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"The EBV-Positive Diffuse Large Cell Lymphoma of the Elderly" in a Young Patient : A Rare Case Report

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""The EBV-Positive Diffuse Large Cell Lymphoma of the Elderly" in a Young Patient : A Rare Case Report

Cover Page Footnote

From: Abdulkadir Yasir Bahar, MD, PhD Department of Pathology Kahramanmaraş Sütçüimam University Kahramanmaraş, Turkey Tel: (+90) 5313819711 February 23, 2016 To: Editor-in-Chief Tennessee Medicine e-Journal Dear Editor: Re: Submission of Manuscript Dear Editor, We are submitting a manuscript entitled ""The EBV-Positive Diffuse Large Cell Lymphoma of the Elderly" in a Young Patient: A Rare Case Report " to be considered for publication in Tennessee Medicine e-Journal . We believe this work is scientifically valid, and all authors have sufficiently contributed to data collection/analysis and manuscript preparation. We have no financial interest or conflict of interest in association with this work. This manuscript has not been published previously and is not being considered for publication by another journal. Dr. Bahar will serve as the corresponding author. Sincerely Yours, Abdulkadir Yasir Bahar

"The EBV Positive Diffuse Large Cell Lymphoma of the Elderly" in a Young Patient: A Rare Case Report

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ABSTRACT

EBV-positive diffuse large cell lymphoma (DLBCL) of the elderly is a specific and a very aggressive form of clonal B-cell proliferation which generally observed over 50 years of age and without any known previous lymphoma or immunodeficiency. Rarely, it may be observed in younger individuals. Our case was a 24-year-old male. Histopathologic examination revealed atypical pleomorphic bizarre cells which were positive for CD45, CD20, CD79a immunohistochemically and positive for ın situ hybridization(ISH) for "Epstein-Barr virus-encoded mRNA (EBER)." The case is reported with diagnosis and discriminative diagnosis.
Keywords: DLBCL, Lymphoma, EBV positive
Abbreviations: EBV-Epstein-Barr virus; DLCBL-diffuse large B-cell lymphoma

INSTRUCTION

EBV-positive diffuse large cell lymphoma (DLBCL) of the elderly is a specific and a very aggressive form of clonal B-cell proliferation that observed in patients older than 50 years [1,2]. It may be observed in the young extremely rare. And therefore, this topic was considered in "2015 United States and Canadian Academy of Pathology (USCAP) Annual Meeting," and was decided to remove the word "elderly" [3]. For the diagnosis, other EBV -positive B cell lymphomas should definitely be excluded. Also, the patient shouldn't have a known immunodeficiency or lymphoma.

CASE

A 24-year-old male patient was admitted with abdominal pain, fever and fatigue complaints. Physical examination revealed scleral icterus, abdominal ascites, systolic cardiac murmur (2/6) hepatomegaly and splenomegaly. Laboratory examination revealed a decreased hemoglobin 8,1 g/dL (12-15 g/dL); high lactate dehydrogenase 753 IU/L (135-225 IU/L); high aspartate aminotransferase 271 IU/L (0-55 IU/L) and alanine aminotransferase 205 IU/L (0-55 IU/L); elevated serum total bilirubin 11 mg/dL (0,3-1,2 mg/dL) and direct bilirubin 8,4 mg/dl (0-0,5 mg/dL); and significant elevated serum ferritin 10800 ng/mL (18,5-306 ng/mL). White blood cells and platelets were normal range. On serological tests HBsAG, Anti-HBs, Anti-HCV, Anti-HIV were negative. Computed tomography (CT) examination revealed hepatomegaly with homogeneous parenchyma (craniocaudal diameter 181 mm), splenomegaly (craniocaudal diameter 180 mm), multiple paraaortic and mesenteric lymph adenomegaly (the largest one was 8x7cm dimension). Color-Doppler ultrasound examination revealed portal vein diameter 15mm, splenic vein diameter 12 mm, and intra-abdominal free fluid accumulation. The patient underwent excision of mesenteric lymphadenopathy and was referred to our clinic for consultation.

Microscopic examination revealed a complete impairment of the lymphoid structure. Atypical lymphoid proliferation was observed that formed by large atypical cells accompanying numerous small lymphocytes and histiocytes. These atypical cells are enlarged basophilic or amphophilic cytoplasms with large, vesicular nuclei which irregular in outline and have centrally located single nucleoli. Additionally, numerous mitosis and apoptotic bodies were observed (Figure 1). Immunohistochemically, CD 20 (Figure 2), PAX5, CD79a, and CD45 were positive, and CD3, CD5, CD10, BCL-6, CD15, CD30, ALK-1, CD138, (EBV)LMP1, MUM1 and cycline-D1 were negative in the large atypical cells; EBER in situ hybridization revealed almost complete positive reaction in atypical cells (Figure 3).

The differential diagnosis of cases is presented in Table 1 with the histomorphological and immunohistochemical findings.

DISCUSSION

The pathogenesis of EBV-positive diffuse large cell lymphoma (DLBCL) of the elderly is the decreased function of the immune system by age, and the loss of control for the B cell clone under the stimulatory effect of EBV. EBV-positive diffuse large B-cell lymphoma of the elderly is commonly observed among Eastern Asian countries (8-10% of DBBHLs) [4]. The cases from Western countries were reported and based on these limited number of studies; EBV-positive DLBCL seems to represent <5% of DLBCL cases in patients without immunodeficiency [5,6]. Recently, the cases from Turkey have been reported that 'Epstein–Barr virus-positive DLBCL of the elderly' were comprised 6.7% (12／178) of immunocompetent patients above the age of 50 years, 4.7% (12／257) of all cases without immunodeficiency or prior lymphoma and 3.5% (12／340) of all cases of DLBCLs [7]. It is often extranodal (70%), but lymph node involvement may be observed as well. In 30% of the patients, only lymph nodes are affected. Mean survival is two years. "International Prognostic Index" and histopathological subtypes are ineffective in the prognosis, and the presence of B symptoms and age over 70 are indicative of bad prognosis [4, 8]. Our patient died six days after diagnosis.

Although not clinically important, EBV-positive diffuse large B-cell lymphoma of the elderly is classified morphologically in two subtypes as polymorphous and large cell lymphoma. Both subtypes include large transformed cells/immunoblasts and Hodgkin and Reed Stenberg-like giant cells (HRS). In addition, both subtypes may show large geographic necrosis. In the polymorphous subtype, B cell maturation, small lymphocytes in varied rates, plasma cells and histiocytes are observed. In large cell lymphoma subtype, the cells generally have transformed appearance. The discriminative diagnoses of the cases are presented in Table 1 with the histomorphological and immunohistochemical findings [9]. According to this information, our case is compatible with the polymorphous subtype.

The largest study of the literature on the subject was conducted by Oyama et al. in 2007 on seven patients younger than 40 years with no immune failure [4]. In 2011, Beltran et al. have presented 3 cases between 25 and 34 years of age, who had no immune failure [1]. Recently in 2014, Qilin et al. have presented a case of 17 years of age with no immune failure [10]. Our case is a 24-year-old male who had no detected immune failure; however, he was a Syrian refugee which we suspected to may be an originating factor for tumor development, but we don't know the incidence of EBV infection in the refugee camp.

CONCLUSION

This case was presented to suggest that EBV-positive diffuse large B-cell lymphoma of the elderly is extremely rare in young patients with no immunodeficiency, and should be considered in discriminative diagnosis in patients examined for the lymphoma subtype.

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FIGURE LEGENDS

1: Lymph node microscopic examination, there is atypical lymphoid proliferation and atypical large, bizarre pleomorphic cells (Hematoxylin And Eosin, 200x)

2: Large pleomorphic cells are positive for CD20 (Immunohistochemistry, 200x)

3: In situ hybridization(ISH) for “Epstein-Barr virus-encoded mRNA (EBER)” positive cells (ISH-EBER, 200X)