly those who are treated with immunosuppressive drugs to prevent rejection after solid organ transplantation. All these viruses are characterized for encoding their own battery of genes, which imitate cellular processes and allow chronic infections to be established, lasting the entire lifetime of the host. The same genes that perpetuate life of the infected cell and interfere in its process of replication are the oncogenes responsible for its malignant transformation. Understanding these persistent viral mechanisms will provide a significant control of the associated diseases.

Currently, EBV is recognized as the oncogenic agent most strongly related with pediatric cancers. In children, this agent is associated with a set of diseases ranging from infectious mononucleosis to lymphomas, particularly in immunosuppressed individuals. This special issue of the *Boletín Médico del Hospital Infantil de México (BMHIM)* has the objective of highlighting the growing importance of viral agents in the development of neoplasms in the pedia-

tric population, mainly EBV, but also of other members of the herpesviruses family. These neoplasms include post-transplant lymphoproliferative disease and different types of lymphomas, including Burkitt's lymphoma, Hodgkin's lymphoma and diffuse large B-cell lymphoma. More recently, EBV is also recognized as the causal agent of a fraction of the T-cell lymphomas and NK cell lymphomas and a new entity called hemophagocytic lymphohistiocytosis. This issue of *BMHIM* gathers original articles, review articles and clinical case reports of researchers located in different research centers and hospitals worldwide who share their experiences in the study, diagnosis and treatment of this set of diseases.

Chabay and Preciado present the epidemiological panorama of pediatric lymphomas associated with EBV in Argentina.¹ This work represents one of the few reports of pediatric lymphomas and EBV done in developing countries and out of Africa. It shows that in a Latin American country the epidemiological behavior of these neoplasms is different from that of developed countries, with a higher incidence of EBV-positive cases and with an earlier presentation.

Presenting part of the experience of the medical centers to which they are affiliated, Martín-Mateos and Piquer from Spain² and Lee and Ko from South Korea³ present case reports of common variable immunodeficiency and chronic active EBV infections, respectively: two diseases that have been relatively recently recognized as important risk factors in the development of lymphomas. Jiménez-Hernández et al. from Mexico present a case of hemophagocytic lymphohistiocytosis probably associated with EBV.⁴ This case highlights that these types of diseases also occur in Mexico, up to now mainly studied in Asian countries or in the U.S. Reyes-Pérez et al., in an original article, approach the importance of continuous CMV monitoring in pediatric patients who are pharmacologically immunosuppressed due to a solid organ transplantation. This article also confirms the importance of monitoring drug levels in the blood and to not be based solely on the dosage given.⁵

In an interesting review article, R. Rochford, of the University of Denver, discusses epidemiological and experimental evidence on the probable mechanisms of

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transformation that occur in endemic Burkitt's lymphoma of Equatorial Africa.⁶ In this specific type of lymphoma, co-infection with the *Plasmodium falciparum* parasite, which causes malaria, is a critical factor. Taking into consideration the article by Chabay and Preciado, who arrive at the conclusion that the incidence of lymphomas associated with EBV is very high in Argentina and its presentation is earlier than in developed countries,¹ it would be important to identify which infections act as co-factors in the development of Burkitt's lymphoma in countries in which malaria is not prevalent, but where the incidence of this EBV-positive lymphoma is high in pediatric populations.

The Rouce working group from Baylor College of Medicine, Houston, a world leader in the area of immunotherapy against cancer, presents an opinion based on their personal experience on risk factors, diagnosis and management of posttransplant lymphoproliferative diseases and EBV.⁷ Finally, J.M. Mejía-Aranguré discusses a model of causality of pediatric acute leukemias that includes infections as possible risk factors in their development.⁸

In summary, lymphomas are the third most common type of cancer in the pediatric population and leukemia is the most common. This special edition emphasizes the importance of viral infections, especially by members of the herpesviruses family, in the development of lymphomas, with the objective of intensifying its study, especially in developing countries such as Mexico, with very poor understanding in this regard. The study of viruses associated with malignant processes has resulted in the Nobel Prize for Dr. Harald zur Hausen for the discovery of the human papilloma virus and for Dr. Luc Montagnier for the discovery of the human immunodeficiency virus. This knowledge has also resulted in the generation of two vaccines that will help in the control of cervical cancer and liver cancer. In the future, it is advisable to have better tools for the control of pediatric malignancies, which are importantly associated with viral infections.

References

1. Chabay P, Preciado MV. Epidemiology of Epstein-Barr virus-associated pediatric lymphomas from Argentina. *Bol Med Hosp Infant Mex.* 2016;73:47-54.
2. Martín-Mateos MA, Piquer Gibert M. Primary immunodeficiency syndromes and B-cell lymphomas. *Bol Med Hosp Infant Mex.* 2016;73:18-25.
3. Lee TH, Ko YH. Chronic active EBV infection: the experience of the Samsung Medical Center in South Korea. *Bol Med Hosp Infant Mex.* 2016;73:10-7.
4. Jiménez-Hernández E, Martínez-Villegas O, Sánchez-Jara B, Martínez-Martell MA, Hernández-Sánchez B, Loza-Santiago PR, et al. Epstein-Barr virus-associated hemophagocytic lymphohistiocytosis: response to HLH04 treatment protocol. *Bol Med Hosp Infant Mex.* 2016;73:26-30.
5. Reyes-Pérez H, Sánchez-Huerta JL, Varela-Fascinetto G, Romo-Vázquez JC, Morales-Sánchez A, Fuentes-Panana EM, et al. Correlation between viralload of cytomegalovirus and tacrolimus and sirolimus levels in transplanted pediatric patients. *Bol Med Hosp Infant Mex.* 2016;73:4-9.
6. Rochford R. Epstein-Barr virus infection of infants: implications of early age of infection on viral control and risk for Burkitt lymphoma. *Bol Med Hosp Infant Mex.* 2016;73:41-6.
7. Aguayo-Hiraldo P, Arasaratnam R, Rouce R. Recent advances in the risk factors, diagnosis and management of Epstein-Barr virus post-transplant lymphoproliferative disease. *Bol Med Hosp Infant Mex.* 2016;73:31-40.
8. Mejía-Aranguré JM. Molecular epidemiology of acute leukemia in children: causal model, interaction of three factors—susceptibility, environmental exposure and vulnerability period. *Bol Med Hosp Infant Mex.* 2016;73:55-63.

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