Burkitt’s lymphoma of the base of the tongue: A case report and review of the literature

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Abstract
Burkitt’s lymphoma is a highly aggressive, mature B cell non-Hodgkin’s lymphoma that is rare outside Africa. We report a case of Burkitt’s lymphoma presenting as a rapidly expanding tongue-base mass that caused airway obstruction in an 80-year-old Palestinian man living in California. According to our review of the literature, this is only the third reported case of Burkitt’s lymphoma arising in the base of the tongue. We also discuss the incidence, epidemiology, genetics, prognosis, and treatment of this malignancy. Because Burkitt’s lymphoma is one of the fastest-growing tumors in humans, rapid diagnosis and treatment are important. Treatment involves brief-duration, high-intensity chemotherapy and central nervous system prophylaxis. It is important for the otolaryngologist to recognize this disease and to understand the steps necessary to treat this aggressive tumor.

Case report
An 80-year-old Palestinian man presented to our clinic with a 3-month history of a muffled voice, odynophagia, cough, and snoring. Physical examination revealed that a large mass had arisen from the right side of the base of the tongue; the mass crossed the midline and extended to the vallecula. On computed tomography (CT) of the tongue base, the mass measured 4.3 × 2.4 × 2.8 cm (figure 1, A).

The patient underwent local tracheotomy and endoscopy (figure 2) with biopsies. Pathologic examination of the biopsy specimens revealed a diffuse monomorphous population of small and medium-size lymphocytes with round to oval nuclei, prominent basophilic nucleoli, coarse chromatin, and a thick nuclear membrane; abundant mitotic figures and tingible-body macrophages were easily identified, giving rise to the classic “starry-sky” appearance (figure 3). A moderate amount of amphophilic cytoplasm was identifiable. Flow cytometry demonstrated expression of CD10, CD19, and CD20 antigens with monoclonal restriction of the lambda light chain. Tumor staging was performed on the basis of findings on lumbar puncture, bone marrow biopsy, liver function tests, chest x-ray, positron-emission tomography (PET), and CT of the head, chest, abdomen, and pelvis. All staging workups were negative (including a normal lactate dehydrogenase level), and imaging confirmed that the lymphoma was confined to the area of the tongue base. The patient was found to have microcytic anemia, and further workup revealed a beta-thalassemia trait.

The patient was treated with a modification of the Stanford regimen plus rituximab for a total of 3 cycles of chemotherapy. Involved-field radiation was planned.

The first cycle of chemotherapy involved the administration of R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) in addition to both intravenous and intrathecal methotrexate. Despite growth-factor support, the patient developed febrile neutropenia and was admitted. The second cycle of therapy consisted of R-CHOP and intrathecal methotrexate, and the patient again experienced febrile neutropenia despite growth-factor

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support. The third cycle consisted of R-CHOP in lower doses; the intrathecal methotrexate was omitted. Again, despite the dose reduction and the omission of intrathecal chemotherapy, the patient experienced febrile neutropenia.

Following the third cycle, PET and CT (figure 1, B) of the neck demonstrated that the tumor had resolved completely. Therefore, the decision was made to cancel the involved-field radiation.

At the 2½-year follow-up, the patient exhibited no signs of residual lymphoma.

Discussion
Burkitt’s lymphoma is the fastest-dividing lymphoma, with 100% of cells being in a cell cycle at any given time; it has been considered one of the most rapidly growing tumors in humans. The tumor was first described as a neoplasm arising in the jaws of African schoolchildren. Subsequently, a neoplasm of identical histology was identified in the United States. In 1994, the International Lymphoma Study Group published the revised European-American lymphoma (REAL) classification system for lymphoid neoplasms. In this system, lymphomas were classified according to morphologic appearance, immunophenotype, and genetic features. In 2001, the REAL classification system was updated by the World Health Organization, which classified Burkitt’s lymphoma together with Burkitt’s leukemia as a mature (peripheral) B cell neoplasm. Previous classification systems had also included “Burkitt’s-like lymphoma,” but this entity was subsequently considered to be the same as Burkitt’s lymphoma.

Morphologically, Burkitt’s lymphoma cells have round nuclei with clumped nucleoli and an abundant basophilic cytoplasm that contains lipid vacuoles. The tumor has a diffuse pattern of infiltration. The starry-sky appearance under low magnification is caused by the presence of macrophages that contain ingested apoptotic tumor cells. Burkitt’s lymphoma cells express surface IgM, bcl-6, CD10, CD19, CD20, CD22, and CD79a; they lack CD5, CD23, and TdT.

Burkitt’s lymphoma arises from activation of the c-myc oncogene, most often as a consequence of a chromosomal

![Figure 1. A: The tumor is seen on pretreatment contrast-enhanced CT. B: Post-treatment CT demonstrates that the tumor has resolved completely.](image1)

![Figure 2. Endoscopic views show the tumor in the base of the tongue.](image2)
translocation between chromosome 8 and chromosome 14, 2, or 22; in 80% of cases, it is translocation (8;14). In the endemic and sporadic variants, the location of this translocation is different. Epstein-Barr virus (EBV) is strongly associated with the endemic variant, being present in 80 to 90% of tumor cells. EBV is less strongly associated with the sporadic variant, being present in only 15 to 20% of tumor cells. It is not known what role EBV plays in the pathogenesis of Burkitt’s lymphoma. EBV nuclear antigen, a viral protein consistently expressed in Burkitt’s lymphoma cells, has been shown to be required for the survival of tumor cells.

Endemic Burkitt’s lymphoma is commonly seen in equatorial Africa, where it accounts for 50 to 70% of all pediatric malignancies. The mean age at presentation is 7 years. The disease frequently involves the jaw and kidney; jaw involvement occurs in approximately 50% of cases. The ileum, cecum, ovary, and breast may also be involved, and invasion of the cerebrospinal fluid is common.

Nonendemic Burkitt’s lymphoma accounts for 1 to 2% of all adult lymphomas in Western Europe and the United States. The mean age at presentation is 11 years. Most of these tumors (56%) arise in the abdomen. Involvement of extranodal sites in the head and neck occurs in fewer than 25% of cases. Jaw involvement occurs in only 7% of cases. Bone marrow and central nervous system (CNS) involvement occurs in 30 to 38% and 13 to 17% of adult cases, respectively.

Only 2 cases of Burkitt’s lymphoma of the tongue base have been previously reported in the English-language literature. Other sites of involvement in the head and neck include the parapharyngeal space, tonsil, mandible, maxilla, skull, maxillary sinus, nasopharynx, mastoid, orbit, and nasal cavity. In a study of 80 children with Burkitt’s lymphoma, 31 (38.8%) had involvement of the head and neck region, including 10 (12.5%) who had primary jaw tumors, a finding that is consistent with other reports of sporadic Burkitt’s lymphoma.

Immunodeficiency-associated Burkitt’s lymphoma generally occurs in patients with human immunodeficiency virus (HIV) infection. In a series of 399 patients with acquired immunodeficiency syndrome who presented with head and neck manifestations, 8% had Burkitt’s lymphoma as a rapidly enlarging neck mass. Unlike other HIV-associated lymphomas, however, Burkitt’s lymphoma tends to occur in patients whose CD4 counts exceed 200 cells/mm³. These patients—like those with sporadic Burkitt’s lymphoma—typically present with extranodal disease that most commonly involves the abdomen.

The Murphy/St. Jude’s staging system is commonly used to stage non-Hodgkin’s lymphomas in children (figure 4). In adults, the Ann Arbor staging system, which was originally developed for Hodgkin’s lymphomas, is often used. The usefulness of the Ann Arbor system is limited by the fact that Hodgkin’s lymphoma and non-Hodgkin’s lymphoma have different patterns of spread. For this reason, the Murphy/St. Jude’s system is sometimes used in...
adult studies of Burkitt’s lymphoma. In the past, Burkitt’s lymphoma was treated with a prolonged regimen of high-intensity chemotherapy—including induction, consolidation, and maintenance phases—similar to those used for patients with acute lymphoblastic leukemia. But this regimen was ineffective, and it gave way to a regimen of high-intensity chemotherapy over a short duration. The chemotherapeutic agents include cyclophosphamide, doxorubicin, vincristine, methotrexate, and cytarabine. Current therapy does not involve routine debulking surgery because the chemotherapy itself is effective and because early surgery is associated with an increase in complications.

In children with advanced-stage Burkitt’s lymphoma, 2-year disease-free survival ranges from 75 to 89%. In adults, who have a higher incidence of CNS and bone marrow involvement, treatment also includes intrathecal chemotherapy. With this treatment, 65 to 100% of adults have achieved a complete response, and 47 to 86% of patients remained in remission after treatment. Many of the chemotherapeutic regimens currently used in adults are based on principles previously developed for the treatment of childhood Burkitt’s lymphoma. The addition of rituximab (an anti-CD20 monoclonal antibody) to chemotherapy has greatly improved the outcome of treatment for non-Hodgkin’s lymphoma. Similarly, our patient was treated with 3 cycles of R-CHOP, with and without intrathecal methotrexate, and he experienced a complete response to therapy.

Lymphoma is two to four times more common in patients of Middle Eastern descent than others, and extranodal manifestations are more common, as well. Several series have examined the incidence of Burkitt’s lymphoma in the Middle East. In these series, patients’ ages ranged from 2 to 50 years, and median ages ranged from 7 to 15 years. In the Middle East, Burkitt’s lymphoma has shown characteristics intermediate between the American and African types in both the age at presentation and the site of involvement. Our patient was an adult of Palestinian descent, and his tumor was negative for EBV, which made his tumor more similar to the endemic variant.

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doubt, complete detachment with formal canthopexy is the treatment of choice because it will obviate the need for repeat surgery.

References