Posttransplant CD30+ (Ki-1) Anaplastic Large Cell Lymphoma

A Case Report and Review of the Literature

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Posttransplant CD30+ (Ki-1) anaplastic large cell lymphoma (ALCL) is rare. A review of the literature revealed only 3 such cases. All 3 cases were developed after single-organ transplantation. We describe CD30+ (Ki-1) ALCL in a dual-organ (liver and heart) transplantation recipient. The patient was a 68-year-old white female who underwent an orthotopic heart transplantation in 1999 and a liver transplantation in 2000. She presented with nausea and was found to have CD30+ (Ki-1) ALCL by pathologic examination of the gastric antrum biopsy specimen. To our knowledge, this patient represents the first reported case of posttransplant CD30+ ALCL following a dual-organ transplantation.

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Most posttransplant lymphoproliferative disorders are Epstein-Barr virus (EBV)-associated B-cell proliferation. The T-cell origin is rare. Although it has been reported that T-cell lymphoma accounts for 14% of the posttransplant malignant lymphomas, only a few cases have been detailed. Posttransplant CD30+ (Ki-1) anaplastic large cell lymphoma (ALCL) is rare. It is characterized by the proliferation of large lymphoid cells with a strong expression of the cytokine receptor CD30. A review of the literature revealed only 3 such cases. All 3 cases were developed after single-organ transplantation; 2 of these cases involved a renal transplant recipient, and the other case involved a heart transplant recipient. We describe CD30+ (Ki-1) ALCL in a dual-organ (liver and heart) transplantation recipient.

REPORT OF A CASE

The patient was a 68-year-old white female with a past medical history of type 1 diabetes mellitus, coronary artery disease status postmyocardial infarction, and ischemic cardiomyopathy with congestive heart failure (CHF) who underwent an orthotopic heart transplantation in November 1999 for end-stage CHF. She subsequently had an orthotopic liver transplantation in March 2000 for cirrhosis from vascular outflow secondary to heart failure. Immunosuppressive therapy consisted of Prograf (FK506), prednisone, and azathioprine. In August 2000, the patient presented with severe nausea. Endoscopy evaluation revealed an antral nodule, which was biopsied.

MATERIALS AND METHODS

The biopsy specimen was fixed in 10% buffered formalin, processed in a standard fashion, and embedded in paraffin. Microscopic sections were stained with hematoxylin-eosin. Immunohistochemistry was performed on paraffin-embedded material using a standard avidin-biotin immunoperoxidase technique. The antibodies used in this study were as follows: CD3, CD5, CD43, CD45RO, LCA, L26, CD79a, Ki-1, EBV, CK, AE1/AE3, S100, HMB-45, and anaplastic lymphoma kinase (ALK). In situ hybridization was performed on paraffin-embedded material using a probe for EBV messenger RNA.

RESULTS

Histologically, the lamina propria of gastric mucosa is diffusely infiltrated by discohesive pleomorphic cells (Figure, A). The neoplastic cells are large with moderate to abundant cytoplasm. The nuclei are chromatin-poor, large, irregular, and sometimes lobulated, with prominent and multiple nucleoli. In this study, the patient’s condition was initially diagnosed as poorly differentiated adenocarcinoma. However, the tumor cells demonstrated an anaplastic lymphoma phenotype with strong cytoplasmic and membranous positivity for CD30 (Figure, B) and faint positivity for CD5 (Figure, C), CD43 (Figure, D), and ALK (Figure, F). The cells were negative for CD20 (Figure, E), CD45RO, CD3, CD79a, EBV, in situ hybridization for EBV early RNA, cytokeratin, and HMB-45. A diagnosis of posttransplant CD30+ (Ki-1) ALCL was then established.

COMMENT

Posttransplant lymphoproliferative disorders represent an immunophenotypic, genotypic, and clinical spectrum of diseases seen in patients after solid organ and bone marrow transplantation. This spectrum of lesions ranges from polyclonal lymphoid proliferation to monoclonal lymphoma. The reported incidences of posttransplant lymphoproliferative disorder vary from 2% to 10%, depending on the type of transplant, with an even higher incidence in some circumstances. The incidence of and interval involved in lymphoma development are most likely influenced by the type of immunosuppression. Most cases of posttransplant lymphomas are EBV-associated B-cell lymphomas. T-cell lymphoma accounts for only 14% of the cases and was reviewed by van Gorp et al in 1994.
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A. The lamina propria is infiltrated by large tumor cells with chromatin-poor, large, irregular, and sometimes lobulated nuclei containing prominent and multiple nucleoli (hematoxylin-eosin, original magnification ×400). B, The tumor cells show strong cytoplasmic and membranous positivity for CD30 (immunoperoxidase, original magnification ×400). C and D, The tumor cells are positive for CD5 and CD43 (immunoperoxidase, original magnification ×400). E, The tumor cells are negative for the B-cell marker CD20 (immunoperoxidase, original magnification ×400). F, The tumor cells are positive for anaplastic lymphoma kinase (ALK) (immunoperoxidase, original magnification ×400).

Its etiology remains unclear. Like posttransplant B-cell lymphoma, posttransplant T-cell lymphomas also predominantly present as extranodal lesions. In contrast to posttransplant B-cell lymphoma, however, few posttransplant T-cell lymphoma cases are associated with EBV. Most posttransplant T-cell lymphomas appear to be monoclonal and generally have a poorer prognosis.

ALCL usually derives from cytotoxic T cells and rep-
represents a group of large cell lymphomas. Defining features consist of a proliferation of predominantly large lymphoid cells with a strong expression of the cytokine receptor CD30 and a characteristic sinusoidal or perivascular growth pattern of tumor cells. Extranodal involvement is frequent. Three subtypes of ALCL have been identified by molecular and clinical criteria: primary systemic ALK⁺ ALCL, primary systemic ALK⁻ ALCL, and primary cutaneous ALCL. ALK expression is caused by a chromosomal translocation, most commonly t(2;5). The translocation results in the fusion of an ALK gene with a nuclear protein nucleophosmin gene. The fusion gene produces a novel chimeric protein p80 nucleophosmin gene/ALK, which has ALK activity. The mechanism by which the ALK fusion proteins cause malignant growth is as yet unknown. The 3 cases of posttransplant ALCL reported in the literature were not investigated for ALK. ALK⁺ ALCL generally has a favorable prognosis if treated with chemotherapy. Our case was positive for ALK; however, because of the rarity of posttransplant ALCL and differences in the therapeutic measures in reported cases, the prognosis of posttransplant ALK⁺ ALCL is unclear.

Two of the 3 cases reported were negative for EBV. The third case was not investigated. In our study, immunohistochemical staining for EBV latent membrane proteins and in situ hybridization for EBV early RNA were performed and showed an absence of EBV.

In summary, we describe a rare case of posttransplant CD30⁺ ALCL developing after heart and liver transplantation. Posttransplant lymphoproliferative disorders may respond to a decrease in immunosuppression. This entity should be considered in the posttransplant setting to ensure appropriate diagnosis and therapy.

References