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Case report

Hypertensive retinopathy as the initial presentation of neuroblastoma

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ABSTRACT

Purpose: To describe a case of a patient who presented with hypertensive retinopathy and was found to have neuroblastoma.

Observations: Neuroblastoma has three main ocular presentations. As a primary disease, it can present with a paraneoplastic syndrome in the form of opsoclonus, or it can present as a Horner's syndrome from its effect on the cervical sympathetic ganglia. Metastatic disease can present as a triad of periorbital edema, ecchymosis and proptosis from orbital bone involvement. Hypertension is a rare systemic presentation of neuroblastoma. We report the case of a two-year-old girl whose initial presentation of neuroblastoma was hypertensive retinopathy.

Conclusions and importance: To our knowledge, this is the first reported case of neuroblastoma presenting as hypertensive retinopathy. Our case highlights the importance of a multidisciplinary approach and thorough systemic work up of ocular findings in order to arrive at an appropriate diagnosis.

1. Introduction

Neuroblastoma is a neuroendocrine tumor that most commonly originates in the adrenal glands, but can also develop anywhere along the sympathetic nervous system in the neck, chest, abdomen or pelvis. The three main ocular presentations include opsoclonus secondary to a paraneoplastic syndrome[1]; the triad of periorbital edema, ecchymosis or proptosis from orbital bone involvement[2] and Horner's syndrome from involvement of the cervical sympathetic ganglia.[3] Both opsoclonus and Horner's syndrome usually are associated with non-metastatic disease, while orbital ecchymosis is a sign of metastatic disease. The purpose of our report is to describe an additional initial presentation of neuroblastoma in the form of hypertensive retinopathy.

Hypertension can be a manifestation of neuroblastoma, occurring in 10–27% of patients,[4,5] and frequently results from renal artery compression with resulting stimulation of the renin-angiotensin system and hyperaldosteronism, or less commonly directly from increased catecholamine secretion, which usually only causes mild elevations in blood pressure.[6] Increased catecholamine production can be seen in up to 95% of patients with neuroblastoma.[7] Hypertension can be the presenting sign of neuroblastoma. A case report in the literature describes seizures in the context of hypertensive encephalopathy as the presenting sign of neuroblastoma.[8] There has also been a report of a child with neuroblastoma presenting with severe heart failure from malignant hypertension.[9] Although there have been various presentations of neuroblastoma-induced hypertension, there are no prior reports of hypertensive retinopathy as the initial presentation.

2. Case report

A 2-year-old girl presented to the emergency room with bilateral optic nerve edema. She was referred by an outside ophthalmologist who saw the child because the mother thought the child had deterioration in her vision over the past week. She has a history of congenital left upper lid ptosis, but no significant medical or surgical history. A complete eye examination was done previously at our institution at 7 months of age and was normal except for 2 mm of left upper lid ptosis.

Eye exam upon admission showed vision was fix and follow bilaterally. Pupils were equal round and reactive without anisocoria or an afferent pupillary defect. Anterior segment examination was normal except for 2 mm of left upper lid ptosis. Dilated fundus exam showed bilateral optic disc margin blurring, nerve head elevation, disc hemorrhages, dense peri-papillary cotton wool spots, arterial narrowing and retinal exudates including a macular star in the right eye. There was no proptosis, periorbital ecchymosis or abnormal eye movements.

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Review of systems revealed that she also had significant weight loss, decreased appetite and irritability over the last five months. She was more thirsty and urinating more frequently as well. On physical exam, the emergency room physicians noted that she had cervical, auricular and inguinal lymph nodes and a palpable left upper quadrant abdominal mass. MRI of the brain and orbits with contrast showed prominence of both optic discs and the superior ophthalmic veins (Fig. 1). There were no other signs of increased intracranial pressure on MRI: there was no evidence of an empty sella, no fluid distension around the optic discs, no tortuosity of the optic nerves and no flattening of the globe. Initial blood pressure was recorded as normal (104/76 mmHg), but during the course of hospitalization, systolic blood pressure ranged from 140 to 208 mmHg and diastolic blood pressure ranged from 86 to 151 mmHg. Echocardiogram showed mild left ventricular hypertrophy, mildly depressed left ventricular systolic function and mild-moderate dilated coronary arteries.

MRI of her abdomen showed a 11 cm × 8 cm × 6 cm lobulated heterogeneous retroperitoneal mass with calcifications, which extended across the midline to the right of the upper lumbar vertebral bodies deviating the aorta and inferior vena cava anteriorly. The mass also demonstrated encasement of the left renal vessels with invasion of the renal hilum. Laboratory work up showed elevated serum normetanephrine 1678.0 pg/ml (normal 0–145.0 pg/ml) and lactate dehydrogenase 315 U/L (normal 135–225 U/L) but normal serum aldosterone 63.6 ng/dl (normal 5.0–80.0 ng/dl) and metanephrine 56.0 pg/ml (normal 0–62.0 pg/ml). Random spot urine showed elevated vanillylmandelic acid 92.2 mg/g Cr (normal <16.0 mg/g Cr), homovanillic acid 153.3 mg/g Cr (normal <25.0 mg/g Cr), norepinephrine 1269 mcg/g Cr (normal 25–210 mcg/g Cr) and dopamine 2834 mcg/g Cr (normal 86–1861 mcg/g Cr). The differential diagnosis for these findings includes neuroblastoma, pheochromocytoma and adrenal cortical adenoma. Biopsy of the abdominal mass revealed neuroblastoma tumor cells. Bone marrow biopsy did not reveal any tumor cells. The patient was transferred to another hospital for further management of the systemic disease, and was lost to ophthalmologic follow up.

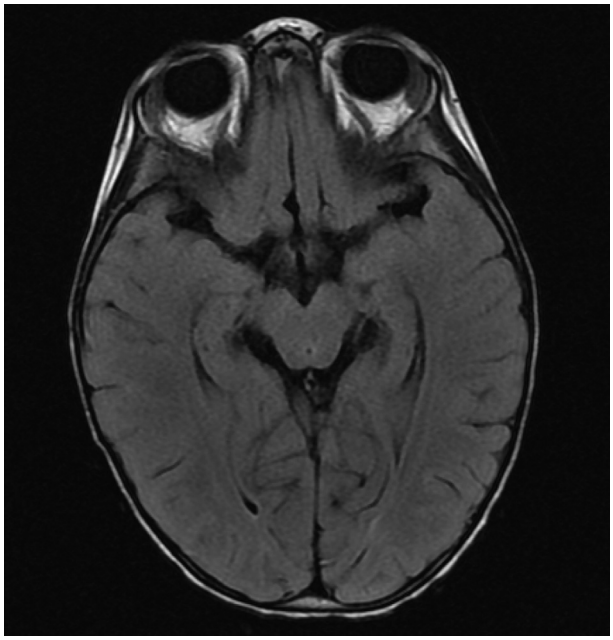

Fig. 1. Axial T1 magnetic resonance imaging of the brain and orbits with fat suppression demonstrating bilateral superior ophthalmic vein dilatation.

3. Discussion

Our patient had fundus findings consistent with accelerated malignant hypertension presenting with grade 4 hypertensive retinopathy, as outlined by the Modified Scheie Classification System.[10] Her initial blood pressure recording was within normal range, but upon repeat examination was actually consistent with malignant hypertension. Her echocardiogram also showed changes of hypertensive cardiomyopathy. Her imaging and laboratory workup confirmed the diagnosis of an adrenal gland tumor, which was confirmed to be neuroblastoma by pathologic examination. The exact cause of this child's hypertension was thought to be the increase in the catecholamine production and not compression of the renal artery by the tumor since the aldosterone levels were normal. Serum renin levels were also drawn on this child but the specimen was lost. The renin levels in this child should have also been normal since the serum aldosterone levels were normal.

There have been numerous case reports in the literature of pheochromocytoma presenting as hypertensive retinopathy with and without loss of vision,[11,12] but no cases of neuroblastoma presenting as hypertensive retinopathy. Although it was difficult to assess her vision, the presenting chief complaint according to the family was poor vision, as the family noted that she was not following targets appropriately or reliably fixating on objects directly in front of her. One other possible explanation for this child's presentation of neuroblastoma with hypertensive retinopathy is the possibility that this child harbored a mixed tumor containing neuroblastoma and pheochromocytoma cells, a very rare occurrence.[13] This tumor was extremely large and despite multiple biopsies, there is the small possibility that a focus of pheochromocytoma tumor cells may have been missed.

4. Conclusions

Neuroblastoma can present with a variety of ocular manifestations. The most commonly associated findings of primary disease are opsoclonus and Horner's Syndrome or the triad of periorbital edema, ecchymosis and proptosis in the setting of metastasis. This is the first reported case of hypertensive retinopathy as the initial manifestation of neuroblastoma.

5. Patient consent

This report was consulted with our Institutional Review Board (IRB). Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Conflict of interest

The authors have no conflicts of interest or financial interests to disclose.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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None.

Literature search

The authors have performed an extensive literature search on the Pubmed Database with search terms such as neuroblastoma and hypertensive retinopathy, retinopathy, ocular, eye, hypertension without any articles in the search engine results.

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