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Case Report

Burkitt Lymphoma Involving Bilateral Maxilla and Mandible: A Rare Presentation

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Abstract

A 4-year-old boy is reported with Burkitt lymphoma involving bilateral maxilla and mandible. The initial clinical diagnosis was dentoalveolar abscess since the patient had multiple carious teeth in relation to jaw swellings. The incisional biopsy was performed and histopathological analysis, including immunohistochemistry, confirmed Burkitt's lymphoma. The patient was referred to National Cancer Institute for further management. The occurrence of Burkitt lymphoma involving all four quadrants of the maxilla and mandible is unusual.

Keywords: Burkitt Lymphoma; Maxilla and Mandible Involvement; Child

Introduction

In 1958, Denis Burkitt, an Irish surgeon, first described Burkitt Lymphoma (BL) in African children presenting with rapidly growing jaw and abdominal tumors [1,2]. It is highly aggressive, B cell lymphoma, which is categorized under non-Hodgkin lymphoma. According to WHO classification, there are three epidemiological variants of Burkitt lymphoma. These are 'Endemic' (associated with malaria endemicity), 'Sporadic', and 'Immunodeficiency-related' [2]. Morphology, Immunophenotype, and Genetic features are similar in the above types and most of the cases are associated with Epstein Barr Virus (EBV). It is the first human tumor that is associated with a virus, and it is the fastest growing human tumor [2,3]. Early treatment provides a better prognosis [3].

Case Report

Clinical features

A 4year old boy was brought by parents to the Oral and Maxillo-Facial (OMF) Unit, District General Hospital, Kalutara, complaining of gum swelling and pain in upper and lower jaws for six months duration which had increased with time. There were some carious teeth which were painful. Since the child was complaining of pain in relation to gingival swelling, the parents consulted a general practitioner one month ago. Since the condition was unresponsive to ongoing treatments, the patient presented to the OMF unit. The patient did not have significant pain in this region at the time of examination, but there was bleeding from the gums when brushing and child had been incorporative for a proper brushing. There was no history of low-grade fever and recent rapid weight loss.

The patient didn't have any significant past medical history and he was not on regular long-term medication except the medication given by general practitioner. There was no allergic history to drugs. Previously he has not undergone any surgeries under general or local anesthesia.

General examination showed that the child was active and corporative but still in discomfort having meals due to gingival hyperplasia. On examination of the oral cavity, all primary teeth and first permanent molars were present except the lower left quadrant. Gingival swellings were present in relation to D and E teeth bilaterally in relation to upper and lower posterior quadrants. Lesions were firm, hyperemic, inflamed and having spontaneous bleeding. All Ds and Es were grossly carious. There was a slight mobility of maxilla at the level of le-fort I. The remaining teeth were not mobile (Figures 1-3).

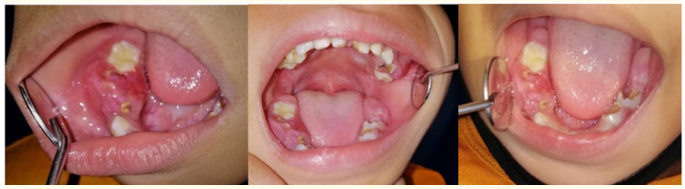


Figure 1-3: Gingival swelling present in all four quadrants with grossly carious D and E.

Bilateral cervical lymph nodes were palpable in levels IA and IB. Consistency of lymph nodes were soft, non-tender and they were mobile; which gave the impression of reactive nodes.

The clinical differential diagnosis were Hereditary gingival fibromatosis, leukemic deposits, lymphomas and Granulomatosis with polyangiitis.

Following a proper clinical examination, the patient underwent serological investigations (Full blood count, Liver Function Test, Renal Function Test and PT/INR) and imaging. Plain radiographs of the skull and cervical spine, and CECT of head and neck were arranged.

Full blood count showed high counts of white blood cells and Lymphocytes. Blood picture was normal. Among the liver enzymes, ALP and AST was significantly high. Serum creatinine level was low.

The CECT finding was as follows, Infiltrative soft tissue mass with bony destruction involving bilateral maxilla and mandible. It is associated with waylayer's ring/adenoid enlargement.

The CECT features were favorable to Burkitt lymphoma or Acute Lymphoblastic Lymphoma which was involving both the maxilla and mandible associated with adenoid enlargement.

There was no evidence of cerebral metastasis. There were no radiological abnormalities observed in the plain radiograph of the cervical spine and skull.

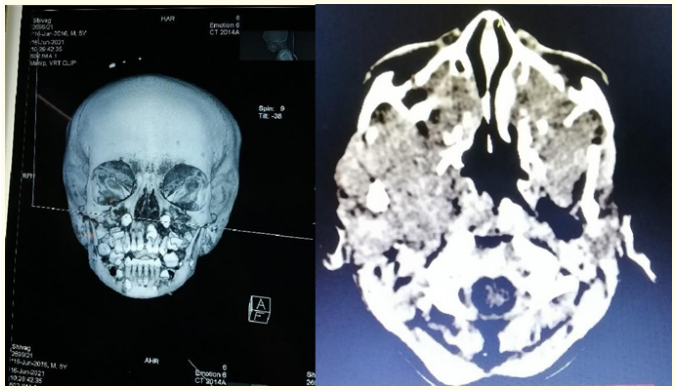


Figure 4

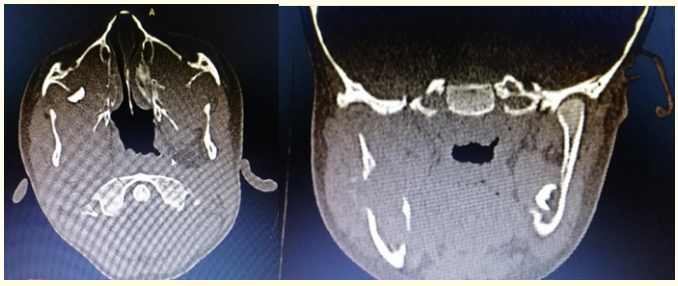


Figure 5

With the provisional differential diagnoses, an incisional biopsy from a gingival overgrowth of both upper and lower quadrants and removal of septic roots were planned under general anesthesia. The patient underwent surgery following pre-operative anesthetic evaluation. The postoperative course was uneventful and the pa-

tient was discharged on third post operative day, with oral antibiotics and analgesics.

Histologic findings

Following Histological evaluation of soft tissue specimens, it showed diffuse infiltrate of atypical lymphocytes of intermediate size, these lymphoid cells contain irregular enlarged nuclei with prominent nucleoli. The cytoplasm was present in scant to moderate amounts. There were numerous cells undergoing apoptosis. Some areas showed "starry sky" appearance. Frequent mitoses were present. There were some entrapped bone fragments too. The possibilities were acute lymphoblastic lymphoma or Burkitt lymphoma.

Further immunohistochemical studies were carried out to arrive at a definitive diagnosis.

CD 20	Positive
CD 10	Positive
BCL 6	Positive
CD 3	Negative
CD 5	Negative
BCL 2	Negative
Tdt	Negative
CD 34	Negative
CD 99	Negative
Ki 67	100%

Table 1: Types of immune stains carried out and results.

With the above results the definitive diagnosis was established as Burkitt lymphoma. Bone marrow aspiration and Trephine Biopsy was arranged for further evaluation and staging of the disease. There was no bone marrow infiltration.

Treatment plan

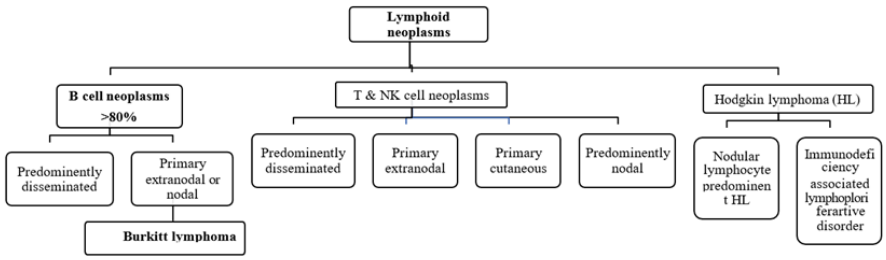
Following investigations were completed, the case was discussed among experts. Then patient was sent to National Cancer Institute for further management.

Discussion

Malignancies of oral and maxillofacial region are very rare in pediatric population. The incidence is ranging approximately from 0.5% - to 6% [4]. The main affected anatomical sites are the oropharynx(38.18%), followed by salivary glands (30.91%), maxillofacial bone (20%), and oral cavity (10.91%)(4).The most prevalent pediatric cancers in developing countries are Leukemia (18-41%), Lymphoma (13-24%), and Central Nervous System Tumors (7-17%) [3].

In 4th edition of WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, lymphoid neoplasms have been classified in to 3 major categories [5].

Lymphoma classification mainly based on morphologic features, immunophenotypic features and genetic characteristics in accordance with the clinical features. So, lymphoma can be classified broadly into Non-Hodgkin Lymphoma (NHL) and Hodgkin Lymphoma (HL). Burkitt lymphoma comes under the category of NHL [5].



NHL shows extra nodal involvement in 20% - 30% of cases. The most common extra nodal sites are the gastrointestinal tract, central nervous system, bone, skin and non-lymphatic structures of head and neck. The oral cavity as a primary site constitutes only 2% of all extra nodal NHL [6,7].

	Endemic type	Sporadic type	Immunodeficiency type
Epidemiology	Regions where malaria endemicity is present, Africa and Papua New Guinea	Predominantly north America and northern and East Europe, EastAsia, no special climate or geographical links	Most often associated with HIV
Association to EBV	>90%	Rarely associated with EBV	<40% US and European cases associated with EBV
Age	Peak incidence is 6yrs	Peak incidence in 3-12 years Median age – 30yrs 1-2% adult lymphomas 30-40% of NHL in childhood	Median age – 44yrs
Gender predilection	Twice common in boys	3.5 times common in boys than girls	Associated with higher CD4 counts >100/mm3
Incidence	5-10: 100000	2 - 3:1000000	22:100000

Table 2: Tabulates the noticeable features of different types of Burkitt lymphoma [1,2,8].

	Endemic type	Sporadic type	Immunodeficiency type
Common site of presentation	Jaw involvement is more frequent, common in young children (3-7 yrs.) 2nd commonest is abdomen	Abdomen (60 - 80%) 2nd commonest is head and neck (25%)	Nodal presentation is more common
Associated symptoms	Jaw involvement- periorbital swelling sudden paraplegia and incontinence Bone marrow involvement is common in recurrent or treatment resistant disease.	Abdomen - abdominal pain (25% have ileocecal disease) Head and neck - lymphadenopathy, involve nasal, oropharynx, tonsils OR sinuses Bone marrow involvement (15%) - bone pain	Bone marrow and CNS is also involved
Genomics	MYC mutation 100%; ID3 and/or TCF3 mutations 40%; CCND mutations 1.8%	MYC mutation 100%; ID3 and/or TCF3 mutations 70%; CCND mutations 38%	MYC mutation 100%; ID3 and/or TCF3 mutations 67%; CCND mutations 67%

Table 3

Our patient was not related to any malaria endemic area and HIV screening was negative. We were not able to arrange EBV screening due to limited laboratory facilities.

Oral signs of Burkitt lymphoma are gingival enlargement, swelling of alveolar regions and jaw, loosening of teeth, premature shedding of primary molars and premature eruption of permanent molars [9]. Some cases have been reported with nasal obstruction, unilateral tonsillar enlargement, cervical lymphadenopathy, otitis media and hypo nasal speech [10]. In the present case, gingival hyperplasia in all four quadrants was the main clinical presentation of the disease. In addition, there was significant mobility of maxilla which was a rare presentation.

The plain radiographs like Intra Oral Peri Apical (IOPA) views, Dental Panoramic Tomogram (DPT) and OM views can be arranged as a basic radiologic investigation. In plain radiographs, destruction of lamina dura around the tooth can be seen. With the tumor progression, the teeth and tooth buds are displaced and multiple radiolucencies that coalesce and gives the "teeth floating in air "appearance. When the tumor enlarge, it infiltrate subperiosteally, and induce reactive bone formation. This is described radiologically as sunray spicules. Root resorption is not a feature associated with this tumors [11]. However, in some articles, it has been mentioned that plain radiographs have limited usefulness when the lesions located laterally, because of super imposition of other structures. This is mostly related to maxilla [12].

To assess the disease extent the patient should undergo CT and MRI. CT is widely available and superior for imaging of bone. On MRI, enlarged lymph nodes and soft tissue masses seen as homogenous enhancements without central necrosis. In sporadic form of Burkitt lymphoma, waldeyer ring is the most common site of extra nodal disease. It doesn't show any skull base erosions but it fills the adjacent spaces e.g.- nasal cavity. The brain involvement is very rare in sporadic form. In immunodeficiency type of BL, involvement of the central nervous system and calvarial bone marrow may be observed [13].

Radiological changes can be seen before significant clinical findings in endemic cases [11] and it commonly presents with bone erosion around the jaw and orbit? [13].

Following successful chemotherapy, with the clinical regression of the tumor, there is radiological evidence of formation of lamina dura and reformation of normal architecture of the bone [12].

The PET scan, bone marrow aspiration and CSF evaluation will help to assess the whole-body involvement [8].

In this patient, occipitomental view didn't show any significant finding. Contrast Enhanced Computed Tomography (CECT) of head and neckshowed soft tissue mass infiltrating both maxilla and mandible bilaterally and also involving waldeyers ring. There was no involvement of brain. This gave a clue which was more in favor of Burkitt lymphoma. Other radiological differential diagnosis was acute lymphoblastic leukemia.

The low power magnification of hematoxylin and eosin stain showes classic "starry sky" appearance which is a classic feature of Burkitt lymphoma. Starry sky appearance is due to scattered tangible body laden macrophages, which contain apoptotic tumor cells [2,10,14]. Present case showed above features in histology.

As Burkitt lymphoma biologically derived from germinal center B cell, the cells are positive for CD 10, CD 20, CD 45, CD 79a and BCL 6. The cells are negative for BCL 2 and Terminal deoxynucleotidyl transferase (Tdt). Growth fraction is measured by Ki67. It approaches 100% [1]. In our case table 1 shows the types of immune stains we carried out to arrive at diagnosis. Results of BCL 6, BCL 2, CD 20 and Ki 67 were compatible with Burkitt lymphoma.

Bone marrow aspiration and Trephine biopsy were carried out to find any bone marrow involvement. According to the literature percentage of Bone Marrow involvement in Burkitt lymphoma is >40% [15]. But some authors say it is around 16% in pediatric cases and around 65% in adult cases [16]. The present case didn't show any bone marrow involvement.

There are several staging systems to stage non-Hodgkin lymphoma eg- Ann Arbor staging system, St Jude staging system, Murphy staging system and newly proposed International pediatric Non- Hodgkin lymphoma staging system [17].

According to the newly proposed International pediatric non-Hodgkin lymphoma staging system, our patient is having stage 1

disease, because he showed involvement of jaw bones only. There were no involvement of central nervous system, chest, abdomen, long bones or bone marrow.

Patient was transferred to specialized cancer treatment center for further management and he is currently undergoing chemotherapy.

Conclusion

The occurrence of Burkitt lymphoma in head and neck is rare. The involvement of bilateral maxilla and mandible is even rarer. The dental surgeons may be the first medical contact to see such cases presenting with gingival hyperplasia as in this case report. Therefore, the dental surgeons must be well aware and vigilant on investigating and managing this kind of cases due to the fact that Burkitt lymphoma carries good prognosis if it is identified early and treated promptly.

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