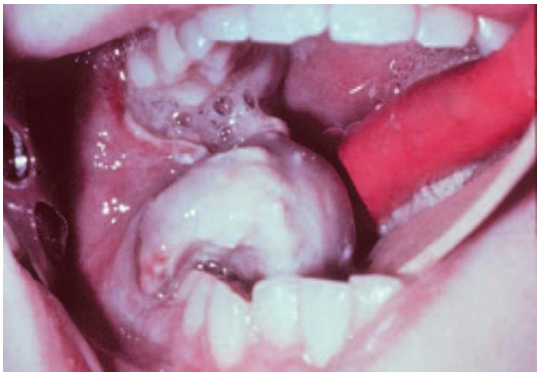
Malignant tumors of the bone

Ewing's Sarcoma

Ewing's sarcoma (the name come from American pathologist James Ewing who first described the tumor in 1921). The pathogenesis of tumor is unknown, the cell of origin is uncertain. Ewing's sarcoma has a common chromosome translocation t(11;22)(q24;q12) in approximately 85% of cases and t(21;22)(q22;q12), found in 10% to 15% of cases. Ewing's sarcoma accounts for approximately 6% of all malignant bone tumors mostly involve the bones of the lower extremity or pelvis. When the jaws are involved, the predilection is for the ramus of the mandible, with few cases reported in the maxilla. Because Ewing's sarcoma has a propensity to metastasize to other bones, the possibility that jawbone involvement represents metastatic disease from another skeletal site should always be considered.

Clinical Features

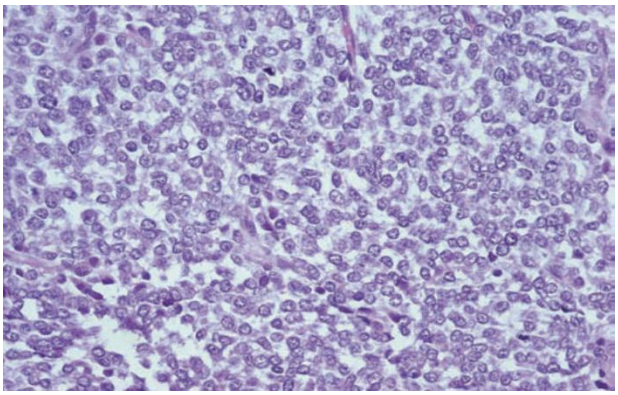
Ewing's sarcoma is the second most common sarcoma in bone and soft tissue in children. Ninety percent of Ewing's sarcomas occur between the ages of 5 and 30 years, and more than 60% affect males. The mean age of occurrence for primary tumors involving bones of the head and neck is 11 years. Pain and swelling are the most common presenting symptoms. Involvement of the mandible or maxilla may result in facial deformity, destruction of alveolar bone with loosening of teeth, and mucosal ulcers. A significant number of patients also have a soft tissue mass.



Radiographic findings in the jaws are nonspecific and may simulate an infectious or malignant process. The most characteristic appearance is that of a moth-eaten destructive radiolucency of the medullary bone and erosion of the cortex with expansion. A variable periosteal onion-skin reaction also may be seen.

Histopathology

Ewing's sarcoma characterized microscopically by proliferation of uniform, closely packed cells that may be compartmentalized by fibrous bands. The round to oval nuclei have finely dispersed chromatin and inconspicuous nucleoli. The cytoplasm stains with the periodic acid– Schiff stain but is digested with diastase, indicating the presence of glycogen. Although glycogen staining by this technique is helpful in diagnosis, some otherwise histologically acceptable cases of Ewing's sarcoma have yielded negative results. In addition, other tumors that mimic Ewing's sarcoma may contain glycogen. CD99 is highly expressed in most Ewing's sarcomas and PNETs (primitive neuroectodermal tumor). cytogenetics to identify the characteristic chromosome translocations are needed to establish the diagnosis.



Ewing's sarcoma demonstrating characteristic round-cell cytologic morphology

Differential Diagnosis

Microscopically, Ewing's sarcoma simulates other small round cell tumors that occur in childhood and adolescence which include (lymphoma/leukemia, metastatic neuroblastoma, mesenchymal chondrosarcoma, small cell osteosarcoma, and although rare for this age group, metastatic carcinoma). Routine light microscopy, electron microscopy, immunohistochemistry, and cytogenetics often used to reach a conclusive diagnosis.

Treatment and Prognosis

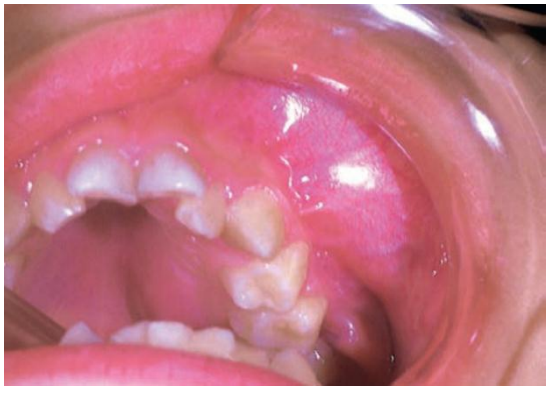
The highly malignant nature of this sarcoma is reflected in its propensity for metastasis, especially to lungs, other bones, and lymph nodes. Multiple-method treatment protocols, involving surgery or radiation for local control and chemotherapy for systemic micro-metastases, have dramatically improved the formerly dismal 10% 5-year survival rate. With these newer intensive therapies, 80% 2-year disease-free survival rates and 60% 5-year actuarial survival rates have been reported.

Burkitt's Lymphoma

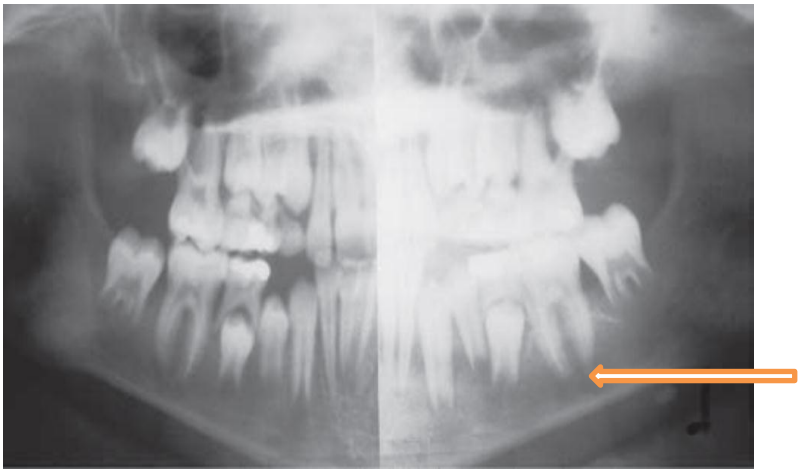
Burkitt's lymphoma is a high-grade non-Hodgkin's B-cell lymphoma that is **endemic** in Africa and occurs only **sporadically** in North America and Western Europe. It was first described in 1958 by the surgeon Denis Burkitt as a jaw malignancy occurring with high frequency in African children. Both sporadic and endemic forms of Burkitt's lymphoma are characterized by a translocation of the distal part of chromosome 8 containing the (c-myc) oncogene to the immunoglobulin heavy chain gene locus on chromosome 14. These translocations may be directly involved in the enhanced tumor cell proliferation of Burkitt's lymphoma, which has been shown to have one of the highest proliferation rates of any neoplasm in humans, with a potential doubling time of 24 hours and a growth fraction of nearly 100%.

Clinical Features

In Africa, lymphoma accounts for 50% of all childhood malignancies, but it constitutes only 6% to 10% of childhood malignancies in the United States and Europe. Whereas the endemic form of Burkitt's lymphoma has a peak incidence between 3 and 8 years of age and a 2:1 male predominance, the sporadic form affects a slightly older age group, with a mean age of 11 years, and has no gender predilection. Endemic Burkitt's lymphoma typically involves the mandible, maxilla, and abdomen. The incidence of jaw tumors in endemic Burkitt's lymphoma is related to the age of the patient; 88% of those younger than 3 years of age and only 25% of those older than 15 years of age show jaw involvement. Involvement of the jaws is relatively uncommon in the sporadic form of this disease, occurring in approximately 10% of cases. Sporadic Burkitt's lymphoma presents most often as an abdominal mass involving the mesenteric lymph nodes or ileocecal region, often with an intestinal obstruction. A notable difference between endemic and nonendemic forms of Burkitt's lymphoma is that the Epstein-Barr virus genome can be detected in 95% of endemic cases but in only 10% of sporadic cases. When the mandible and the maxilla are involved, the initial focus is usually in the posterior region, more commonly in the maxilla than in the mandible. Tumors in the sporadic form appear more localized, whereas in the endemic form, they more commonly involve all four quadrants. The usual signs associated with jaw lesions are an expanding intraoral mass and mobility of the teeth. Pain and paresthesia are occasionally present.



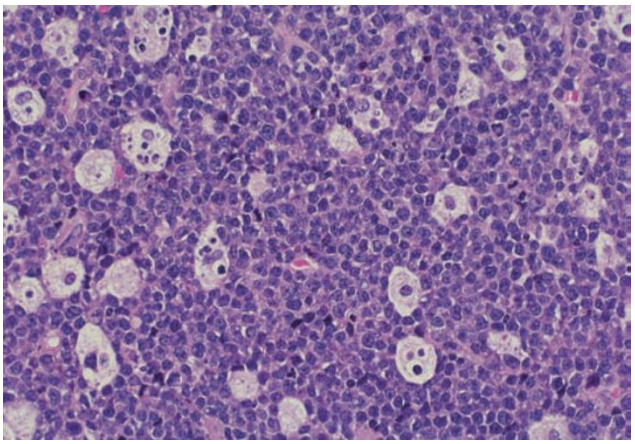
Radiographically, a moth-eaten, poorly marginated destruction of bone is observed. The cortex may be expanded, eroded, or perforated, with soft tissue involvement.



Burkitt's lymphoma presenting as a periapical radiolucency (mandibular left first molar). The patient also had lip paresthesia.

Histopathology

Burkitt's lymphoma is a neoplastic B-cell proliferation that contains cell-surface B-lineage differentiation antigens and monoclonal surface immunoglobulin. The proliferation is extremely monomorphic, composed of medium-sized lymphocytes with round nuclei and three to five small basophilic nucleoli. Throughout the lymphoid proliferation are numerous scattered macrophages containing nuclear debris, contributing to the so-called starry sky appearance. By immunohistochemistry, tumor cells express the B-cell markers CD20 and CD10. Almost all the cells are dividing and the almost uniform expression of the proliferation marker Ki-67 protein can be useful in diagnosis. The histologic differential diagnosis includes other subtypes of non-Hodgkin's lymphoma, undifferentiated carcinoma and sarcoma, metastatic neuroblastoma, and acute leukemia.



Burkitt's lymphoma exhibiting starry sky effect. Pale cells are macrophages.

Treatment and Prognosis

Burkitt's lymphoma was always fatal within 4 to 6 months of diagnosis. However, because of its high proliferation rate, Burkitt's lymphoma has proved to be extremely sensitive to combination chemotherapy, and therefore is potentially curable. The endemic and sporadic forms of Burkitt's lymphoma show similar excellent response rates to chemotherapy, with similar rates of relapse and survival. With combination chemotherapy, the overall 2-year survival rate is 55%, with a range of 80% for low stage disease and 40% for advanced-stage disease.