

Case Report

EBV Associated Diffuse Large B cell Lymphoma in a Child Mimicking Hodgkin Lymphoma - A Rare Case Report

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ABSTRACT

Pediatric EBV+ DLBCL (Ebstain bar virus associated diffuse large B cell lymphoma) is a rare disease in non immunocompromised hosts of less than 10 years of age. This was a case of 6 years old boy having abdominal pain, fever, cervical and abdominal lymphadenopathy which on cytomorphology basis was diagnosed as Classical Hodgkin's lymphoma, but latter was confirmed as EBV+DLBCL on histopathology and IHC (immunohistochemistry). This report concluded that reactivation of EBV infection may lead to development of disease and EBV associated DLBCL affecting the paediatric patients had remarkable histologic, immunohistochemical, and molecular similarities to EBV+DLBCL of the elderly making the outcome comparable to the elderly counterpart.

Keywords: Pediatric EBV+ DLBCL, EBV+DLBCL of the elderly, Lymphadenopathy, Classical Hodgkin's Lymphoma, IHC (Immunohistochemistry).

INTRODUCTION

Paediatric EBV+ DLBCL (Ebstain bar virus associated diffuse large B cell lymphoma) is rarely seen in non immunocompromised hosts of less than 10 years of age with strong histological and immunohistochemical resemblance with EBV+DLBCL of elderly. EBV⁺ DLBCL of the elderly, first described by Oyama et al, [1] is a provisional entity in the 2008 World Health Organisation (WHO) classification of lymphoid neoplasm, accounting for 3% to 14% of DLBCL cases. Only few studies have identified EBV⁺ DLBCLs in paediatric and young age patients without known immunodeficiency. [2] Those reported cases showed more frequent type III EBV latency and aggressive clinical behaviour, but the small number of cases analyzed and the

cases with low percentage of EBV⁺ cells limits firm conclusions regarding this disease in young patients.

CASE REPORT

A 6 years old male presented with cervical and abdominal lymphadenopathy, loss of weight, fever and abdominal pain. Complete blood count was in normal limit with slight raised absolute lymphocyte count. Patient was advised for ultrasonography of neck and aspiration cytology of cervical and abdominal lymph nodes. Ultrasonography excluded granulomatous lesion and in cytology it was reported as possibility of Hodgkin's lymphoma (Figure 1). Further CECT abdomen was done, suggesting hepatosplenomegaly and multiple enlarged

lobulated enhancing lymph nodal masses along left common iliac vessels, pre/para aortic and peri pancreatic regions with possibility of lymphoproliferative disorder. Left cervical node biopsy was done.

Initially, it was reported as Classical Hodgkins Lymphoma. Whole body PET-CT was done and showed bilateral level IV and supraclavicular nodes enlargement. Later on case was reviewed and on histopathology and immunohistochemistry, it was reported as stage IV EBV associated B cell proliferation favouring diffuse large B cell lymphoma having classical Hodgkin lymphoma like pattern i.e. diffuse, polymorphous lymphoid proliferation with admixture of CD20/CD30 and EBV positive cells, macrophages and CD3 positive cells. Dominant population were the EBV infected B immunoblasts. Mib 1 index was 60% (Figure 2).

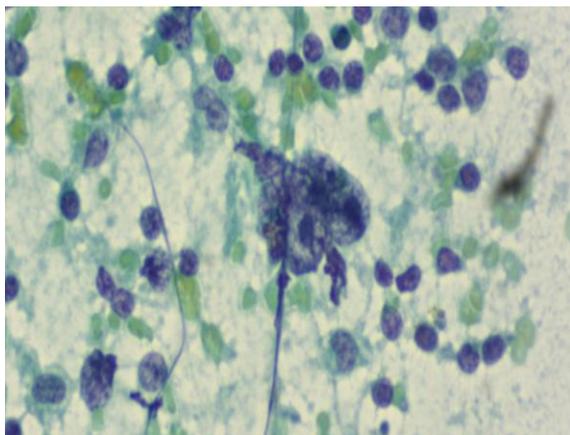


Figure 1: 40X, FNAC, MGG stain, microscopy showing polymorphous cell population, large atypical cell resembling Reed-Sternberg like cell in a haemorrhagic background.

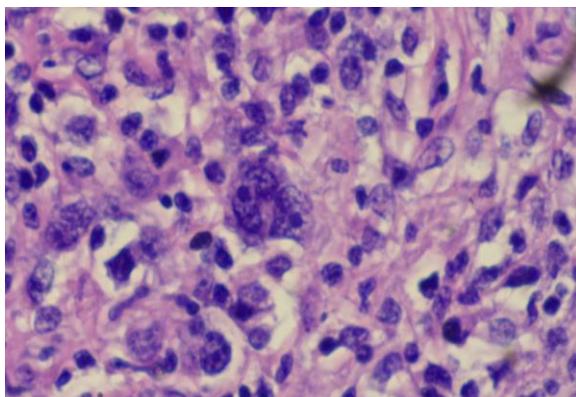


Figure 2: 40X, H& E: microscopy showing diffuse pattern of polymorphous lymphoid population with atypical binucleated cells having irregular nuclear margins, vesicular chromatin and prominent nucleoli, resembling Reed-Sternberg cells (RS Cells). EBV infected B immunoblasts, macrophages and mature lymphocytes were also seen.

DISCUSSION

In immunocompetent hosts of paediatric age group, EBV+ DLBCL is a rare disease. [1] Due to preferential infection of B cells, the most common forms of EBV-associated lymphoproliferative disorders are B cell lymphomas: Hodgkin lymphoma, non-Hodgkin lymphoma, including Burkitts lymphoma and diffuse large B cell lymphoma. [2] EBV plays a role not only in lymphomagenesis, but also in non neoplastic cell proliferation. EBV may induce the expression of cytokines and trigger an exuberant reactive process. Virus infects neoplastic and non neoplastic cells and expresses a range of latent cycle viral proteins including latent membrane protein-1, [2,3] leading to activation of nuclear factor-kappa B pathway.

WHO classification (2008) pointed out that DLBCLs formed a large heterogeneous group of hematologic neoplasm's, including a number of separate pathological entities, among them the below described forms are associated with EBV infection. Mostly, all of the EBV-positive lymphomas are CD10- and MUM1+, have an aggressive clinical phenotype showing poor prognosis. [4]

EBV+DLBCL of the elderly is usually present in lymph nodes and extra nodal locations as an infiltrate of polymorphic, large lymphoid cells, plasmacytoid cells with an inflammatory background. The Reed-Sternberg (RS cells) like cells which leads to the misdiagnosis of classical Hodgkin's lymphoma(HL) in paediatric or young patients, express CD20, CD79a, EBER, and LMP1, and lack expression of CD 15 antigen to differentiate it from classical Hodgkin lymphoma. The presence of geographical necrosis is also suggestive more towards EBV+DLBCL. [5]

The EBV-positive Reed-Sternberg cells (RS cells) in HL show positivity of LMP-1, EBER, EBNA-1, and LMP-2A. RS cells are mostly found in HL patients older than 75 years (45%–80%) as well as in the patients below 10 years of age (40%–85%). EBV infection is rare in nodular

lymphocyte-predominant HL and is infrequently found in nodular-sclerosis HL (15%–20%). It is more commonly associated with mixed-cellularity HL and lymphocyte-depleted HL (especially in patients under 14 years of age and between 40–54 years of age).^[5,6]

Other one, the monomorphic type pattern of DLBCL needs to be differentiated as they may be EBV-Negative DLBCL or may be case of Lymphomatoid granulomatosis.^[7]

Lymphomatoid granulomatosis is extranodal ,mostly involving brain, liver, kidneys lungs, skin , have Pleomorphic, angiocentric morphology and are CD45 β , CD20 β , MUM1 β , CD30 β /- , CD79a- β , LMP β /- , EBER β .

Because of the young age of the patients, infectious mononucleosis can also be considered as a possible differential diagnosis but it can be ruled out by the total effacement of the involved lymph nodes, by nodularity of the lesions, by abundance of large tumor cells and by extensive coagulative necrosis. A mixture of latency II and III and a lytic EBV gene is observed in both young patients and older than 50 years.^[6] This finding suggests that the entity EBV+DLBCL of elderly can occur in paediatric and young immunocompetent patient^[5] and might conclude that EBV+DLBCL is a single disease that can appear at any age.

DLBCL associated with chronic inflammation is usually extranodal located mostly in articular cavities, pleural cavity, skin or serous membranes and have variable morphology on histopathology with immunophenotype showing positivity for CD45, CD20, CD30, MUM1, sometimes CD138 and negativity for CD20.^[5,7]

Primary effusion lymphoma is mostly present in body cavities, has Immunoblastic, anaplastic morphology on histopathology and immunophenotypically are CD20- , CD45 β , CD138 β , MUM1 β , PAX5- , CD30 β , CD19- , CD20- , CD79a- .^[5]

Primary DLBCL of central nervous system is also extranodal having Polymorphic morphology and are Bcl-6 β , Mum-1 β , sometimes CD10 β .^[5]

Plasmablastic lymphoma is usually extranodal involving oral cavity, alimentary tract. They have Immunoblastic plasmablastic morphology and are CD20- , CD45- , CD38 β , CD45 β , CD138 β , PAX5- , CD79a β , and CD30 β .

Staging of EBV + DLBCL diagnosed cases depends upon lymph nodes involved i.e. stage 1(only 1 group of lymph nodes affected), stage 2(2 or more groups of lymph nodes affected either below or above the diaphragm), stage 3(lymph nodes affected on both sides of the diaphragm) or stage 4(lymphoma is found in organs outside the lymphatic system or in the bone marrow).^[5,6]

CONCLUSION

In summary, EBV+DLBCL in young patients are not a distinct disease entity. It can occur in younger patients, and may also be noted in paediatric age. Most of them are presented as a nodal disease and can be confused with other lymphoproliferative disorders like Hodgkins Lymphoma. The concept of EBV+ DLBCL as a disease of the elderly requires reassessment.

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