Statement of Editorial Purpose

The Hospital Physician Hematology Board Review Manual is a study guide for fellows and practicing physicians preparing for board examinations in hematology. Each manual reviews a topic essential to the current practice of hematology.

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Post-transplant Lymphoproliferative Disorders

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INTRODUCTION

There is an increased risk of malignancy after both solid organ transplantation (SOT) and hematopoietic cell transplantation (HCT). In patients who undergo SOT, the second most common malignancy after nonmelanoma skin cancers is post-transplant lymphoproliferative disorders (PTLD). The term PTLD includes disorders ranging from benign hyperplasia to malignant lymphomas occurring in the setting of immunosuppression during SOT and HCT. The first cases of PTLD were described in renal transplant recipients in the late 1960s. Since then, PTLD has remained a serious and sometimes fatal complication in the post-transplant setting.

EPIDEMIOLOGY

PTLD is the most common malignancy in children who undergo SOT. Primary Epstein-Barr virus (EBV) infection after transplantation is the cause of this high incidence. In adults, PTLD is seen in up to 10% of all SOT recipients. However, different types of transplants result in varying degrees of risk of PTLD; this is thought to reflect the characteristics of both the specific tissue type and the immunosuppressive regimen used in different transplants. The incidence of PTLD is highest after small bowel transplantation (20%), followed by lung (10%), heart (6%), and liver transplants (2.8%). The incidence of PTLD is lowest in renal transplant recipients (2.3%). Historically, the incidence of PTLD has been highest during the first year post-transplant. A collaborative transplant study reported a PTLD incidence of 224 per 100,000 in the first year post-transplant, 54 per 100,000 in the second year, and 31 per 100,000 in the sixth year. This study also demonstrated that the incidence of PTLD during the first year after transplant was higher in combined heart-lung and lung recipients, which was attributed to more aggressive immunosuppression within the first year. However, more recent series show a median time to PTLD onset after SOT of 30 to 40 months.

PTLD is comparatively less common after allogeneic HCT, although it is still a potentially fatal complication in this setting. In large retrospective studies, PTLD occurred in 0.5% to 2.5% of patients after HCT, with the peak incidence occurring between 2 and 6 months post-transplant. Nearly all cases of early-onset PTLD after HCT are associated with EBV infection. Late-onset PTLD following HCT can also occur, with some cases being EBV-negative or of T-cell origin in this setting.

CLASSIFICATION AND PATHOLOGY

The classification of PTLD is based on the histopathologic appearance of the tumor and is categorized according to the 2008 World Health Organization (WHO) classification. The 4 WHO categories of PTLD are early lesions, polymorphic PTLD, monomorphic PTLD, and classical Hodgkin lymphoma. In the United States and Europe, most PTLD lesions (>85%) are of B cell origin, and more than 80% of these are EBV-positive. Early lesions maintain normal tissue architecture and present with 2 histological patterns—plasmacytic hyperplasia and an infectious mononucleosis-like form. Polymorphic PTLD is composed of a combination of lymphoid cells including small- to medium-sized lymphocytes, immunoblasts, and mature plasma cells with degradation of the underlying architecture. Polymorphic lesions may be either polyclonal or monoclonal but do not meet the diagnostic criteria for B-cell or T/NK cell lymphoma.

The most common form of PTLD is monomorphic PTLD. Monomorphic lesions include monoclonal lymphoid proliferations and are divided into B-cell PTLD and T-cell PTLD. Monomorphic B-cell PTLDs include diffuse large B-cell lymphoma (DLBCL), the largest category of monomorphic lesions, followed by Burkitt lymphoma. Monomorphic B-cell PTLD also includes plasma cell myeloma and plasmacytoma-like lesions. Monomorphic T-cell PTLD, including T/NK...