CASE REPORT

Burkitt Lymphoma of Oral Cavity in Myanmar.

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Abstract

Burkitt lymphoma is a highly aggressive but curable lymphoma, composed of monomorphic medium sized B cells with basophilic cytoplasm and numerous mitotic figures. It has endemic, sporadic, and human immunodeficiency-associated subtypes. The African or endemic variants frequently involves the maxilla and other facial bones, while head and neck manifestations in sporadic Burkitt lymphoma are rare. We present the case of a 41-year-old woman with a rapidly growing buccal mucosal growth, leading to swallowing difficulties within one month. There was no palpable lymphadenopathy or organomegaly. Serology tests for HBs antigen, HCV antibody, and HIV antibody were negative. The histological section of the biopsy tissue from the buccal mucosal growth showed infiltrating diffuse sheets of neoplastic cells. These cells appeared as monotonous, medium-sized lymphoid cells, displaying numerous apoptotic bodies and numerous tangible body macrophages, indicative of a high proliferation rate. Immunohistochemical staining of the tumor cells revealed positivity for CD20, CD10, BCL6, and CMYC, while BCL2 was negative. Additionally, the Ki67 proliferation index was exceptionally high, nearly 100%, consistent with Burkitt Lymphoma. The true incidence of Burkitt lymphoma in Myanmar is unknown due to a lack of reported cases. This underscores the importance of early diagnosis and immediate, appropriate management of the disease. The definitive diagnosis was confirmed through a meticulous histopathological examination combined with immunohistochemistry.

Keywords: *Burkitt Lymphoma; CMYC expression; highly aggressive lymphoma; high Ki67 expression; monomorphic medium sized B cells.*

Introduction

Burkitt lymphoma is a highly aggressive yet curable lymphoma, composed of monomorphic medium sized B cells with basophilic cytoplasm and numerous mitotic figures [1]. This lymphoma has endemic, sporadic, and human immunodeficiency-associated subtypes. The African or endemic variants frequently involves the maxilla and other facial bones, while head and neck manifestations in sporadic Burkitt lymphoma are rare [2]. Burkitt lymphoma is characterized by its rapid progression of symptoms and frequent multifocal extranodal involvement. Within the oral cavity, this tumor can progress rapidly, presenting as facial swelling or an exophytic mass involving the jaws [3].

Case report

We presented a 41-year-old lady who came to the maxillofacial clinic with buccal mucosa swelling. The swelling rapidly progressed, resulting in swallowing difficulty within one month. She denied history of fever, night sweats, respiratory, or gastrointestinal symptoms. In the first week of her clinical course, she applied indigenous medicine on her right cheek due to discomfort on that side of her face, but it did not provide relief. In the second week, she sought a general practitioner and received anti-inflammatory drugs and antibiotics for three days, but her symptoms did not improve. She experienced no relief during this time and began to feel toothache-like pain on the right side of her face**.** She gradually shifted to a soft and liquid diet during this week. When she came to the maxillofacial clinic, given the rapid growth, she was referred to the clinical haematology ward to be investigated for any involvement of haematological malignancy. On examination, a loculated buccal mucosa mass (approximately 6 x 7 cm) occupying the right buccal cavity, which limited mouth opening and swallowing, was observed (Figure1). The surface of the mass has ulcerated mucosa epithelium, and a small necrotic area was noted. There was no palpable lymphadenopathy or organomegaly. Laboratory investigations revealed the haemoglobin level was 12.1 mg/dl, white cell count was 9 x 10^9/L, and platelet count was 405 x 10^9/L. Renal and liver function showed no abnormalities. Serology tests for HBs antigen, HCV antibody and HIV antibody were negative. Plasmodium falciparum-Plasmodium vivax immunochromatographic test was negative. Chest X-ray and ultrasound abdomen showed no evidence of distant metastasis. The histological section of biopsy tissues from the buccal mucosa mass showed proliferation of diffuse sheets of medium-sized lymphoid cells. In some areas, they exhibited vaguely nodular growth patterns, admixed with salivary glands and fat. The proliferating lymphoid cells were distributed in diffuse sheets in most areas of the tumor, with tangible body macrophages infiltrating into the tumor sheets, creating a starry sky pattern. These lymphoid cells appeared monotonous, with basophilic cytoplasm and round nuclei featuring finely clumped and dispersed chromatin. They had small, pericentrally located nucleoli. These cells displayed some degree of cohesion (Figure 2.A, B). Immunohistochemical staining of these neoplastic lymphoid cells revealed CD20+, CD10+, strong CMYC+ expression, and 100% Ki67 expression (Figure 2. C, D, E, F). They also tested positive for BCL6 and MUM1, and negative for CD3, CD5, CD23, BCL2, cyclinD1, and EBV/LMP1. These findings are indicative of Burkitt lymphoma. Treatment started with CHOP (Cyclophosphamide, doxorubicin, Oncovin, Prednisolone) but during the first cycle of treatment, the patient developed neutropenic septicaemia. The clinical condition deteriorated, and she expired.

Discussion

Burkitt lymphoma is a highly aggressive non-Hodgkin B-cell lymphoma and is the fastest growing tumour. Adult Burkitt lymphoma represents 1-2% of non-Hodgkin lymphoma in adults or the elderly [4]. In many equatorial Africa countries and in Papua New Guinea, Burkitt lymphoma is the most common childhood

cancer, and is considered the endemic type [5]. In other regions, Burkitt lymphoma is less common in children and is considered the sporadic type [6]. Most cases of sporadic Burkitt lymphoma present with abdominal masses, but it is very rare in facial structures, particularly the jaws. The ileocecal region is the most frequent site of involvement. Similar to endemic Burkitt lymphoma, sporadic cases may also affect the ovaries, kidneys, and breasts [7]. In immune deficiency setting, Burkitt lymphoma typically exhibits a higher likelihood of nodal involvement, although extranodal involvement is also commonly observed [8].

In the presented case, an immunocompetent adult woman with a previously healthy medical history, developed a rapidly increasing buccal mucosa growth that limited her mouth opening within one month. This is a rare presentation of oral cavity Burkitt lymphoma. According to a report by Jan. Ahmed. et al., oral sporadic Burkitt lymphoma acts as a rapidly growing, aggressively expanding tumor, leading to a dull, toothache-like pain, teeth malposition, and challenges in chewing and bite alignment [9].

The correlation between Epstein-Barr Virus (EBV) infection and Burkitt lymphoma exhibits significant variation across different regions of the world [10]. The risk factors for endemic Burkitt lymphoma include *Plasmodium falciparum* (malaria) and EBV infections. However, the factors contributing to Burkitt lymphoma in regions with low incidence, such as Europe, Asia and South America, remain poorly understood. In sporadic Burkitt lymphoma, EBV is detected in at most 20% of cases [6].

In our case, there is no immunoexpression of EBV/LMP1 on the tumor cells, indicating this is not associated with Epstein Barr virus infection. However, it is worth noting that EBV in situ hybridization method of viral RNA detection is better than EBV/LMP1 for detection of EBV virus association.

It has been suggested that there may be a hit and run mechanism involved by EBV infection. That mechanism is supported by recent evidence suggesting that EBV may play an initiating role in oncogenesis, but the viral genome is subsequently lost as neoplastic cells acquire stable (epi) genetic changes [11].

Benjamin Emmanuel et al stated that there is an association between the complexity of malaria infection and Burkitt lymphoma risk. Here in our case, the malaria ICT test was negative. [12].

In the typical or classic form of Burkitt lymphoma, neoplastic cells are characterized by their monotonous medium-sized appearance, featuring round nuclei and multiple peripheral nucleoli, surrounded by scanty cytoplasm with clear vacuoles. Mitotic figures are abundant, and at low-power microscopy, one can observe the presence of many tangible body macrophages containing phagocytosed apoptotic debris, creating the distinctive "starry sky" pattern [13]. Our case exhibits the same morphology as the classic form of Burkitt lymphoma. Unlike classic Burkitt lymphoma, the atypical form of Burkitt lymphoma shows more nuclear pleomorphism and has fewer, but more prominent nucleoli, although its immunophenotypic and molecular features are characteristic of typical Burkitt lymphoma. Some Burkitt lymphoma cases with plasmacytoid differentiation contain cells with eccentric nuclei, often featuring a single nucleolus [14].

Regarding the immunophenotype, Burkitt lymphoma tumor cells typically express B cell antigens such as CD19, CD20, CD22, CD79a, and PAX5, along with germinal center markers like CD10 and BCL6. CD38, CD77, and CD43 are also frequently positive. On the other hand, the neoplastic cells are usually negative for CD5, CD23, CD138, BCL2, and TdT. The immunophenotype may exhibit more variability in sporadic Burkitt lymphoma in older patients [15]. Almost all Burkitt lymphoma have strong expression of MYC protein in most cells. The proliferation rate is exceptionally high, with nearly 100% of the cells positive for Ki-67 [16].

In our case, positive expressions of CD20, CD10, BCL6, MUM1, CMYC, and a very high Ki67 index were observed. Notably, the expression of CMYC on the tumor cells is strong. Based on the

combined assessment of morphology and immunophenotyping, a diagnosis of mature B cell neoplasm, Burkitt lymphoma, was made.

The prognosis for Burkitt lymphoma is influenced by various factors including the extent of the disease, the patient's age, and the timing of the diagnosis [9].

For the initial stages of the disease (I, II), the prognosis is highly favorable, with event-free survival rates ranging from 85% to 100%. In contrast, for the advanced stages (III, IV), the survival rate ranges from 75% to 85% [17].

Burkitt lymphoma is an extremely rapidly growing tumor and is highly sensitive to chemotherapy. However, drug resistance can develop quickly. The real incidence of Burkitt lymphoma in Myanmar is unknown because of a lack of reported cases. This underscores the importance of early diagnosis and the need for prompt and appropriate management of the disease. The definite diagnosis was established through a thorough histopathological examination combined with immunohistochemistry. The use of extended immunohistochemical staining markers is still limited in Myanmar and that is the major challenge for the definite diagnosis of lymphoma entity based on definitions of World Health Organization. The drug anti-CD20 (Rituximab) is still expensive for some patients and this is also one of the limitation in the management of malignant B cell lymphoma.

Statement of ethics

The authors have no ethical conflicts to disclose. Informed consent was obtained from the patient.

Conflict of interest

The authors declare no conflict of interest.

Author contributions

WMO performed concept designing, laboratory diagnosis by histologic morphology, immunohistochemical study and confirmation of the case diagnosis. AA performed case investigation, case review and clinical management. NCA performed literature search and manuscript preparation.

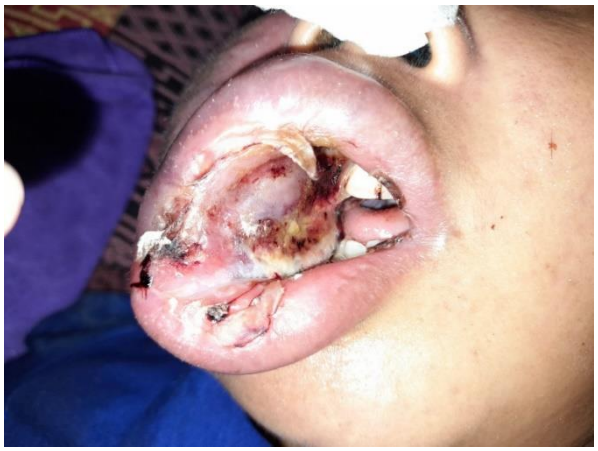

Figure 1. Large ulcerative and necrotic buccal mucosal mass occupying the right buccal cavity which limits mouth opening and swallowing.

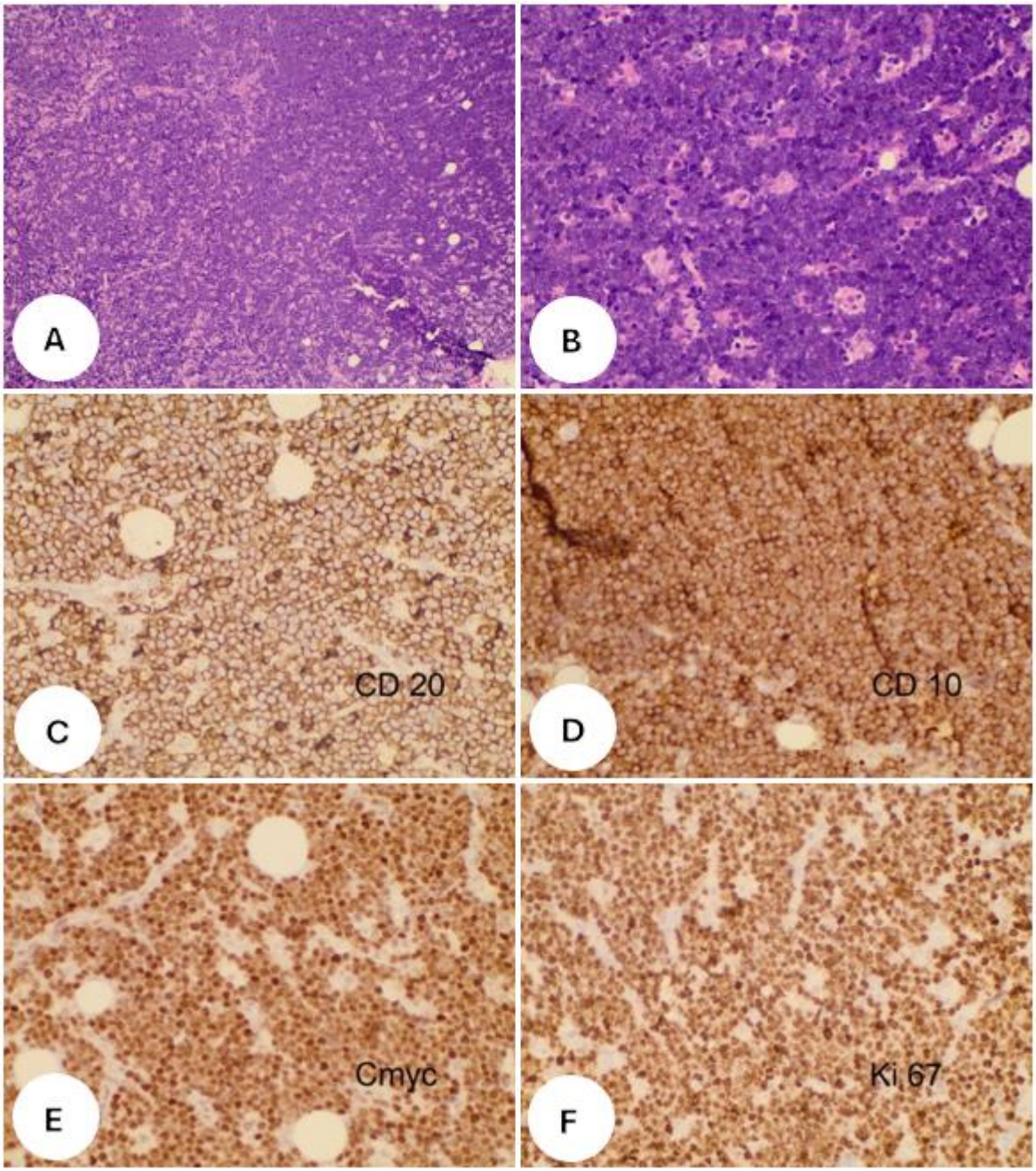

Figure 2 (A-F). Histologic section of buccal mucosa growth biopsy showing diffuse sheets of neoplastic medium sized lymphoid cells with numerous tangible body macrophages forming starry sky pattern, **A**. Lower power view 40x magnification and **B**. 400x magnification, Tumor cells are positive for **C**. CD20, **D**. CD10, and **E**. Cmyc. **F**. They have high Ki67 expression.

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