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Plasmablastic lymphoma in pediatric patients: clinicopathologic study of three cases ☆

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ABSTRACT

Plasmablastic lymphoma (PBL) is an aggressive high grade non-Hodgkin lymphoma which occurs predominantly in adult patients who are concomitantly afflicted with HIV infection. In contrast to several reports and studies of PBL in adult patients, PBL has very rarely been reported in *pediatric* patients. This article hereby provides collaborative clinicopathologic information of de novo PBL diagnosed in 3 *pediatric* patients with concomitant HIV infection. Cognizance of this rare tumor in the pediatric population coupled with antiretroviral therapy and prompt initiation of multimodality treatment may, in the future, facilitate improved outcome in pediatric patients with PBL.

1. Introduction

Plasmablastic lymphoma (PBL) is an aggressive, high grade non-Hodgkin lymphoma (NHL) which was initially considered to be a variant of diffuse large B-cell lymphoma (DLBCL). However, the most recent 2008 World Health Organization classification of tumors of hematopoietic and lymphoid tissues recognizes PBL as a distinctive mature B-cell lymphoma, having been separated from the category of DLBCL [1]. PBL is most commonly diagnosed in immunocompromised adult patients and is very rarely reported pediatric patients.

This article focuses on collaborative clinicopathologic information of de novo PBL diagnosed in three pediatric patients, all of whom have concomitant HIV infection.

1.1. Patient 1

The first patient was an 11-year-old boy with background history of HIV infection. The patient presented with a right-sided orbital mass and an incisional biopsy thereof confirmed the presence of high grade NHL characterized by the presence of starry sky appearance at low power microscopic examination (Fig. 1). The tumor comprised a sheet-like population of large atypical lymphoid cells with vesicular nuclei and prominent nucleoli, the latter varying from single to multiple. The cells displayed intermittently eccentric nuclear displacement and distinctly amphophilic cytoplasm. In some cells, paranuclear hofs were discernible. The high-grade nature of the tumor was supported by the presence of abundant apoptotic debris, numerous interspersed tingible body macrophages and coagulative tumor necrosis.

The immunophenotypic features included immunoreactivity for MUM1 and Vs38C (Fig. 2A and B) as well as epithelial membrane antigen (EMA) and CD10 expression. The tumor displayed leukocyte common antigen (LCA) membrane immunoreactivity which varied from weak to moderate intensity. CD20, CD79a, ALK, Epstein-Barr virus (EBV) LMP1, human herpesvirus 8 (HHV-8), and CD3 immunostains were negative within tumor cells. The tumor proliferation index, assessed using Ki67 immunohistochemistry, was close to 80% (Fig. 2C). Epstein Barr Virus mRNA in situ hybridisation (EBER ISH) was subsequently performed and the tumour cells displayed diffusely positive nuclear signaling. The diagnosis of PBL was confirmed. At diagnosis, the patient had normocytic normochromic anemia. However, there was no associated renal dysfunction or hypercalcemia.

At presentation, the disease was St Judes stage 2, and the patient was treated with the (Berlin-Frankfurt-Munster) BFM '86 B NHL protocol. Highly active antiretroviral therapy (HAART) was commenced and the CD4 count was 221cells/mm^3 at lymphoma diagnosis. Unfortunately, the patient demised 6 months after lymphoma was diagnosed.

1.2. Patient 2

The second patient was a 14-year-old male adolescent who presented with upper respiratory tract symptoms related to the presence of left sided nasal, maxillary, and orbital mass which resulted in proptosis of the left eye. The patient had HIV infection and the CD4

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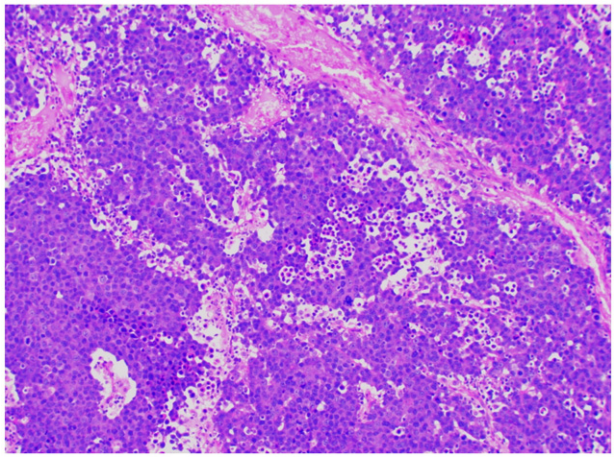

Fig. 1. Sheets of tumor cells with interspersed tingible body macrophages creating a starry sky appearance (scanning magnification).

count (1 month after the initial diagnosis of lymphoma) was 237 cells/mm^3. Biopsy of the mass confirmed the presence of high grade NHL with morphologic features of PBL (Fig. 3). Areas of plasmacytic differentiation were evident and comprised the presence of smaller tumor cells with distinctive plasmacytic features dispersed among plasmablasts and immunoblasts. The immunophenotype was similar to that seen in patient 1 in that the tumor cells were immunoreactive for Vs38C and EMA. Furthermore, there was faint membrane staining with LCA and diffuse nuclear staining with MUM1. The tumor cells lacked immunoreactivity for CD20, EBV LMP1, HHV-8, TdT, CD10, and CD3. At initial presentation, there was no associated anemia, renal dysfunction or hypercalcemia. There was also no bone marrow involvement by tumor.

One year after initial diagnosis and treatment, the patient presented with recurrence of the left sided maxillary sinus tumor and enlarged (level II) cervical lymph nodes. Biopsy of the maxillary sinus mass and lymph nodes confirmed PBL with features similar to those seen in the initial biopsy. Furthermore, the tumor demonstrated immunophenotypic evidence of light chain restriction with diffuse cytoplasmic Kappa staining. There was high proliferation index of approximately 95% and the tumor cells lacked ALK immunoreactivity EBER ISH confirmed nuclear signaling within the tumour (Fig. 4). The lymph nodes displayed no features of Castleman disease or Kaposi sarcoma.

The disease at presentation was St Judes stage 2. The patient was treated with the BFM '86 B NHL protocol and completed 8 cycles of chemotherapy. HAART was commenced at initial lymphoma diagnosis. Unfortunately, death ensued 15 months after lymphoma was initially diagnosis.

1.3. Patient 3

The third patient is a 9-year-old girl with background HIV infection who presented with a scalp mass. The CD4 count before presentation of the mass lesion was 592 cells/mm^3, and the patient received HAART before the diagnosis of lymphoma. Core biopsy of the scalp mass confirmed the presence of high grade NHL with typical plasmablastic morphology. Moreover, in some of the tumor cells, there was plasmacytic differentiation (Fig. 5). Apoptotic debris and mitotic figures were frequent. The tumor cells displayed diffuse immunoreactivity for MUM1 and focal CD138 expression. The tumor proliferation index was close to 95%.

CD20, CD3, ALK, HHV-8, myeloperoxidase, EBV LMP1, and TdT immunostains were negative. EBER ISH demonstrated diffusely positive nuclear signaling within tumour cells. These features confirmed the diagnosis of PBL. The hematological workup revealed no evidence of bone marrow involvement and there was no light chain restriction on flow cytometry of peripheral blood. There was no anemia and biochemistry confirmed the absence of derangement in renal function as well as an absence of hypercalcemia.

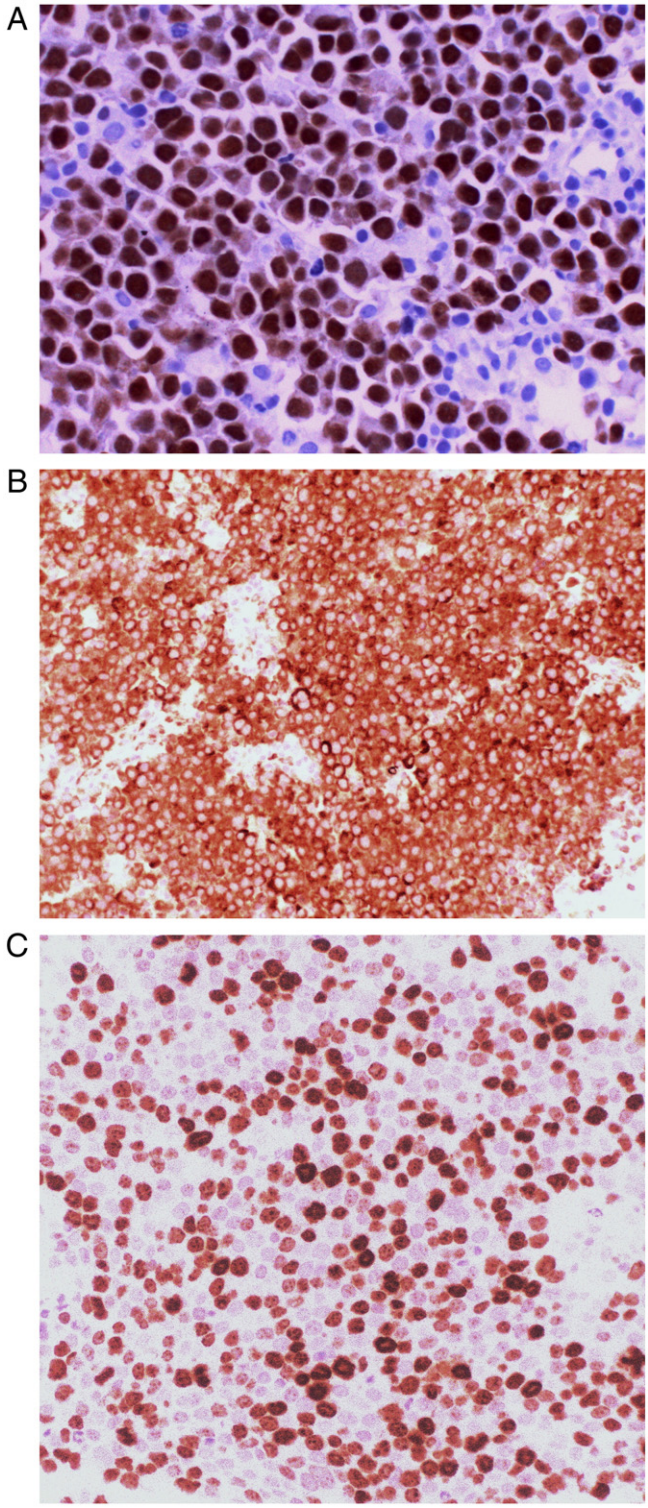

Fig. 2. A, Diffuse MUM1 nuclear immunoreactivity. B, Vs38C immunoreactivity in PBL. C, High tumor proliferation index Ki-67.

The disease was St Judes stage 3. The patient has completed treatment with the BFM '95 B NHL protocol. 6 months after diagnosis the patient remains well and has had an excellent clinical response to treatment. Radiological remission assessments are underway.

Table 1 contains a clinicopathologic summary of the findings.