Primary Involvement of Allografted liver in Post-Transplant Lymphoproliferative Disorders, Report of Two Pediatric Cases and Review of the Literature

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ABSTRACT

Post-transplant lymphoproliferative disorder is a lymphocyte proliferating disease, usually of B cell origin, and rarely of T cell. Involvement of liver itself in liver transplant recipients as the primary organ is not common. Herein we report our experience in two patients who primarily presented in the allografted liver, both of whom were promptly diagnosed after liver biopsy and treated successfully. Now after a few months; both of the patients are alive with normal liver function tests and negative imaging studies.

Keywords: Liver; Lymphoproliferative Disorders

1. Introduction

Post-Transplant lymphoproliferative disorder (PTLD) consists of a heterogeneous group of lymphoproliferative disorders which occurs in 1.4-7% of orthotopic liver transplantations (OLT) and its incidence depends on the age of patient and immunosuppressive therapy used (1). PTLD in OLT patients typically presents as a systemic illness and it rarely presents with involvement of hepatic allograft (2). Among more than 1000 OLT patients in our center we had two patients presented with PTLD in the allografted liver. Herein we report our experience with these two liver transplant patients who had biopsy proven liver involvement.

2. Case Presentation

2.1. Case 1

A 3-year-old boy underwent OLT for cirrhosis secondary to tyrosinemia (HBS and HCV negative). His immediate post-transplant course was unremarkable. After 6 months he developed constipation, vomiting and fever (T> 38°C). At that time he was receiving Tacrolimus, mycophenolate mofetil and prednisolone. His laboratory findings are summarized in Table 1. Liver ultrasonography showed a hypoechoic lesion measuring 14x16 mm in medial segment of left lobe. Liver biopsy was performed which showed severe infiltration of highly atypical mononuclear cells in the portal tracts with parenchymal involvement (Figure 1).
All of these cells were reactive with B cell markers such as CD 20 and CD 79 (Figure 2). LMP-1 antigen of EBV was positive in some of the above mentioned atypical cells. EBV-PCR was also positive in the liver tissue.

3. Discussion

PTLD is a potential complication of transplanted patients with varying incidence based on the transplanted organ and immunosuppressive regimen (3). PTLD in OLT patients typically presents as a systemic illness with rare presentation in the hepatic graft (4). PTLD in the allografted liver as a part of systemic disease or alone has been reported from 0 to 8% in pediatric group from different centers (5-7). Therefore, it seems that liver localized PTLD as the first presentation in pediatric age group is rare (2). There are rare reports concerning the differences between PTLD presenting in the liver allograft and systemic PTLD. Capello et al (8) in their report have described this
issue and concluded that liver allograft PTLDs are of donor origin, mostly B cell type, early onset and pathogenetically related to EBV infection as our two patients.

In an OLT patient, PTLD with liver involvement presents with variable symptoms such as fever, chills, nausea and jaundice (9). Both of our patients presented with fever and abnormal liver function tests and liver biopsy was performed to exclude a rejection episode and to diagnose the source of fever. EBV plays a special role in the pathogenesis of lymphoproliferative disorders that develop in the grafted liver (9,10). EBV has the ability to stimulate B cells to proliferate and transform. After primary infection, EBV persists in the B cells and causes a latent infection. In the process of latency during reactivation after immunosuppression, it can cause lymphoproliferative diseases such as PTLD (11). In both of our cases association with the EBV was definite, because the EBV-PCR in the liver tissue was positive. Some authors believe that the type of immunosuppressive regimen play a crucial role in the pathogenesis of PTLD specially OKT3, antilymphocyte globulin (ALG) and antithymocyte globulin (ATG), but others found no significant association except for treatment with antithymocyte globulin (1,12).

The first step of the treatment in PTLD is decreasing immunosuppression (11). In none of our patients, this was curative and both of them required chemotherapeutic regimen including Retuximab and standard protocol. After that a clear regression of liver lesions was noticed and liver function tests became normal. According to our experience, the liver localization of PTLD does not change with immunosuppressive regimen, i.e. chemotherapy and decreasing immunosuppression can induce subsequent remission without graft rejection. This finding has also been reported in previous studies (12,13). Our experience in these two patients insists on the value of the early diagnosis of PTLD by performing liver biopsy, so clinicians taking care of the OLT patients should consider PTLD with liver involvement or liver localized PTLD as the possible cause of abnormal liver function test and fever (14,15).

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