INDEX OF SUSPICION

Abducens Nerve Palsy in a 4-month-old Girl

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PRESENTATION

A previously healthy 4-month-old girl with a history of left torticollis, positional plagiocephaly, and nevus simplex on the left upper eyelid presents to the clinic for a health supervision visit. Over the last 2 months, her mother reports that the infant's left eye does not seem to track leftward. Review of systems is otherwise normal. She is developing appropriately and meeting her expected milestones, including bringing both hands together, laughing and vocalizing, attempting to roll, and bearing weight on both legs. She has no other known past medical history. She is not taking any medications or supplements. Her family history is normal. Her weight and length are tracking in the 80th percentile, whereas her head circumference is tracking in the 57th percentile. Physical examination is notable for right occipital flattening with anterior displacement of the right forehead and right ear. She preferentially holds her head tilted to the left and rotated to the right. Her pupils are equal, round, and reactive to light, with red reflexes present bilaterally. She turns her entire head to the left to track objects in her left temporal visual field. She is able to adduct her right eye but is unable to abduct her left eye when attending to visual stimuli on the left with her head restrained. She has normal range of motion, tone, and strength of all four extremities. She has normal symmetric patellar reflexes and upgoing plantar reflexes without ankle clonus bilaterally. She has a less than 1-cm, faintly pink blanching macule with irregular feathery borders on her left upper eyelid that has been present since birth, and she does not have any hemangiomas or port-wine birthmarks. An urgent ophthalmologic evaluation confirms the suspected abducens nerve palsy of the left eye. A magnetic resonance imaging scan of the brain and orbit reveals diffuse leptomeningeal enhancement involving the right posterior temporal, parietal, and occipital lobes with regional parenchymal volume loss.

DISCUSSION

Differential Diagnosis

The abducens nerve (cranial nerve VI) innervates the ipsilateral lateral rectus muscle, resulting in abduction of the eye. Any deficit would impair abduction unilaterally, resulting in diplopia. Causes and etiologies of abducens nerve palsy can be broadly classified into acquired or congenital causes.

Common causes of acquired unilateral abducens nerve palsies include neoplasms, trauma, and microvascular insults. Bilateral abducens nerve palsies commonly develop in the setting of increased intracranial pressure. (1) Acquired causes will typically present with other neurologic signs and symptoms depending

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on the anatomical location of the lesion. For example, concurrent symptoms of hemiparesis, ataxia, or vertigo with multiple cranial nerve deficits would suggest brainstem involvement. (1) Lethargy, meningismus, or papilledema would suggest involvement of the subarachnoid space. Recently, acute abducens nerve palsy has also been described in the setting of SARS-CoV2 infection, suggesting a direct viral infection or immunologic cause. (2)

Congenital causes need to be considered, particularly in the pediatric age group. Duane retraction syndrome (also known as co-contraction syndrome) is a congenital restrictive strabismus secondary to cranial nerve dysinnervation. (1) Individuals present with limited abduction, adduction, or both owing to co-contraction of horizontal recti muscles. (3) Moebius syndrome has been associated with nonprogressive abducens and facial nerve palsies that can improve through early rehabilitation. (4)

Mimics of abducens nerve dysfunction include diseases such as myasthenia gravis, which affects the neuromuscular junction and would be expected to cause intermittent symptoms. Disease states affecting the extraocular muscles, such as idiopathic orbital myositis or thyroid gland-associated eye disease, can result in a restrictive orbitopathy. (1) Infantile esotropia is a common condition in which the eye deviates inward and can mimic the appearance of an abduction deficit but is rarely caused by abducens nerve palsy. (5)(6) Congenital oculomotor apraxia and disorders causing delayed myelination could also present with isolated deficits in abduction, but they typically manifest with more global deficits in voluntary and purposeful eye movements. (3)

Actual Diagnosis

Ophthalmologic evaluation and neuroimaging with direct visualization of the abducens nerves did not identify an obvious cause of the patient's left abducens nerve palsy. However, the neuroimaging findings were diagnostic for type 3 Sturge-Weber syndrome (SWS).

It is still currently unclear whether there is a causative association between the patient's underlying SWS and her left abducens nerve palsy or whether the abducens nerve palsy represents an incidental finding and a "red herring" of sorts. Regardless, it highlights the importance of a thorough neurologic history and examination when evaluating a suspected cranial nerve palsy.

Condition

SWS is a rare neurocutaneous syndrome classically associated with a facial port-wine birthmark and leptomeningeal angiomatosis. It occurs sporadically and is caused by a somatic mutation in the G protein subunit α q (*GNAQ*) gene. (7) The incidence in newborns is estimated to be one in every twenty to fifty thousand live births. (8) In children who are born with a port-wine birthmark in the distribution of the ophthalmic branch of the trigeminal nerve, the risk of having SWS is estimated to be 26%. (8) Port-wine birthmarks need to be distinguished from other common vasculature malformations, including nevus simplexes, which are not associated with SWS.

Nevus simplexes will fade and regress over time, whereas port-wine birthmarks continue to grow in proportion with the child's growth and often become thicker and darker over time. The most common neurologic manifestation of SWS is seizures in the first months of life. (8) Over time, affected individuals are at increased risk for developing additional neurologic symptoms, including hemiparesis, intractable headaches, and migraines. Developmental surveillance is critical because SWS is often associated with developmental delay and cognitive impairments. Neuropsychological evaluation is also recommended given reports of higher rates of depression and development of aggressive behaviors. Additional organ system involvement includes ophthalmologic complications such as glaucoma and endocrinological abnormalities. Studies have reported an 18-fold greater prevalence of growth hormone deficiency in patients with SWS compared to the general population. (9)

SWS is divided into three subtypes. Type I, the most common, manifests with a facial port-wine birthmark involving the ophthalmic division of the trigeminal nerve and leptomeningeal angiomas. Although the location of the port-wine birthmark corresponds to the course of the trigeminal nerve, ongoing studies have now suggested that the distribution follows the embryonic vasculature of the face. (10) Type 2 presents with isolated facial angiomas. Type 3, the rarest, presents with isolated leptomeningeal angiomas. (8)(11)

Type 3 SWS presents the greatest diagnostic challenge because patients do not have the classic cutaneous or ocular manifestations such as the port-wine birthmark, venous-capillary abnormalities of the eye, or glaucoma to warrant neuroimaging. (8) Seizures are the most common neurologic manifestation of type 3 SWS in the first few months of life. (12) In the absence of seizures, diagnosis is frequently delayed until a much later age, when patients are evaluated for persistent neurologic symptoms such as headaches, migraine-like bouts, or hemianopias. (11)(13)(14)

Treatment and Management

SWS is associated with devastating neurologic impairments such as epilepsy, stroke-like episodes, visual field defects, glaucoma, and cognitive disability. (14)(15) Early diagnosis

is crucial for patients so that they can be connected with specialists and start receiving appropriate treatment and therapies. Furthermore, for the safety of the child, it is crucial that the parents are educated on how to recognize seizures, including education regarding how seizures in infants are typically subtle, with rhythmic, twitching movements, and how to appropriately use rescue medication. (14)

Previous studies have shown that seizures occur in ~75% of patients with unilateral brain involvement and ~95% of patients with bilateral brain involvement. (14) Given the high rates of epilepsy secondary to SWS, initiation of anticonvulsants before the onset of seizures is an option. Aspirin can be considered to reduce the risk of stroke-like episodes. (14) Surgical resection may be considered for patients with intractable epilepsy refractory to multiple anticonvulsants. Ophthalmologic involvement, including glaucoma, can be managed with medicated eye drops or surgical interventions. The port-wine birthmark can be treated with oral propranolol or laser therapy. Additional multidisciplinary care with physical and occupational therapy and early educational intervention is critical.

Patient Course

After the imaging findings, the patient was urgently referred to neurology. An electroencephalogram did not reveal epileptiform discharges; therefore, she was not immediately started on an anticonvulsant. However, she was given rectal diazepam to use as a rescue medication in the event of seizures. She continued to be followed by ophthalmology for her left abducens nerve palsy. She continued with physical therapy for her residual torticollis. Four months after diagnosis, she presented with her first seizure characterized by repetitive movements of the right arm, head tilt to the left, and left gaze deviation. She was started on levetiracetam at that time. She has continued to have breakthrough seizures and is now also on oxcarbazepine.

Lessons for Clinician

- Comprehensive evaluation of abducens nerve palsy should include prompt neuroimaging to evaluate for congenital or acquired causes.
- SWS should be included in the differential diagnosis when evaluating infants with a variety of neurologic or ophthalmologic presentations (gaze palsy, hemiparesis, glaucoma), even in the absence of a facial port-wine birthmark or seizures.
- Type 3 SWS presents the greatest diagnostic challenge because patients do not have the typical cutaneous or ocular manifestations.

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