Introduction

Burkitt lymphoma (BL) is a highly aggressive subtype of non-Hodgkin lymphomas (NHL). The World Health Organization (WHO) classification recognizes three clinical variants of BL: sporadic, endemic, and immunodeficiency related [1]. The immunodeficiency related BL is more common in patient with human immunodeficiency virus (HIV), in whom the lifetime incidence of BL has been estimated at 10-20% [2]. Granulomatous reaction usually indicates a chronic inflammation caused by microorganisms and inert foreign bodies. Lymphoma related granulomatous reaction rarely occurs in sporadic BL, suggesting limited stage disease and good prognosis [3]. From our review of relevant literature, a total of 15 cases of sporadic BL with granulomatous reaction have been reported in English literature [3-7]. Herein, we report the first case of HIV related Burkitt lymphoma with florid granulomatous reaction.

Case report

A 41-year-old Chinese male presented lymphadenopathy in the right cervical lymph node for 3 months. Initial clinical examination revealed the enlargement of right side cervical lymph node 1.5 cm in diameter, hard and painful. He underwent a complete excision of the lymph node and was diagnosed as tuberculous lymphadenitis in other hospital. Subsequently, the case was sent to us for consultation. The morphology, immunophenotype, special staining, interphase FISH analysis and blood tests confirmed a diagnosis of HIV related Burkitt lymphoma with granulomatous reaction. Without radiotherapy and chemotherapy, the patient was alive and well with no evidence of lymphoma during the observation period of 24 months. The case suggested that lymphoma with florid granulomatous reaction can easily be misdiagnosed as benign lesions since the large number of epithelioid granulomas could obscure the primary lesion. Moreover, the granulomatous reaction may be an indicator for favorable prognosis in HIV related Burkitt lymphoma.

Keywords: Human immunodeficiency virus related Burkitt lymphoma, granulomatous reaction, prognosis
HIV-related Burkitt lymphoma with florid granulomatous reaction

growth pattern. The atypical lymphocytes showed round or oval nuclei with finely clumped and dispersed chromatin and 2~4 basophilic medium sized, centrally situated nucleoli. The cytoplasm was scarce to moderate and basophilic (Figure 1C, 1D).

By immunohistochemical staining, the atypical lymphocytes were positive for CD20, CD10 and BCL6 and negative for CD3ε, BCL2 and MUM1. Nearly 100% of atypical lymphocytes expressed Ki-67 (Figure 2A-C). In addition, Ziehl-Neelsen, periodic acid-Schiff, and Grocott stainings did not found the evidence of microorganism infection.

In situ hybridization for EBV

In situ hybridization indicated positivity for EBV presence in the nuclei of atypical lymphocytes by using the in situ hybridization detection kit (A300K.9901; Panpath, Holland) (Figure 2D). However, histiocytes around the atypical lymphocytes were negative.

Interphase fluorescence in situ hybridization (FISH) analysis

FISH analysis was performed on 4 μm thick paraffin-embedded tissue sections. All of the FISH probes were obtained from Vysis/Abbott, Downers Grove USA. FISH using LSI MYC dual-color break-apart rearrangement probe showed 1 orange, 1 green and 1 orange/green fusion (1O1G1F) signal pattern (Figure 3A) indicating the presence of MYC translocation. FISH using IGH/MYC dual color, dual-fusion translocation probe revealed 1 orange, 1 green and 2 orange/green fusions (1O1G2F) signal pattern (Figure 3B) indicating translocation between MYC and IGH. FISH using BCL2 dual-color break-apart probe and BCL6 dual-color break-apart probe presented 2 two orange/green fusion signals pattern (Figure 3C, 3D) indicating atypical lymphocytes.

Figure 1. Prominent granulomas of different size are identified (H&E × 100) (A). Langhans giant cells are fairly easy to be observed in granulomas (H&E × 400) (B). “Starry sky” pattern is obviously seen (H&E × 200) (C). Medium sized cells present round or oval nuclei with finely clumped and dispersed chromatin and 2~4 basophilic (H&E × 400) (D).
HIV-related Burkitt lymphoma with florid granulomatous reaction

Figure 2. Immunohistochemistry (A-C). Atypical lymphocytes are positive for CD20 (A), CD10 (B), and nearly 100% of atypical lymphocytes are positive for Ki-67 (C) (× 200). EBER-ISH shows positive signal in atypical lymphocytes, while histiocytes are negative (D) (× 200).

Phocytes absence of BCL2 and BCL6 translocation respectively.

Clinical follow-up

Without radiotherapy and chemotherapy, the patient was alive and well with no evidence of lymphoma during the observation period of 24 months. Follow-up including blood tests, imaging examinations and bone marrow biopsy were performed every 6 months.

Discussion

Lymphoma related epithelioid cell granuloma occurs in T-cell-derived NHL, Hodgkin lymphoma (HL) and some B-cell-derived NHL [8, 9]. Granulomatous reaction indicates different clinicopathological significances in different lymphomas. Granulomatous reaction may reflect the disease progression of follicular lymphoma (FL) in large B-cell lymphoma [10]. Conversely, granulomatous reaction suggests limited stage disease and good prognosis in cases of sporadic BL and HL [3, 9]. Unfortunately, lymphomas with accompanying florid granulomatous reaction are easily misdiagnosed as benign lesions due to the fact that the primary pathology is obscured by a large number of granulomas. To make the correct diagnosis may be a challenge on fine needle aspiration biopsy. Immunohistochemical staining, special staining and molecular tests are possessed of very important in accurate diagnosis.

A review of the literature revealed isolated case reports of florid granulomatous reaction in sporadic BL. These cases typically present with limited stage disease and have an especially good prognosis [3]. Some studies revealed a close association between EBV infection and granulomatous reaction, one of them suggested that the granulomatous reaction may represent an interaction between CD4+ helper T cells and EBV nuclear antigen 1 (EBNA1) due to...
the lack of LMP1 expression in tumor cells [3]. However, a recent study reported a case of florid granulomatous reaction in primary gastric BL without EBV infection [6]. Furthermore, Hossain et al. showed that BL was deficient in HLA class II-mediated Ag presentation [11]. The exact causes of granulomas in BL became vaguer.

The case under discussion exhibited three particular features which are rare in this entity. First, the patient infected with HIV had subnormal CD4 cell count. Owing to EBER positivity was detected only in tumor cells and the CD4 cell count was subnormal, we expect that CD4+helper T cells don’t play the key role for formation of the florid granulomatous reaction. BL related epithelioid cell granuloma is more likely to result from cytokine production by tumor cells. Second, without radiotherapy and chemotherapy, the patient revealed no evidence of BL involvement during the next 24-month. It seems that there is an association between the granulomatous reaction and the favorable outcome in case of HIV related BL. Third, the granulomas occupied a significant area in the lymph node, which created troubles to make the accurate diagnosis. The presence of atypical lymphocytes in the context of a granulomatous reaction aroused our suspicion, and immunohistochemical staining, special staining and FISH analysis are useful to establish an accurate diagnosis.

In summary, we describe the first case of HIV related BL with accompanying florid granulomatous reaction which almost obscured the primary pathology. Pathologists need to be aware of the presence of large number of prominent granulomatous reaction. The first temptation is to think about an infectious disease. Special stains are required to rule out the possibility of infection. Any presence of atypical lymphocytes in the context of a granulomatous reaction should be considered suspicious. The patient
HIV-related Burkitt lymphoma with florid granulomatous reaction had a good prognosis suggesting an association between the granulomatous reaction and the favorable outcome in case of HIV related BL. Many possible mechanisms of genesis of granulomas in BL have been postulated. However, more cases and further research are needed to elucidate the exact causes of granulomas in cases of BL which may provide some new insights into the treatment of BL.

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Disclosure of conflict of interest

None.

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References