ASSOCIATION OF EPSTEIN–BARR VIRUS AND LYMPHOPROLIFERATIVE DISEASES IN IMMUNE DEFICIENT PERSONS

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SUMMARY

Multiple immune responses ordinarily provide tight security against life-threatening Epstein–Barr virus (EBV)-induced diseases. However, studies performed predominantly during the recent decade have demonstrated that individuals with acquired or inherited immune deficiency disorders are subject to life-threatening diseases related to EBV. The diseases seem to result depending on the type and degree of the immune deficiency and when the immune deficiency occurs with respect to primary infection by the virus. The X-linked lymphoproliferative syndrome (XLP) serves as a model demonstrating that immune deficient individuals can develop a spectrum of diseases including acquired agammaglobulinemia, aplastic anemia, red cell aplasia, or proliferative disorders such as chronic or fatal infectious mononucleosis, pseudolymphoma or malignant B cell lymphoma. Similarly, renal transplant recipients can develop a fatal infectious mononucleosis-like disease in young seronegative patients, whereas older individuals tend to show reactivation of virus and develop malignant lymphomas. Patients with AIDS have also developed EBV-carrying malignant lymphomas. The serological findings in immune-deficient patients usually reveal excessively high or low antibody titers. The conversion from polyclonal B cell proliferation to monoclonal B cell malignancies probably occurs as a result of cyto-
genetic and/or molecular changes involving immunoglobulin gene loci and oncogenes, such as c-myc. Recognition that EBV can induce life-threatening diseases can lead to development of rational strategies for preventing immune deficiency and also for treating patients before they develop the life-threatening diseases.

INTRODUCTION

The immune competence and age of a person determine the clinical consequence when primary infection by Epstein-Barr virus (EBV) occurs. Although mainly malignant B cell disorders will be dealt with, a variety of EBV-associated diseases which affect human beings will also be summarized. Thereby, I intend to illustrate the biological bridges between benign disorders and lymphoma which are found in an individual or within families or in communities and are associated with immune deficiency and viral infection (Purtilo and Sakamoto, 1982; Purtilo, 1984a).

PREGNANCY, THE FETUS, EBV, AND BIRTH DEFECTS

Owing to physiological immune suppression accompanying normal pregnancy (Purtilo et al., 1972), the virus frequently becomes reactivated (Sakamoto et al., 1982). Reactivation of EBV in pregnant women has been linked with an increased frequency of pathologic births (Icart and Didier, 1981). Others (Goldberg et al., 1981) have noted that congenital heart disease can arise when the mother becomes infected by EBV early in pregnancy. Maternal antibodies to the virus increase during pregnancy. They are passed transplacentally to the fetus (Sakamoto et al., 1982).

PASSIVE AND ACTIVE PERIODS OF PROTECTION AGAINST EBV

The transplacental passage of neutralizing EBV antibodies protect the child from primary infection for periods up to 10 months. Seldom does an infant develop infectious mononucleosis or Burkitt's lymphoma prior to approximately four months, nor do phenotypes of the X-linked lymphoproliferative syndrome (XLP) appear. Children, until approxima-