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Case Report

A RARE CASE OF BURKITT'S LYMPHOMA

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ABSTRACT

Aim: The aim of this paper is to report a rare case of sporadic Burkitt's lymphoma of the maxilla and its response to chemotherapy and emphasize the importance of early diagnosis in the treatment and prognosis.

Objective: The objective of this paper is to present a rare case of sporadic Burkitt's lymphoma. This type of Burkitt's lymphoma is seen in other parts of the world except equatorial Africa where Endemic form is found. Sporadic Burkitt's lymphoma usually presents in the abdominal organs, mostly in the ileocecal area, but, in our case, it occurred in the maxilla. Endemic type of Burkitt's lymphoma is reported to respond well to chemotherapy, whereas this form is not reported to behave so.

Results: The case reported herewith was referred at the earliest for chemotherapy and it responded well to the currently used CODOX-M/IVAC regimen. There has been no short term recurrence in this case for 6 months.

Conclusion: It is important to remember not to delay time in leisurely investigations in Burkitt's lymphoma cases, in order to achieve complete remission and a better prognosis.

Keywords: Burkitt's Lymphoma, Non-Endemic Burkitt's Lymphoma, Sporadic Burkitt's Lymphoma, Non-Hodgkin's Lymphoma, Malignant Tumors Of Maxilla.

INTRODUCTION

Burkitt's lymphoma (BL) is a highly aggressive form of B cell lymphoma that usually occurs in children and young adults and to a lesser extent in middle aged adults¹. Denis Burkitt's, a British surgeon, working in central Africa in Kampala, was the first to describe Burkitt's lymphoma in 1956. In 1964, Epstein along with his colleagues, identified a virus in culture cell lines of the tumor, from patients' samples obtained from Denis Burkitt's. The virus was later named Epstein-Barr virus (EBV) and was proposed to be oncogenic. Burkitt's lymphoma is estimated to account for only 1 to 5% of all non-Hodgkin lymphomas in adults. Burkitt's lymphoma may present at extranodal sites or as an acute leukemia. Childhood non-Hodgkin lymphomas are a heterogeneous group of malignancies that arises from T-cells, B-cells or natural killer (NK) lymphocytes. Burkitt's lymphoma is a B cell lymphoma genetically characterized by a chromosomal translocation that results in de-regulation of the c - MYC oncogene, and is the most common neoplastic disease of childhood in Africa. . It is reported to account for 30 to 50% of all childhood cancers in equatorial Africa².

Three clinical variants of BL are recognized: endemic BL, sporadic BL and immunodeficiency associated BL. Endemic BL is the form that occurs in African children, involving the mandible and other facial bones in 50% of the cases. It is invariably associated with Epstein Barr Virus infection. Malaria also appears an important co factor in oncogenesis. In contrast, the sporadic (western) variety is associated with Epstein Barr Virus in only 20% of cases².

Sporadic BL is seen worldwide, mainly in children and young adults involving the abdominal organs, mostly the ileocaecal area³. It accounts for 1-2% of lymphomas in adults and up to 40% of lymphomas in children in the United States of America and Western Europe.

Immunodeficiency-associated Burkitt's lymphoma occurs mainly in patients infected with HIV but also occurs in allograft recipients and individuals with congenital immunodeficiency. Burkitt's lymphoma accounts for 30-40% of non-Hodgkin's lymphoma in HIV positive patients². Burkitt's lymphoma represents the initial AIDS-defining illness³.

We are presenting herewith a rare case of BL of sporadic form occurring in the maxilla, in a patient who is neither HIV

positive nor with any history of congenital immunodeficiency or receiving allograft. The tumor responded well to chemotherapy.

CASE REPORT

A 12 year old boy reported to the Department of Oral Medicine and Radiology, Tamil Nadu Government Dental College and Hospital, Chennai with the chief complaints of pain and swelling on the left side of the face of duration of two months. The patient gave history of exfoliation of left upper back teeth. The swelling was initially small, asymptomatic and rapidly increased over a period of 15 days to attain the present size. There was no history of paresthesia or bleeding. Past medical, surgical and drug histories were non-contributory. The patient's family history was not significant.

Extra oral examination showed a solitary diffuse swelling (Fig.1 (A)) measuring approximately 6 x6 cm in size present on the left maxillary region extending superiorly till the infra orbital region, medially till ala of the nose, inferiorly till the commissure of the lip. Skin over the surface of the swelling appeared smooth, stretched and normal in color. Left side ala of the nose appeared elevated with a deviated nasal septum. On palpation, there was no warmth and the swelling was slightly tender. It was firm in consistency, not fluctuant, not compressible, not reducible, and no discharge was present. The swelling was fixed to the underlying structures.

Intra oral examination revealed that all the teeth were present except 23, 18,28,38,48 were not erupted. Grade 1 mobility was noted in 24. Soft tissue examination revealed a solitary, well-defined, lobulated, erythematous, mass measuring approximately 6 cm × 6 cm in the left maxillary region. The mass extended antero-posteriorly from 21 to 26 region involving the hard palate and buccal vestibule obliterating the buccal sulcus and covering the occlusal surface of the teeth.. The surface of the swelling appeared irregular (Fig.1(B)) and on palpation, the mass was non-tender, soft to firm in consistency. There was no compressibility, reducibility or fluctuation. The patient's oral hygiene was fair. There was generalized gingival bleeding on gentle probing.

History and clinical examination were suggestive of a malignant mesenchymal neoplasm arising from the maxilla. A differential diagnosis of Burkitt's lymphoma, Non- Hodgkin's lymphoma, fibro-sarcoma and angio-sarcoma was made.

Hematological investigations were carried out. Mild degree of microcytic, hypochromic anemia with atypical lymphocytes - 15%. Total WBC count was 4000cells/mm³. ESR was 45mm/hr. Hb% was 7.6gms/dl. Packed cell volume was 24%. Platelet count 1.3lakhs cells/mm³. Blood urea was 28 mgs%, Serum creatinine was 0.8mgs%

Maxillary occlusal view radiograph revealed discrete peri-apical radiolucencies in relation to 22, 23,24 with loss of lamina dura and widening of periodontal ligament space(Fig.2(A)).

Panoramic radiograph showed displaced left maxillary canine and interdental bone loss in 23, 24,25,26,27 region and soft tissue radiopacity involving the left maxillary antrum. Disruption of posterior wall of maxillary antrum was seen above the root apices of 26, 27(Fig.2 (B)).

CT scan revealed a homogeneous soft tissue density lesion involving left maxillary alveolus with destruction of buccal and palatal cortical plates and extension to the soft tissues (Fig.3(A)). The mass involved the entire left maxillary antrum with destruction of medial wall with extension to the left nasal cavity (Fig.3(B)) and destruction of some areas of the postero-lateral wall as seen in some of the axial sections (Fig.3(C)). These features were suggestive of a malignant neoplasm involving the left maxillary alveolus and maxillary antrum with extension to the soft tissues.

Incisional biopsy of the intraoral mass was performed. Histopathological sections showed monotonous proliferation of small, round, blue cells resembling lymphocytes and scattered macrophages within it resembling "starry- sky" appearance, consistent with the classical picture of Burkitt's lymphoma (BL)(Fig.4). The histopathology report was that of Burkitt's lymphoma (BL).

A final diagnosis of Burkitt's lymphoma (BL) was considered based on the clinical, hematologic, radiographic, histopathologic investigations.

The patient was referred to Medical Oncology Department, Government General Hospital, where 4 cycles of chemotherapy was instituted. Patient was administered **CODOX-M** protocol (cycle 1&3) and **IVAC** protocol (cycle 2&4). At the end of four cycles of chemotherapy, the swelling showed complete regression both intra (Fig.5 (A)) and extra-orally (Fig.5 (B)).

DISCUSSION

Burkitt's lymphoma (BL) belongs to the extended group of Non-Hodgkin's lymphoma (NHL) which is a solid tumor of lymphoid organs. NHLs are clonal malignancies of the multiple cellular components of the normal lymph node, spleen or thymus. Burkitt's lymphoma arises as a clonal transformation that occurs at a particular stage of normal B cell differentiation during antigenic stimulation⁴. It is composed of monomorphic medium-sized transformed cells with basophilic cytoplasm and shows a high mitotic rate. Translocation of MYC oncogene is considered to be a hallmark of Burkitt's lymphoma². 80% of cases of BL carry translocations between c-myc proto-oncogene and IgH gene t (8; 14) (q24.1; q32.3)⁴.

The aetiological factors of Burkitt's lymphoma differ depending on the clinical variants as described in the World Health Organization (WHO) classification. However, the major and common aetiological factors are closely and strongly linked with geographical location/climate, immunosuppression and chromosomal abnormalities⁴. The African type (endemic) is commonly found in the malaria belt of Africa and Papua New Guinea. It is associated with low socioeconomic status, undernourishment, malaria holoendemicity and Epstein Barr virus (EBV) infection. The actual age range of occurrence of endemic Burkitt's is 2-16 years but the most common age of occurrence is 4-7 years with a male: female ratio of 2:1⁴. Non-endemic or sporadic Burkitt's lymphoma seen in other parts of the world accounts for 1-2% of lymphoma in adults and up to 40% of lymphoma in the children in the US and Western Europe⁴.

The incidence of BL correlates with the incidence of malaria and with parasitaemia rates. The incidence of BL is less in individuals with sickle cell trait which also protects against malaria. There is also evidence for seasonal variation and for time-space clustering of BL cases⁴.

The clinical presentation of Burkitt's lymphoma varies with depending on the specific variant. Endemic Burkitt's lymphoma presents as a rapidly growing solid tumor or tumors, which are predominantly extra nodal. The clinical history is short and very few patients have symptoms of greater than three months duration. The site of presentation commonly involves the bones of the jaw and other facial bones, as well as the kidneys, gastrointestinal tract, ovaries, breast, and other extra nodal sites. Endemic Burkitt's lymphoma has exquisite sensitivity to chemotherapy unlike sporadic and immunodeficiency-associated types. Short-duration, high-intensity chemotherapy yields excellent survival in children².

Non-endemic Burkitt's lymphomas are believed to be histologically identical to the endemic variety, found predominantly in the equatorial Africa¹.

This form tends to present in the lymphoid tissues of the gut, often presenting as masses in the Waldeyer's ring or the terminal ileum or even with massive abdominal involvement. Bone marrow involvement is common in progressive disease. The most commonly involved sites are the abdomen (especially the ileocecal region), the ovaries, kidneys, omentum and Waldeyer's ring. Lymph node involvement is more common in adults. Children usually present with extra-nodal involvement. In the present case, this sporadic form of Burkitt's lymphoma has occurred in an uncommon site, which is the maxilla¹.

The usual clinical presentation of BL includes:

Swelling of the mandible or maxillae (1-4 quadrants), (which is the commonest presentation in Africa), with loosening of the child's molar or premolar tooth, which is the earliest sign. In the present case there was mobility of left maxillary first premolar. Other manifestations include proptosis, intra-abdominal tumors, especially retroperitoneal lymph nodes or ovaries, extradural lesion causing compression of the spinal cord and paraplegia, less commonly, enlargement of the parotid, thyroid, kidneys, lymph nodes and bilaterally the breasts, however, the child's general condition is usually remarkably good. Metastatic neuroblastoma, Ewing's tumor, Osteolytic osteosarcoma and Non-Hodgkin's lymphoma should be included in the differential diagnosis⁵.

Burkitt's lymphoma is an aggressive tumor that requires a quick and prompt diagnosis and more often Fine Needle Aspiration Cytology (FNAC) is required. Biopsy may also be used in confirmation of diagnosis⁴.

Histopathological features are characterized by a Starry Sky appearance indicating sheets of monomorphic small non cleaved cell with bluish cytoplasm interspersed by cellular debris laden macrophages.

Immunophenotyping shows that the Burkitt's cell is Tdt -ve, but CD10, CD19, CD20, CD22, CD24, CD 37, CD 38 and SIgM positive. In most African BL cases, the cells are CD21 positive, but negative in American BL cases.

Burkitt's Lymphoma is the fastest growing tumor characterized by explosive growth with a doubling time of 24 hours. Hence, there should not be delay in leisurely workup; treatment must be commenced within 24-48 hours. The treatment is divided into: Supportive and Definitive.

Supportive treatment is given to prevent/correct tumor lysis syndrome. Generous hydration is mandatory and Allopurinol must be given at a dose of 10-20 mg/kg daily.

The definitive, mainstay of treatment is Chemotherapy. All reported successful protocols include cyclophosphamide in doses of at least 1 g/m² and either high or intermediate dose methotrexate. Most also include anthracycline. Short duration, high intensity chemotherapy, often combined with CNS prophylaxis yields excellent survival in children. In localized disease a 5 year survival rate of >90%, is achievable.

The more recent, very intensive, highly effective, alternating non- cross resistant regimen developed by Magrath et al is CODOX-M/IVAC regimen. It includes C=cyclophosphamide, O=oncovin/vincristine, Dox=Doxorubicin and M for High dose methotrexate while IVAC → Ifosfomide, Etoposide, Cytosar (high Dose) + IT therapy. In our case, the CODOX-M/IVAC regimen was followed and the tumor showed complete remission clinically

The combination chemotherapy is said to give a high cure rate. However associated toxicities include frequent myelosuppression, severe mucositis, nausea and vomiting, neuropathy and treatment related deaths. Complications include tumor lysis syndrome and hemorrhagic cystitis.

Modern combination chemotherapy results in a 3 year survival rate of 85-100% of those with early stage disease and 75-85% of those with advanced disease without the need for treatment. It is a curable malignancy and if there is no relapse a year after combination chemotherapy, patient has a 90% chance of surviving indefinitely. Prognosis with Cyclophosphamide alone is less favourable.

Relapse in BL may be early or late. In early relapse, tumor regrowth is usually in the same site and occurs at less than 3months post treatment. In our case, the patient was followed up for 6 months after 4 cycles of chemotherapy and till date there has not been any relapse. Late relapse usually arises from a previously uninvolved site and likely to respond to the same agents. It occurs at greater than 3 months post treatment⁴.

CONCLUSION

Sporadic Burkitt's lymphoma is somewhat uncommon in the maxilla, which is a typical site for the Endemic form. Burkitt's lymphoma is an extremely rapidly growing tumor. It has a high sensitivity to chemotherapy but drug resistance can develop quickly. These features necessitate prompt diagnosis and initiation of appropriate therapy essential for an optimal outcome. Prompt diagnosis and treatment may lead to an excellent survival rate.

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IMAGES and LEGEND FOR THE ARTICLE- A RARE CASE OF BURKITT'S LYMPHOMA



Figure 1

Figure 1A : Depiction of extra-oral swelling

Figure 1B : Intra oral view of the growth



Figure 2

Figure 2A: Maxillary occlusal radiograph showing osteolytic areas in relation to the roots of 22,23, 24,25 with loss of lamina dura in relation to 23,24,25 and widening of PDL space in relation to 22.

Figure 2B: Panoramic radiograph showing osteolytic area extending from 22 to 27 region with loss of lamina dura and distal displacement of the root of 23.

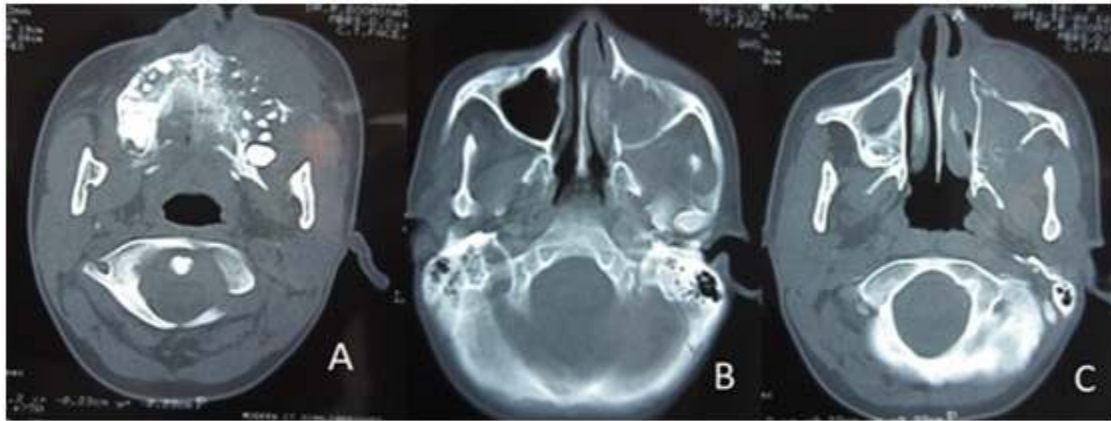


Figure 3

Figure 3A: Axial section of CT scan showing soft tissue density lesion involving left maxillary alveolus with destruction of buccal and palatal cortical plates and extension to the soft tissues.

Figure 3B : Axial section of CT scan showing the mass involving the entire left maxillary antrum with destruction of medial wall with extension to the left nasal cavity.

Figure 3C: Axial section of CT scan showing destruction of some areas of the postero-lateral wall of the maxillary antrum.

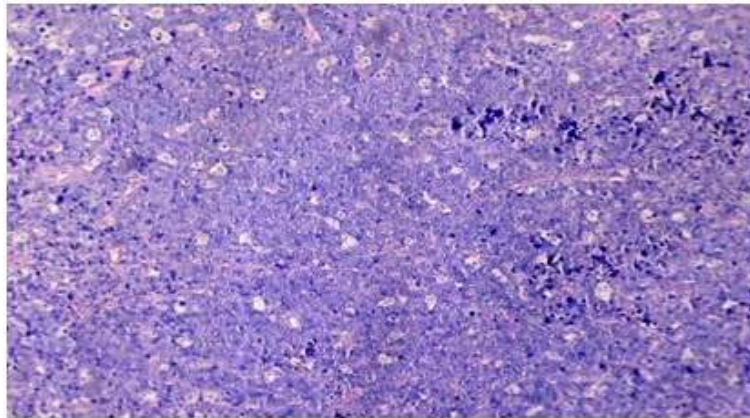


Fig.4: Photomicrograph showing starry sky appearance.

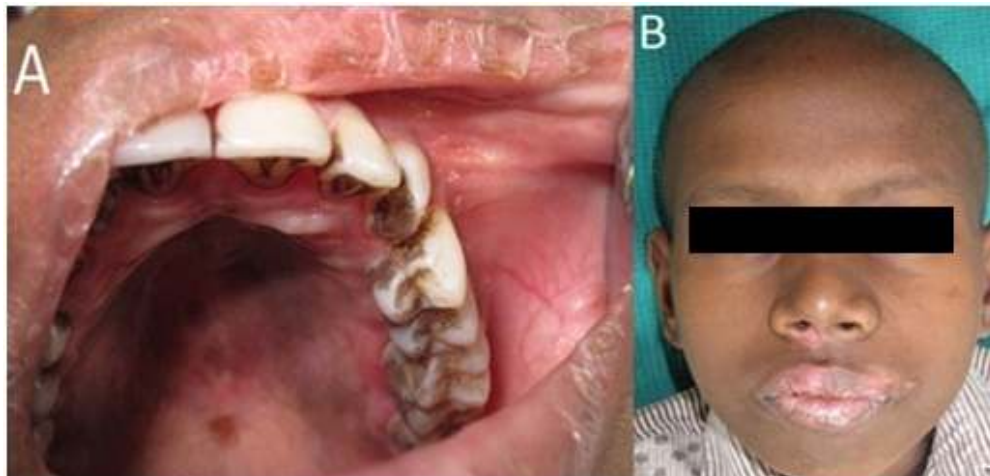


Figure 5

Fig 5A: Post operative intra oral photograph.

Fig 5B: Post operative extra oral photograph.

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