One Approach to Facial Swelling: Tooth or Fiction

Introduction: Facial swelling is a common problem in the pediatric population with a variety of causes, ranging from congenital to acquired diseases. A fundamental understanding of typical clinical presentation helps in narrowing this broad differential.

Case: A 35-month-old, previously healthy, African American boy presented with 2 weeks of intermittent nightly leg pain and 1 week of unilateral, progressive nontender facial swelling. He had severe, achy right leg pain relieved by ibuprofen, which was diagnosed as a sprain at an outside emergency center 2 days before admission. The patient had developed mild, nontender right facial swelling 1 week before admission and had started amoxicillin for a suspected tooth abscess (Fig 1). He developed a fever of 38.7°C 2 days before admission. Because the patient failed to improve with outpatient management, he was admitted for further evaluation.

On admission, the patient appeared well nourished with mild fever of 38.1°C, pulse rate of 108 beats per minute, and blood pressure of 107/64 mm Hg. His physical examination showed enlarged tonsils with no exudates and 1-cm, firm, nonerythematosus soft tissue swelling overlying the right maxilla with no evidence of dental caries or decay. No cervical, axillary, or inguinal lymph nodes were palpated. There were no other signs of constitutional symptoms such as weight loss, night sweats, diarrhea, nausea, or vomiting.

Question: What should be included in an initial differential diagnosis of a patient who presents with facial swelling, and when is imaging indicated?

Discussion: Cases of facial swelling can be divided into 4 groups: acute swelling with inflammation, nonprogressive swelling, slowly progressive swelling, and rapidly progressive swelling. The most common form of facial swelling is acute swelling with inflammation, which typically is caused by lymphadenitis, sinusitis, or a tooth infection. Children who have severe systemic symptoms, concern for an underlying drainable fluid collection, musculoskeletal infection, or orbital involvement should be considered for advanced imaging such as computed tomography (CT) or MRI scan. The patient did have a fever with acute swelling and had previously been diagnosed with a tooth infection. However, he had not responded to antibiotics, and the swelling had been getting progressively worse.

Nonprogressive swelling refers to congenital midfacial masses such as frontoethmoidal cephaloceles, nasal gliomas, and nasal dermoid and epidermoid cysts.
CT and MRI scans are helpful in evaluating the extent of the anomalies and facilitating treatment planning. This patient had no history of any congenital masses and no chronic swelling to suggest any of these causes.

Slowly progressive swelling describes an underlying mass such as neurofibroma, hemangioma, fibrous dysplasia of the bone, and lymphatic or vascular malformation. Depending on the clinical suspicion of expansion or malignancy, advanced imaging should be considered; however, emergent imaging is not required in most cases. The timing of this patient’s presentation with his symptoms did not lead us in this direction.

More worrisome, but less common, are cases of rapidly progressive facial swelling. This type of swelling includes malignancies such as lymphomas, rhabdomyosarcomas, Langerhans cell histiocytosis (LCH), Ewing’s sarcoma, osteogenic sarcoma, and metastatic neuroblastoma. When cranial nerve deficits such as facial numbness or paralysis are present, the index of suspicion rises for malignancy. This patient’s presentation was considered rapidly progressive because it occurred over a 1-week period. With his symptoms of fever and pain despite a course of antibiotics, imaging was warranted.

**Case Continuation:** Laboratory evaluations included the following: white blood cell count, 8.52/μL; hemoglobin, 11.4 g/dL; hematocrit, 33.2%; platelet, 356 μL; erythrocyte sedimentation rate, 25 mm/h mg/L; C-reactive protein, <0.5; aspartate aminotransferase, 265 U/L; alanine aminotransferase, 265 U/L; alkaline phosphatase, 351 U/L; lactate dehydrogenase, 1154 U/L; and uric acid, 4.4 mg/dL. These values revealed no evidence of bone marrow suppression and normal levels of inflammatory markers, but they did reveal transaminitis with elevated levels of lactate dehydrogenase and alkaline phosphatase.

The maxillofacial CT scan with contrast showed a 3.7 cm × 2.9 cm × 4.4 cm enhancing lytic mass in the right maxilla with multiple surrounding lytic areas of bone loss. Subtle spiculated periosteal reaction was also noted by the radiologists. In addition, there was a 1.6 cm × 2.0 cm × 1.1 cm enhancing lytic mass within the left mandible as well as focal lytic destruction of the inner and outer tables of the mandible, with associated focal spiculated periosteal reaction. The underlying maxillary tooth roots showed abnormal lucency on the right side. Otherwise, no definite destructive lytic lesions or abnormal-appearing lymph nodes were identified in the head or neck. The ankle radiograph showed periosteal reaction in the distal diaphysis of the right fibula.

**Question:** Based on these laboratory and radiologic findings, what are the next steps in management?

**Discussion:** Given the radiologic findings, the initial differential included LCH, Ewing’s sarcoma, neuroblastoma, and lymphoma. Our initial management focused on using our radiologic findings and noninvasive diagnostic tests to help narrow the diagnosis.

The patient’s initial presentation of leg and jaw pain was suggestive of multiple bony lesions due to LCH, which is known to present with either solitary or multiple bony lesions as eosinophilic granuloma. This rare disorder generally presents between 5 and 10 years of age, predominantly in males. Clinically, it presents most frequently in the skull (40% to 8% in the jaws), ribs, pelvis, long bones, mandible, and vertebrae. On imaging, the skull lesions classically are punched-out, with a lytic appearance and mandibular involvement simulating the appearance of “floating” teeth.

The patient’s CT scan showed lytic lesions involving the mandible, with abnormal lucency at the maxillary tooth roots commonly found in LCH. With elevated liver transaminase levels, LCH became higher in the differential because liver involvement is a known sequela, especially sclerosing cholangitis, which occurred in as many as 54% of patients with multisystem LCH in 1 case series. An abdominal ultrasound was ordered to detect any changes characteristic of sclerosing cholangitis or any cholestatic features.

The patient’s maxillofacial CT showed some spiculated periosteal reaction with lytic changes that was suspicious for primary Ewing’s sarcoma. Primary
Ewing’s sarcoma normally affects the pelvis, clavicle, and the long bones of the limbs. However, ~2% of cases have involved the face, mostly in the mandible. Of those primary tumors in the face, only 30 cases of primary maxilla involvement have been reported. The most common radiologic signs in cases of primary Ewing’s sarcoma involving the maxilla have been lytic changes with bone destruction and periosteal thickening, described as the “sun-ray” image. This finding contrasts with the characteristic periosteal “onion-skinning” reaction, thickening of the cortical bone, and soft tissue masses seen in more common cases of Ewing’s sarcoma.

Typically, neuroblastoma presents most commonly in the adrenal glands (40%), but 5% of primary lesions arise in the head and neck. Approximately 1% of the cases reveal no primary tumor but instead present as metastatic disease. Given that the patient presented normotensive, with no abdominal mass, periorbital ecchymosis, or any autonomic symptoms, neuroblastoma was less likely, but urine catecholamine levels were analyzed to rule out that remote possibility.

Lymphoma was further down on the differential due to the patient’s presentation without any palpable lymph nodes or other constitutional symptoms. However, lymphoma is 1 of the most common malignancies involving the extracranial head and neck. Hodgkin’s lymphoma presents more commonly in adolescents whereas non-Hodgkin’s lymphoma (NHL) predominates in children aged <10 years. Primary NHL of the bone occurs <3% to 9% of the time in the pediatric population and at 0.6% in the mandible in the overall population. Of all the different types of NHL, endemic Burkitt’s lymphoma (BL) presents more commonly with jaw or facial bone tumors, but our patient had never been in Africa or Papua New Guinea. Sporadic (non-endemic) BL accounts for 30% of all nonendemic pediatric lymphomas but typically presents with abdominal manifestations such as gastrointestinal bleeding, bowel obstruction, and ascites, which were also not present in our patient.

Ultimately, the next management step was a biopsy of the lytic lesions in the patient’s mandible.

Case Resolution: Before the biopsy, results of a liver ultrasound and urine catecholamine levels were both normal. The otolaryngology surgeons were able to obtain 3 biopsy samples from the right maxillary mass. The histologic, genetic, and immunophenotypic components were consistent with BL, including flow cytometry showing a population of mature CD10- and CD20-positive B cells, fluorescent in situ hybridization demonstrating a pattern consistent with an immunoglobulin H–MYC fusion in 91% of cells suggestive of a translocation of chromosome 8 and 14, and immunohistochemical stains demonstrating a “starry sky” pattern of macrophages and tumor cells. Staging was completed, which showed no metastasis or central nervous system involvement, and the patient was subsequently started on an experimental chemotherapy by the hematology/oncology specialists.

Discussion: First characterized >50 years ago in African children, BL is an aggressive B cell NHL endemic in equatorial Africa. BL presents 60% to 80% of the time with jaw or facial lesions at the mean age of 9 years and has an incidence of 50 to 100 per 1 million children. Endemic BL has been well known to be associated with Epstein-Barr virus (EBV), with EBV serology detected in >95% cases, and Plasmodium falciparum malaria, which may directly stimulate B cells or indirectly suppress immune response toward EBV.

A sporadic variant, found outside of Africa, is virtually indistinguishable under the microscope with the same translocation between c-Myc on chromosome 8 and human immunoglobulin heavy chain on chromosome 14. As the third most common childhood lymphoid malignancy among children aged <15 years, sporadic BL represents the most common subtype of NHL in the United States, with an estimated overall incidence of 1 to 3 per 100,000 children. The etiology is still unknown, but risk factors such as male gender, non-Hispanic white race, and early childhood exposure to infection such as HIV and EBV have been identified.

Conclusions: Pediatric facial swelling presents a wide differential, from common benign conditions to more deadly diseases. In most cases, pediatricians will encounter acute infectious processes such as lymphadenitis or tooth infection. However, having a broad differential for the rare but deadlier processes can lead to early diagnosis and treatment. Due to the resemblance of common dental disease, which might also present with acute facial swelling and tenderness, primary NHLs that present in the mandible have an average of 10 weeks between first presentation and final diagnosis, which can delay the correct treatment. In this case, there were very few risk factors
that made us initially think of sporadic BL, but the clinical presentation of rapidly progressing facial swelling with failed treatment of dental abscesses or infection should have been the initial clue.

REFERENCES


