Pediatric

Pediatric mandibular metastasis: A rare finding of neuroblastoma

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A B S T R A C T
We present a case of metastatic neuroblastoma to the mandible in an 11-month-old patient presenting with worsening right-sided proptosis and scalp swelling after a fall 2 weeks prior. Initial evaluation with computed tomography of the head demonstrated soft tissue masses centered at the right sphenoid and right mandible. These masses proved to be metastatic lesions from an intra-abdominal neuroblastoma. Review of the literature revealed 20 cases of neuroblastoma metastasis to the mandible over the past 70 years. To our knowledge, our patient is the youngest reported case with asymptomatic mandibular metastasis related to neuroblastoma and the first to be characterized with magnetic resonance imaging.

Case report

Our patient is an 11-month-old baby who presented to an outside hospital emergency department for worsening right-sided proptosis and scalp swelling after a fall 2 weeks prior. Computed tomography (CT) of the head revealed an aggressive soft tissue mass centered at the right sphenoid extending into the orbit, as well as partial imaging of a separate soft tissue mass with internal calcification centered at the right mandibular ramus (Fig. 1). Osseous structures adjacent to these soft tissue masses showed permissive lytic changes with aggressive periostitis (Fig. 2).

Magnetic resonance imaging (MRI) of the head revealed multiple skull base lesions, with involvement of the orbital walls bilaterally and the sphenoid and occipital bones, as well as of the right mandibular ramus. On nonenhanced T1 sequence, the mandibular lesion was slightly hypointense to gray matter (Fig. 3A and B) and demonstrated heterogeneous enhancement after contrast (Fig. 4A and B). Additionally, the mass displayed mildly increased T2 and diffusion-weighted signal (Figs. 5 and 6). Susceptibility images showed multiple hypointense foci with “blooming” within the mandibular soft tissue mass (Fig. 7). No intra-axial tumor was identified. The diagnosis of metastatic neuroblastoma was suggested based on the constellation of findings on both the CT and the MRI.

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of the head, and not solely on the findings within the mandibular lesion.

Immediate follow-up CT of the chest and/or abdomen and/or pelvis identified a large abdominal mass arising from the left adrenal gland causing focal mass effect and encasing the abdominal vasculature (Fig. 8). Multiple hepatic hypodense lesions and a left pelvic soft tissue mass were also noted. Urine catecholamines were found to be elevated, consistent with the suspected diagnosis of neuroblastoma. Open biopsy of the abdominal mass and bone marrow aspirate was performed, revealing high-risk neuroblastoma due to MYCN amplification. Subsequent MIBG (metaiodobenzylguanidine) scan demonstrated radiotracer accumulation within the bilateral lower extremities, as well as in the known lesions of the abdomen and skull base, consistent with metastatic disease (Fig. 9).

The patient began treatment with cyclophosphamide and topotecan. She is currently being followed as an outpatient approximately 6 months later with overall decreased tumor burden.

Discussion

Neuroblastoma is the most common solid tumor in pediatric patients and the third most common pediatric tumor overall [1,2]. Embryologically, neuroblastomas arise from the ectodermal neural crest cells of the sympathetic nervous system, most commonly in the adrenal medulla, which is the most common location of neuroblastoma. In the United States, the incidence of neuroblastoma is approximately 1 of 7000 [3]. Most cases of neuroblastoma occur sporadically, but approximately 1%-2% exhibit familial transmission [1,3,4]. Approximately 80% of patients with neuroblastoma are diagnosed by 4 years of age, with an average age of 22 months [5,6].

Clinically, patients with neuroblastoma present with palpable abdominal abnormalities and/or complaints related to mass effect on adjacent organ systems, such as extremity edema, shortness of breath, and bone pain [6]. When orbital metastatic disease is present, patients can exhibit proptosis, as seen in our case, or orbital ecchymosis. The diagnosis of neuroblastoma is made with elevated urinary catecholamines and histopathological confirmation or bone marrow aspiration [3]. Metastasis is frequently encountered upon initial presentation (60%-70%), and the extent of metastatic lesions is correlated with prognosis and staging [1].

Detailed neuroblastoma staging is beyond the scope of this report, although briefly, staging of neuroblastoma can be performed by 2 means: postsurgically or presurgically. The International Neuroblastoma Staging System (INSS) is more commonly used and relies on surgical pathologic confirmation. This is in comparison to the more recently created presurgical staging and/or risk stratification system, The International Neuroblastoma Risk Group Staging System (INRGSS). The INRGSS relies on image-defined risk factors obtained from cross-sectional imaging and nuclear scintigraphy, as well as bone marrow sampling.

When comparing the 2 staging systems of neuroblastoma, there are notable differences. For instance, the tumor crossing midline is important for INSS but not so for INRGSS. The nodal lexicon also varies between the 2 staging systems: INSS uses the terms ipsilateral and contralateral, whereas INRGSS uses regional and nonregional. Both systems utilize the “S” qualifier for metastatic disease confined to skin, liver, and bone marrow (less than 10% of the total nucleated cell for INRGSS); however, the age cutoff for “S” used in the INSS is 12 months, whereas INRGSS uses an age cutoff of 18 months [1].

Although approximately 50%-60% of cases of neuroblastoma present with metastatic disease, mandibular metastases

Fig. 1 – Axial computed tomography image shows a soft tissue mass with internal calcification centered on the ramus of the right mandible (arrows).

Fig. 2 – Axial computed tomography image with bone reconstruction shows aggressive periosteal reaction centered at the ramus of the right mandible.
are exceedingly rare [7]. Our literature review yielded 20 reported cases of neuroblastoma mandibular metastases over the last 70 years, with a patient age range between 8 and 102 months. The youngest patient (8 months) reported in the literature with mandibular metastatic disease was symptomatic [8], whereas our 11-month-old patient was asymptomatic. Therefore, to our knowledge, our patient is the youngest with asymptomatic mandibular metastases.

Unfortunately, most of the reported cases in the literature were diagnosed before the common usage of cross-sectional imaging. Most mandibular metastases were originally noted on physical examination or with findings of nonspecific lytic bone lesions found on orthopantomogram films. They were subsequently diagnosed with soft tissue sampling [9]. However, several of the previously reported cases of mandibular metastatic lesions did utilize CT cross-sectional imaging, which showed the lesions to exhibit similar findings to our patient. These lesions appeared as partially calcified soft tissue masses causing significant periostitis [10]. We did not find any reported cases of patients with MRI evaluation of their mandibular metastatic disease, although our MRI findings of the mandibular lesion are largely similar to the MRI findings of abdominal neuroblastoma (T1 isointense, T2 hyperintense, restricted diffusion, and heterogeneous enhancement) [11].

When faced with maxillary and/or mandibular lesions, patient history such as dental history including unerupted teeth or history of dental caries can be helpful for distinguishing primary vs metastatic etiologies. Primary pediatric jawbone lesions can be broadly classified as odontogenic and nonodontogenic. Odontogenic etiologies can be further subdivided into cystic and solid lesions. The cystic entities are benign and most commonly consist of periapical cysts, which occur secondary to poor dentition in older children; solitary bone cysts from trauma; and primordial cysts, which are developmental lesions resulting from incomplete odontogenesis. Benign solid lesions include odontomas, which are hamartomatous lesions with dentin and enamel material usually found in slightly older children; and cementoblastomas, which are

Fig. 3 – (A) Axial T1 image precontrast shows a hypointense expansile soft tissue mass centered at the right mandibular ramus. (B) Coronal T1 precontrast image shows soft tissue expansile mass centered at the right mandibular ramus. Additional masses are noted at the skull base bilaterally.

Fig. 4 – (A) Axial T1 postcontrast image depicts heterogeneous enhancement of the right mandibular expansile soft tissue mass. (B) Coronal T1 postcontrast heterogeneous enhancement of the right mandibular soft tissue mass.
neoplasms of the lining of the roots of the teeth and found in patients younger than 25 years old. Solid lesions are otherwise generally malignant in children and can represent metastatic lesions or, occasionally, lymphoma or leukemia [12].

In 2012, Saxena et al published a case series of pediatric jawbone tumors. In the 61 patients reported, they found that pediatric jawbone tumors of nonodontogenic origin occur almost twice as often as odontogenic, and jawbone tumors more often occur in the mandible compared with the maxilla [13]. It is estimated that up to 30% of malignant mandibular lesions are metastatic from an unknown primary; it is critical to recognize these lesions as metastatic so that the occult primary lesion can be identified [12].

Fig. 5 – Axial T2-weighted image shows mildly increased T2 signal within the right mandibular soft tissue mass.

Fig. 6 – Diffusion-weighted image shows restricted diffusion of the mandibular soft tissue mass.

Fig. 7 – Axial susceptibility weighted image shows presence of blooming artifact within the mandibular soft tissue mass, corresponding to calcifications seen on computed tomography.

Fig. 8 – Axial computed tomography of the abdomen shows large soft tissue mass encasing the arterial vasculature and exhibiting significant mass effect on both kidneys, the aorta, and the inferior vena cava. Additionally, there is a hypodense metastatic lesion noted within the right lobe of the liver.
In 2013, Abramowicz et al discussed the usage of the terms “aggressive” and “nonaggressive,” as opposed to relying on histopathology when describing pediatric primary jaw tumors, as these terms emphasized the biologic and clinical behavior of tumors. Their findings focused on benign tumors where histologic diagnosis of benignity did not necessarily correlate with tumor behavior [14]. In their study of 102 pediatric patients with primary jawbone tumors of benign mesenchymal origin (giant cell lesions, fibro-osseous lesions, and myxofibroid tumors), characteristics such as measurement greater than 5 cm, rapid growth, recurrence after treatment, cortical bone thinning or perforation, dental displacement, presence of root resorption and physical examination findings including pain, soft tissue discoloration or ulceration, tooth mobility, or paresthesia were determined to be particularly concerning. Aggressive jawbone tumors were defined as those possessing 3 or more of these imaging or physical examination findings.

Management has supported the use of the characterization of lesions as either exhibiting nonaggressive or aggressive features. Follow-up of lesions exhibiting nonaggressive features that are treated with enucleation showed no evidence of recurrence, whereas lesions with aggressive features being treated with en bloc resection showed recurrence in approximately 8% [14].

When faced with a lytic jawbone lesion in a pediatric patient, keep in mind that nonodontogenic tumors are reportedly more common than odontogenic, and if a confident diagnosis cannot be made by imaging, the qualifying descriptors “aggressive” or “nonaggressive” may provide clinical management assistance. Differentiating between neuroblastoma and other mandibular bone lesions include characteristic findings on cross-sectional and nuclear imaging (eg, MIBG). MRI, which is frequently the preferred imaging modality used for staging, shows lesions with T1 hypointense signal, T2 hyperintense signal, restricted diffusion, and heterogeneous enhancement.

In our patient, the imaging characteristics that were suggestive of a malignant process included cortical destruction and the presence of multiple similar appearing bone lesions extending into the adjacent soft tissues, with continuation into the intracranial compartment. The location of the lesion within the ramus of the right mandible is suggestive of hematogenously spread primary tumor due to the increased red marrow vascularity of the mandibular body and angle [15].

Although metastatic neuroblastoma without mandibular metastasis has a 3-year event-free survival rate of 15% in children older than 1 year old, mandibular metastases portend a poor
prognosis with death frequently occurring within 12 months of diagnosis [4].

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