Case Report

A case of EBV positive diffuse large B-cell lymphoma of the adolescent

Qilin Ao2, Ying Wang1, Sanpeng Xu2, Ye Tian1, Wei Huang1

1Department of Hematology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1095 Jiefang Da Dao, Wuhan 430030, P. R. China; 2Institute of Pathology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1095 Jiefang Da Dao, Wuhan 430030, P. R. China

Received November 25, 2013; Accepted December 23, 2013; Epub January 15, 2014; Published January 30, 2014

Abstract: EBV positive diffuse large B-cell lymphoma (DLBCL) can happen to the elderly, seldom to the young. The case of EBV positive DLBCL has rarely been reported in the adolescent. We report a rare case of EBV positive DLBCL in a 17-year-old man with normal immune state. He was diagnosed by morphology, immunohistochemistry, in situ hybridization for EBV, Flow cytometer, IG/TCR gene rearrangement and cytogenetic study. The occurrence of this case suggests that EBV-positive DLBCL can happen to adolescent patients with normal immune state and cytogenetic study takes an important role in the diagnosis of adolescent EBV-positive DLBCL.

Keywords: Diffuse large B-cell lymphoma, EBV, the adolescent

Introduction

In the 2008 WHO classification of lymphomas, EBV-positive diffuse large B-cell lymphoma (DLBCL) of the elderly has been included. EBV-positive DLBCL in young immunocompetent individuals has been reported [1]. Case of EBV-positive DLBCL in the adolescent with normal immune state has rarely been reported. We diagnosed a case of the adolescent's EBV-positive DLBCL by morphology and immunophenotyping assisted with the technique in chromosomes. The occurrence of this case suggests that EBV-positive DLBCL can happen to adolescent patients with normal immune state and cytogenetic study takes an important role in the diagnosis of adolescent EBV-positive DLBCL.

Case report

A previously healthy 17-year-old Chinese man presented to our hospital with a 2-month history of right cervical lymph node enlargement, without fever, pain and extra nodal disease in July 2012. He had no abnormal finding in tests of hemogram and blood biochemistry including serum LDH and β2-microglobulin. Chest CT scans and abdominal ultrasound did not display mediastinal and retroperitoneal lymph node. Test of EBV displayed positive serum IgG, negative IgM and negative EBV-DNA. Test of HIV displayed negative result. Cellular immune function was evaluated by analyzing lymphocyte subsets (CD3+, CD3+CD4+, CD3+CD8+, CD3+CD4+/CD3+CD8+, CD16+CD56+ ratio) in Peripheral blood; humoral immune function was evaluated by testing IgA, IgG, IgM and complements C3 & C4. The result showed his normal immune state. Sections of the biopsy from the right cervical lymph node showed the complete effacement of the architecture and a diffusely atypical lymphoid proliferation, which demonstrated medium and large lymphoid cells admixed with small lymphocytes and histiocytes. The predominant larger cells showed abundant basophilic or amphophilic cytoplasm, variably irregular nuclear contours, and vesicular chromatin with a single centrally located nucleolus (Figure 1A). Scattered enlarged cells with prominent nucleoli resembling Hodgkin cells were present. There were abundant mitotic figures, focal necrosis, and apoptotic bodies. Immunohistochemical staining showed the large atypical cells were positive for CD20, CD79a, PAX5, mum-1, EMA and CD30 (Figure 1B-D), but lambda and kappa didn't display
Diffuse large B-cell lymphoma

monoclonality (Figure 1E, 1F), the large atypical cells had no reactivity to antibodies for CD3 (Figure 1G), CD5, CD4, CD8, CD43, CD15, ALK, bcl-6, CD10, CD21. Ki-67 LI values were graded as 70% (Figure 1H). Clonal rearrangement for immunoglobulin heavy and light chain genes was not detectable using PCRs. No abnormal cells with a characteristic phenotype could be identified in lymph node specimens using a multicolor flow cytometric approach. In situ hybridization for EBV RNA using the EBER probe showed positive labeling in almost all of the atypical cells (Figure 1I). On the basis of morphology, immunophenotype and age, the diagnosis of “EBV-associated B immunoblast cells lymphoproliferative disorder consistent with necrosis” was rendered. He was followed with anti-virus treatment and prednisone (30 mg/d). Half a month after cervical lymph node biopsy, cytogenetic analysis of cervical lymph node showed clonal karyotype abnormalities (Figure 2): 50, XXY, del(1)(p32), +9, +19, +21 [13]/46, xy [7]. Because EBV-positive DLBCL in adolescent was rare, pathologist did not correct the diagnosis. One month after treatment, he had no shrink in right cervical lymph node and had enlargement in right subaxillary lymph node. He again presented in September 2012, and received right subaxillary lymph node biopsy. Cytogenetic analysis of subaxillary lymph node showed same clonal karyotype abnormalities: 50, XXY, del(1)(p32), +9, +19, +21 [17]/46, xy [3]. Abnormal cells with a characteristic phenotype could be identified in subaxillary lymph node specimens using a multicolor flow cytometric approach. Gating on the abnormal cluster using SSC/CD45 showed expression of CD19 and CD20, no expression of CD23 and...
Diffuse large B-cell lymphoma

CD5. The abnormal cells to be positive for CD38, CD138 (partly), and KI-67 (78.48%), negative for FMC-7, CD10, CD25, CD103, BCL-2, but lambda and kappa didn’t display monoclonality (Figure 3). Clonal rearrangement for immunoglobulin heavy and light chain genes was not detectable in subaxillary lymph node specimens. Although there were no new findings in morphology and immunophenotype, the diagnosis of “EBV-positive DLBCL, Stage IIB” was rendered. The patient received R-CHOP chemotherapy. Only half month after treatment, the patient was admitted to hospital due to enlarging cervical lymph node and fever (excluding infections), CT scans show obvious mediastinal lymph node enlargement. The patient abandoned treatment.

Discussion

We reviewed case reports of EBV-positive DLBCL in adolescent from the articles listed in PubMed, there was rarely report about EBV-positive DLBCL in adolescent. Case reports of EBV-positive DLBCL in young can be searched in PubMed; the patients with immune deficiency were more than 20 years old [1]. In china, the research showed no EBV positive in pediatric DLBCL [2].

The gold standard test for lymphoma diagnosis is the examination of involved lymph nodes or lymphoid tissue by pathologist. It is difficult for pathologist to give diagnosis only by morphologic analysis and Immunohistochemistry, when they face an infrequent case. Flow cytometric analysis and IG/TCR Gene Rearrangement can provide valuable assistance in the diagnosis of lymphoma [3], but these tests did not provide evidences of monoclonal lymphoma cells for this case. Cytogenetic results showed abnormal karyotypes (97%) in lymphoma [4]. One case of aggressive EBV-associated lymphoproliferative disorder in adolescent was reported. The patient was diagnosed Epstein-Barr virus (EBV)-associated lymphoproliferative disorder consistent with infectious mononucleosis. He had not received cytogenetic analysis. Five months later, based on progressive disease, subsequent right cervical lymph node, liver, and jejunal biopsies showed involvement by diffuse large B-cell lymphoma and the patient expired soon thereafter [5]. If the patient had received cytogenetic analysis, the

Figure 2. abnormal karyotype of the case show 50, XXY, del(1)(p32), +9, +19, +21 [13]/46, xy [7].

309

Diffuse large B-cell lymphoma

Diagnosis would have been done without delay. Lymph node cytogenetic analysis played a key role in early diagnosis of lymphoma. Half a month after cervical lymph node biopsy, cytogenetic analysis of cervical lymph node showed clonal karyotype abnormalities. Because EBV-positive DLBCL in adolescent has rarely been reported, our pathologist did not correct the diagnosis. Cytogenetic analysis of subaxillary lymph node showed same clonal karyotype abnormalities. Although there were no new findings in morphology and immunophenotype, the diagnosis of "EBV-positive DLBCL" was rendered.

In conclusion, our case illustrates that EBV-positive DLBCL can happen to adolescent persons with normal immunologic function. The occurrence of this case suggests that EBV-positive DLBCL can happen to adolescent patients with normal immune state and cytogenetic analysis played a key role in early diagnosis of adolescent EBV-positive DLBCL.

Disclosure of conflict of interest

None.

References


Address correspondence to: Dr. Wei Huang, Department of Hematology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1095 Jiefang Da Dao, Wuhan 430030, P. R. China. Tel: 86-02783663611; Fax: 86-02783662680; E-mail: huangchenxi@medmail.com.cn; Qilin Ao, Institute of Pathology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1095 Jiefang Da Dao, Wuhan 430030, P. R. China. E-mail: aoqilin@263.net
