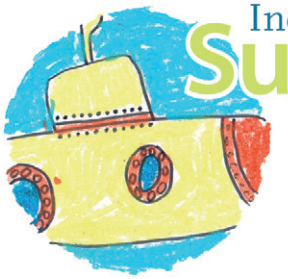

Index of Suspicion

3 Increased Snoring in a 7-year-old Boy

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PRESENTATION

A 7-year-old boy with a medical history of cerebral palsy presents with throat pain of 1 week's duration associated with dysphagia to solids and liquids. He denies any history of fever, joint pain, rashes, or abdominal pain. His illness started approximately 2 months earlier, when he was hospitalized at another institution for difficulty breathing and increased snoring. He was treated with corticosteroids for his airway edema and was discharged with a bilevel positive airway pressure device for possible obstructive sleep apnea, although no sleep study or visualization of airway was performed. One week before this visit, he started complaining of a sore throat and increasing difficulty breathing, for which his pediatrician started him on amoxicillin for presumed streptococcal pharyngitis. Because his symptoms worsened, he was referred to an otorhinolaryngologist, who identified an oropharyngeal mass by nasal endoscopy. He is hospitalized for further evaluation and management.

On hospital admission, his vital signs are stable. He is breathing at a rate of 14 breaths/min, without any distress. He is at the 10th percentile for height (45 in [115 cm]) and the second percentile for weight (40 lb [18 kg]). Examination shows a diffuse, nonfluctuant, firm swelling, approximately 1.5 × 2 cm, over the upper one-third of the right sternocleidomastoid that is not attached to the muscle. No lymphadenopathy is appreciated anywhere else. The rest of the physical examination is benign except for hypotonia due to cerebral palsy.

Initial laboratory evaluation shows a normal complete blood cell count and electrolyte levels, with a C-reactive protein level of 0.2 mg/L (1.90 nmol/L). The lactate dehydrogenase level is elevated at 343 U/L (5.73 μkat/L). Additional evaluation leads to the diagnosis.

The Case Discussion and Suggested Readings appear with the online version of this article at http://pedsinreview.aappublications.org/content/38/12/569.

DISCUSSION

The major differential diagnoses for lateral neck mass are reactive lymphadenitis, malignancies, vascular anomalies, teratomas, thyroglossal duct cysts, dermoid cysts, branchial cysts, and salivary gland infections.

Magnetic resonance imaging showed a solid 5 × 2.2 × 9-cm lesion involving the nasopharynx and the right retropharyngeal and parapharyngeal soft tissues. The mass was biopsied, and the results established the diagnosis of Burkitt lymphoma (BL). Although sporadic BL rarely presents as a parapharyngeal mass, suspicion was high for a malignant lesion in this patient because of the rapid worsening of his symptoms.

His Epstein-Barr virus profile showed evidence of previous infection with the virus. Results of testing for human immunodeficiency virus (HIV) infection were negative. The patient was not taking any immunosuppressive drugs.

The Condition

BL is a very aggressive non-Hodgkin B-cell tumor arising from germinal or postgerminal B cells. Constitutive expression of c-MYC proto-oncogene on chromosome 8 is considered the major genetic change associated with BL. Although c-MYC, which encodes a transcription factor involved in controlling cell proliferation and differentiation, is tightly regulated in normal B cells, translocation of c-MYC gene (from chromosome 8) to a position downstream of a strong promoter, as seen in t(8;14), t(2:8), and t(8;22), results in overexpression of c-MYC. This results in uncontrolled B-cell proliferation. Chronic Epstein-Barr virus infection, which can promote the translocation and also immortalize B cells, is believed to play a crucial role in the pathogenesis.

Three major clinical forms of the tumor are recognized: endemic, sporadic, and immunodeficiency associated. The endemic form, which often presents as jaw mass or facial bone mass with nontender and swollen lymph nodes, is commonly seen in the "lymphoma belt" in equatorial Africa. The sporadic form, which is the form common in North America, usually presents as an abdominal tumor with marrow involvement. Although both the sporadic and endemic forms can occasionally involve the ovaries, kidneys, and breasts, the sporadic form seldom presents as jaw or facial bone mass. Immunodeficiency-associated BL, as seen in patients with HIV infection, presents as lymph node enlargement with bone marrow involvement.

Diagnosis

A high degree of suspicion is needed to diagnose BL in children in the United States because of the rarity of the condition and the protean clinical presentation. Early clinical diagnosis helps in avoiding treatments such as corticosteroids, which can interfere with the histopathological diagnosis and treatment of BL. Histopathology, immunostaining, and cytogenetics are the mainstay of diagnosis. Histologically, numerous intermediate-sized cells with round nuclei and scant cytoplasm are noted in a background of necrotic debris and tangible body macrophages, giving rise to the classic "starry-sky" appearance. The high doubling rate is reflected in the high cell proliferation index. Immunostaining with B-cell markers such as CD10, CD20, CD22, CD79a, and BCL6 is positive. Cytogenetic analysis using fluorescence in situ hybridization demonstrates c-MYC translocation. Although c-MYC translocation is noted in more than 95% of patients with BL, it is not essential to diagnose BL, according to the 2008 World Health Organization classification of lymphoid neoplasms. In addition, patients also need whole-body nuclear scanning and computed tomography to rule out metastases, and magnetic resonance imaging studies to identify the margins of the tumor. Testing for HIV infection and evaluation for immunodeficiency are also warranted in these patients.

Treatment and Prognosis

Patients with BL typically receive chemotherapy for 6 weeks to 8 months, depending on the disease stage. Most of the currently used regimens have evolved from trials conducted by Lymphoma Malignancy B (LMB) group, Berlin-Frankfurt-Munster (BFM) group, and Children's Cancer Group (CCG). After the trials, the mainstay of chemotherapy evolved to use of methotrexate, doxorubicin, and cyclophosphamide. Rituximab is being used in pediatric B-cell tumors, with a considerable increase in overall survival, after the success with rituximab in CD20-positive B-cell lymphoma in adults. Intrathecal chemotherapy has also significantly reduced the use of cranial radiation treatment.

Major complications associated with chemotherapy are acute toxicities from chemotherapeutic agents, tumor lysis syndrome, and infections due to immunosuppression. Tumor lysis syndrome is commonly seen in patients with BL because of the high tumor doubling rate. Aggressive hydration, along with use of allopurinol and/or rasburicase, is the mainstay of preventing this syndrome. Estimated 4-year event-free survival is 98% in patients with early-stage disease and approximately 90% in children with advanced-stage disease.

Our patient was diagnosed as having BL based on clinical and laboratory findings, and he began an R-COPADM (rituximab–cyclophosphamide, Oncovin, prednisolone, adriamycin, and methotrexate) treatment plan. His tumor-reduction chemotherapy

reduced the size of his neck swelling by more than half within a week of starting chemotherapy.

Lessons for the Clinician

- Burkitt lymphoma is an uncommon, rapidly growing, but highly responsive cancer of the B cells.
- Early diagnosis and treatment helps prevent metastases and other complications, such as tumor lysis syndrome, before the tumor burden gets too high.
- It is important to look for the etiology rather than to treat symptomatically.
- More importantly, clinicians should refrain from prescribing corticosteroids in patients such as this when a malignancy is included in the list of differential diagnoses. Treatment with corticosteroids before diagnosis and the initiation of definitive therapy may adversely impact the ability to diagnose and assess response to therapy.

Note: The abstract of this case report was published in the January 2016 issue of the *Journal of Investigative Medicine,* and a talk was presented at the Western Regional Meeting of the American Federation for Medical Research Conference at Carmel, California, on January 28, 2016, was presented under the title "An Unusual Presentation of a Highly Malignant Tumor," by Dr Bhoopalan (presenting author) and Dr Das.

Suggested Readings

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Parent Resources from the AAP at HealthyChildren.org

- Does Your Child Snore?: https://www.healthychildren.org/English/health-issues/conditions/ear-nose-throat/Pages/Does-Your-Child-Snore-Video.aspx
- Childhood Cancer: https://www.healthychildren.org/English/health-issues/conditions/cancer/Pages/Childhood-Cancer.aspx

For a comprehensive library of AAP parent handouts, please go to the *Pediatric Patient Education* site at http://patiented.aap.org.