Case Report

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An Infant with Neuroblastoma Presenting as Intermittent Eye Bruising: A Pediatric Case Report

Urgent Message: Recurrent or unexplained periorbital ecchymosis ('raccoon eyes') in an infant should prompt consideration of metastatic neuroblastoma and escalation for appropriate imaging.

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Abstract

Introduction: The presenting symptoms of pediatric neuroblastoma are highly variable. Patients may first present to urgent care for what they perceive as a minor complaint. These symptoms can include periorbital ecchymosis, which can appear to be trauma-induced. These findings and other presenting symptoms of neuroblastoma can often be due to underlying metastatic disease.

Clinical Presentation: A 10-month-old male presented with a 7-month history of bilateral intermittent eye bruising unrelated to injury. Left upper eyelid bruising had been present for 11 days and right lower eyelid bruising for 2 days. The presenting episode was the 7th known occurrence. The distribution of the bruising had varied between episodes and had typically included the inner upper eyelids and had occasionally spread to lower lids. A raised nodule above the left eyebrow had been present for 3 weeks. No eyelid edema was noted during episodes. The patient had multiple prior visits to a primary care physician and an emergency department (ED) for this concern.

Case Resolution: The patient was transferred to the ED for imaging workup due to suspected oncologic etiology. Initial head computed tomography showed aggressive

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osseous lesions of the left superior orbital margin and anterior lateral roof of the left orbit. Additional imaging noted a large calcified right suprarenal mass concerning for neuroblastoma. Further findings included a moth-eaten, lucent appearance of the left ankle and right tibia concerning for metastatic disease. A biopsy confirmed the suspected diagnosis of neuroblastoma. The patient received chemotherapy, surgical resection, autologous bone marrow transplantation, and radiation therapy.

Conclusion: For pediatric patients with recurrent cases of eye bruising or cases without known mechanisms of injury, neuroblastoma should be considered in the differential diagnosis.

Introduction

Neuroblastoma is a cancer of neural crest cells, which are found in many areas of the body, commonly in the adrenal glands, abdomen, or spine. This condition can occur anywhere within the sympathetic nervous system with the majority of cases presenting in the adrenal glands. Neuroblastoma is the most common form of cancer in children under the age of 1 year,[1] and 66% of cases are metastatic at the time of diagnosis.[2] Because the majority of cases present in the adrenal glands, a palpable abdominal mass is often the earliest sign. However, the presentation of neuroblastoma can be variable, which can make it difficult to diagnose.[1]

Patients with localized neuroblastoma are often asymptomatic at presentation, while patients with metastatic disease can present with systemic symptoms, such as bone pain, painless subcutaneous nodules, and periorbital ecchymosis ("raccoon eyes").[3,4] Periorbital ecchymosis results from the tumor bleeding into the soft tissues of the eyelids and can often be mistaken for trauma. Imaging, primarily computed tomography (CT) scans, is used to diagnose neuroblastomas along with lab tests and surgical biopsies.[3] Stage of malignancy remains the most important prognostic factor, and infants aged less than 1 year have significantly better survival rates than older children with the same disease stage.[5] Low-risk neuroblastoma is usually treated with surgery alone. Intermediate-risk neuroblastoma is treated with a combination of surgical resection and moderate-dose chemotherapy.[6] High-risk neuroblastoma is largely responsive to chemotherapy, yet only 30% to 40% of patients survive long term.[7]

Case Presentation

A 10-month-old male presented to urgent care (UC) with a 7-month history of bilateral intermittent periorbital bruising. The current episode was the 7th known occurrence. Left upper eyelid bruising had been present for 11 days with onset of right lower eyelid bruising for 2 days. The distribution of the bruising had been variable and typically included inner upper eyelids and occasionally spread to lower lids. A raised nodule above the left eyebrow had been present for 3 weeks. No eyelid edema was noted during episodes. The patient's mother denied known injury and reported the infant had normal behavior and appetite. She denied appearance of eye pain or distress. Family history revealed a history of brain tumors in a maternal uncle and paternal grandmother.

The mother reported multiple prior visits to a primary care physician (PCP) and emergency department (ED) for this concern. She was told "the patient is a boy and hitting himself in the eyes with toys" despite this behavior not being witnessed. The patient was seen by his PCP for assessment of the recurrent left upper eyelid ecchymosis and was referred to ophthalmology. The first available appointment was 21 days later. Due to the length of the current episode, the parent did not want to wait, and the patient was brought into UC for further evaluation.

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Physical Exam Findings

The patient presented alert and responsive. Vital signs included: a temperature of 36.2°C; a heart rate of 108 beats per minute; a respiratory rate of 36 breaths per minute; and a blood pressure of 99/80 mmHg (82nd percentile / 99th percentile), which was noted to be elevated. There was a palpable nodule present above the patient's left eyebrow. Left upper and right lower eyelid ecchymoses were present. The patient's pupils were equal, round, and reactive to light bilaterally, and his red reflex was intact. No respiratory distress was noted, and nostrils were free from obstruction. Bilateral capillary refill was measured at 2 seconds.

Medical Decision Making

Given the recurrent nature of the symptoms, the pro-

longed duration of the current episode, and the presence of a palpable nodule above the eyebrow, the patient was transferred to the ED. This decision was prompted by the potential of severe exacerbation and progression of disease with a high clinical suspicion for malignancy. Of note, neuroblastoma can often present with elevated blood pressures due to the catecholamine release by the tumor due to its neural crest origin as was seen in this patient. It is important to note that there is also an association of involuntary rapid eye movements (opsoclonus) and brief twitching (myoclonus) with neuroblastoma.[4] However, these findings were not present for this patient.

Therapeutic Intervention

In the ED, physical examination demonstrated bilateral eye ecchymosis and palpable right abdominal mass with abdominal distension. Pupillary reflex showed a sluggish reaction to light with the red reflex intact bilaterally. This prompted an early working differential including neuroblastoma, non-accidental trauma (NAT), bleeding disorders, and retinoblastoma.

ED workup included the following:

- **Head CT scan:** Indicated for evaluation of tumor vs trauma; revealed aggressive osseous lesions of the left superior orbital margin and anterior lateral roof of the left orbit
- **X-ray skeletal survey:** Indicated for evaluation of NAT; revealed a moth-eaten, lucent appearance of the left ankle and right tibia concerning for metastatic disease
- **Complete blood count**: White blood count, 16.5 x 10^3 cells/uL; absolute neutrophil count, 1.8 x 10^3 cells/mm^3; hemoglobin, 10.5 g/dL; platelets, 493 x 10^3 cells/uL
- **Chemistry**: Sodium, 137 mmol/L; potassium, 4.6 mmol/L; chloride, 105 mmol/L; bicarbonate, 21 mmol/L; blood urea nitrogen, 6 mg/dL; creatinine, 0.23 mg/dL; glucose, 99 mg/dL
- **Coagulation studies:** Prothrombin time, 13.2 seconds; activated partial thromboplastin clotting time, 28 seconds; international normalized ratio, 1.0
- **Urine**: Vanillylmandelic acid / creatinine ratio, 360.8 mg/g (elevated); homovanillic acid / creatinine ratio, 367.7 mg/g (elevated)
- **Other Labs:** Lipase, 54 U/L; aspartate aminotransferase, 60 U/L; alanine aminotransferase, 21 U/L; alkaline phosphatase, 141 U/L; total bilirubin, 0.6 mg/dL; indirect bilirubin, 0.5 mg/dL; direct bilirubin, 0.1 mg/dL

Diagnosis

Exam findings and radiology results were suggestive of metastatic neuroblastoma. The patient was admitted to oncology for further evaluation and management. A CT scan of the chest, abdomen, and pelvis was completed to assess for primary and metastatic disease:

- **Abdomen and pelvis CT scan:** Large right suprarenal mass consistent with neuroblastoma
- **Chest CT scan:** No evidence of pulmonary metastatic disease; however, concerns remained for diffuse marrow infiltration secondary to metastatic disease

The patient underwent an interventional radiology biopsy of the abdominal mass. The final pathology report demonstrated poorly differentiated neuroblastoma with intermediate mitotic-karyorrhectic index and favorable International Neuroblastoma Pathology Classification (INPC) histology, transcription factor *MYCN* amplified positive. Subsequent meta-iodobenzylguanidine (MIBG) single-photon emission computed tomography (SPECT/CT) showed a Curie score of 18, which is a semi-quantitative tool used by oncologists to measure the extent of neuroblastoma.[8] A Curie score of 0 indicates tumor remission with a maximum score of 30 possible. The patient then obtained a bilateral posterior iliac crest bone marrow biopsy. The patient was enrolled in a clinical trial (ANBL2131), and induction of chemotherapy was initiated. The patient was discharged.

Follow-Up and Outcomes

At discharge, the parents received education and were instructed to continue with regular well-child visits. Over the course of 3 months, the patient underwent 5 cycles of chemotherapy followed by right adrenal neuroblastoma resection. Pathology demonstrated treated neuroblastoma with 30% treatment effect, and the patient went on to receive additional chemotherapy.[9] He underwent another MIBG SPECT/CT, which demonstrated residual disease in the left frontal orbital region with a complete response at the primary site (suprarenal mass). The patient underwent a tandem autologous bone marrow transplant. Proton radiation therapy was recommended for residual skull lesions.

Discussion

This case reinforces that recurrent periorbital ecchymosis in infants without a clear traumatic mechanism should not be considered benign until proven otherwise. The intermittent nature of the bruising and lack of witnessed injury could have prompted earlier consideration of non-accidental trauma or pathologic eti-

"This case emphasizes the critical role of urgent care providers in identifying red-flag symptoms that warrant escalation of care."

ologies, including malignancy. The identification of aggressive orbital osseous lesions on head CT was critical, leading to comprehensive imaging that revealed a large suprarenal mass and widespread metastatic disease. By the time of diagnosis, the patient had extensive skeletal involvement, including long bones and frontal skull, consistent with the known tendency of neuroblastoma to metastasize to bone and bone marrow.

Despite advanced disease, the patient's age was associated with a relatively favorable prognosis. Nevertheless, the *MYCN* amplification and high Curie score placed him in a high-risk category, requiring intensive multimodal therapy, including chemotherapy, surgical resection, tandem autologous stem cell transplantation, as well as proton radiation therapy. This case emphasizes the critical role of urgent care providers in identifying red-flag symptoms that warrant escalation of care. While urgent care settings often manage lower-acuity conditions, providers should remain alert for variable presentations of severe disease. Early recognition and timely referral can significantly affect disease trajectory, potentially reducing complications and treatment intensity.

Presenting symptoms of neuroblastoma depend on the location of the primary tumor, presence of metastatic lesions, and systemic symptoms from catecholamine secretion.[10] For the primary tumor, an abdominal mass may be palpable. Metastatic lesions may result in the appearance of periorbital ecchymosis (raccoon eyes) or a palpable bone mass as seen in this patient. Significant eye involvement can lead to opsoclonus-myoclonus. Systemic catecholamine release by the neuroblastoma tumor itself can lead to vital sign abnormalities including prolonged hypertension and tachycardia. Given this patient's specific presentation of periorbital ecchymosis and hypertension, prompt referral to the emergency department for imaging and oncologic evaluation was essential. Increased awareness of this presentation among urgent care, emergency, and primary care providers may help reduce diagnostic delays and improve outcomes for patients with neuroblastoma.

Ethics Statement

Informed consent for publication was obtained from the patient's mother. She said she hoped that reporting about her son's condition would help others to see fewer healthcare providers before obtaining a diagnosis.

Takeaway Points

- Recurrent eye bruising or bruising without a clear cause should prompt immediate referral or ED transfer for imaging and full oncologic assessment.
- Early recognition of neuroblastoma and timely referral can significantly affect disease trajectory, potentially reducing complications and treatment intensity.
- Urgent care providers should remain alert for neuroblastoma in presentations of recurrent periorbital ecchymosis in infants without a clear traumatic mechanism. ■

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