CASE PRESENTATION:

SEPTO-OPTIC DYSPLASIA

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Abstract

This is a case report of a child diagnosed with septo-optic dysplasia. The terms septo-optic dysplasia and deMorsier's syndrome have been used to encompass a variety of clinical findings in patients with bilateral optic nerve hypoplasia in conjunction with a spectrum of midline brain anomalies. This case is presented to demonstrate the significant findings associated with this syndrome.

Key Words

septo-optic dysplasia, deMorsier's syndrome optic nerve hypoplasia, corpus collosum

In 1956 deMorsier first described septo-optic dysplasia as a pathologically distinct entity. It is characterized by an absent or hypoplastic septum pellucidum, partial or complete agenesis of the corpus collosum, a primitive optic vesicle, and dysplasia of the optic nerve, chiasm and optic tracts.[1] The association of septo-optic dysplasia and hypopituitary dwarfism was first reported by Hoyt and associates in 1970.[2] A wide variety of pituitary hormone deficiencies have since been identified in patients with septo-optic dysplasia.[3] Over the last decade, magnetic resonance imaging (MRI) has emerged as a sensitive diagnostic tool for delineating subtle congenital central nervous system malformations.[4,5] The use of MRI's in patients with septo-optic dysplasia has shown such central nervous system anomalies as schizen-cephaly, posterior pituitary ectopia, and infundibular hypoplasia.[5] The terms septo-optic dysplasia and deMorsier's syndrome have been used to describe a variety of clinical conditions in patients with bilateral optic nerve head hypoplasia in conjunction with a spectrum of midline brain defects with or without endocrine abnormalities.[6]

CASE PRESENTATION

A 1-year-old male infant presented to the University Optometric Center's Infant Vision Clinic at the State University of New York, State College of Optometry for a second opinion regarding poor vision and nystagmus. The child had been evaluated by an ophthalmologist at the age of 5 months and informed the parent that the child was partially blind.

History

The pregnancy was reported to be normal until the 7th month when sonogram testing indicated hydrocephalus. The child was delivered full term by scheduled Caesarian section. The birth weight was 5 pounds 11 ounces. A CAT scan and MRI were performed within the first week of life. Hydrocephalus and agenesis of the corpus collosum were diagnosed. The patient had major developmental delays in all areas. A flaccid muscle tone was noted to be more pronounced on the left side than the right side of the body.

Optometric Evaluation

Pendular nystagmus was evident in both eyes. The patient displayed an alternating esotropia (25Δ to 40Δ) with a hyper component (2Δ to 6Δ), with a preference for OD fixation. Cycloplegic refraction revealed +7.50 –0.50 x 180 in each eye. Visual acuity attained by forced preferential looking (FPL) was 20/710 OU using Teller Acuity cards. The child could localize a transilluminator target when presented in each field; however, the response to the stimulus was delayed.

Pupillary responses were present, but sluggish. The external and anterior segment examinations were unremarkable. The dilated fundus examination revealed a clear media in each eye. The discs were gray and hypoplastic with moderately defined margins. Disc pallor was also noted in each eye. The artery to vein ratio was 1:2 and there was mild tortuosity of the vessels in each eye. The diagnoses was hypoplastic discs and hyperopia. A prescription of +6.00 spheres was recommended for full-time wear.

The parent reported improvements in the child's visual awareness at follow-up examinations performed at 13 months of age and 18 months of age. The prescription of +6.00 spheres was worn full time. Upon examination the patient readily fixated and followed a transilluminator target. At the age of 18 months marked developmental delays were still evident, i.e., unable to sit without support and unable to walk.

A VEP performed at the age of 3 years showed no response to pattern, and an abnormal response to flash. The visual acuity was estimated to be between 20/400 to 20/1000.

Our last follow-up examination was performed when the patient was 3 years 11 months old. The patient was able to fixate and follow both a penlight and a small toy. The visual acuity was measured as 20/300 by FPL using Cardiff Cards at 50 cms. A reliable response could not be obtained using the Teller Acuity cards.

The patient is followed on a regular basis by both his pediatrician and a neurologist. At the time of our last examination the patient's medical history was positive for asthma. A gastric tube had been surgically implanted because the child aspirated on both liquids and solids. Severe developmental delays were present. The patient was still unable to sit unsupported, and was not talking. No endocrine abnormalities have been noted.

The patient has been diagnosed with Septo-optic dysplasia.

DISCUSSION

Septo-optic dysplasia represents a spectrum of midline developmental anomalies that include optic nerve hypoplasia and possible endocrine abnormalities. Common usage of the term today includes three well-documented subgroups: 1) Patients with optic nerve hypoplasia, endocrine abnormalities and normal midline brain anatomy on CT scanning. 2) Patients with optic nerve hypoplasia, midline brain anomalies and normal endocrine function. 3) Patients with optic nerve hypoplasia, endocrine abnormalities and midline brain anomalies.[7,8]

The case presented is an example of the second subgroup. The patient has bilateral optic nerve hypoplasia, agenesis of the corpus collosum, a midline brain anomaly, and normal endocrine function.

It has been presumed that those patients in the first group actually do have brain midline structural anomalies, but are below the resolution of the CT scan.[8] A study done by Kaufman and associates using MR imaging of these patients failed to visualize the pituitary stalk.[8] This discrete midline brain anomaly of pituitary stalk hypoplasia has been further evidenced in studies by Zeki,[9] and by Brodsky[5] of patients with septo-optic dysplasia and endocrine abnormalities.[5,9] Until the use of MR imaging, it was not known whether patients within the first subgroup of optic nerve hypoplasia, endocrine abnormalities and normal midline brain anatomy on CT scanning had endocrine disturbances secondary to a functional or structural defect.[8] The MRI results demonstrating pituitary stalk hypoplasia or posterior pituitary ectopia support the theory that the endocrine sequelae in septo-optic dysplasia are indeed secondary to abnormal midline brain anatomy.[8]

Theories

The etiology of septo-optic dysplasia is due to an unknown pathological process that interferes with normal embryologic midline brain structure.[8] The extent of anatomical disruption is dependent upon the severity of this process.[8] Optic nerve hypoplasia is associated with all subgroups of septo-optic dysplasia. Consequently the pathological process involves the optic nerves, the optic chiasm and the optic tracts. If the insult extends superior to the chiasm, the septum pellucidum, corpus collosum or the third ventricle could be affected.[8] Endocrine disturbances result if the hypothalamus, pituitary stalk or pituitary gland is involved in the anatomic disruption.[8]

There are several theories regarding the pathological process. Since all the tissues involved arise from different precursor stem cells, a primary agenesis is unlikely to be the cause.[8] The "Developmental Theory" suggests that some type of interference such as teratogenic, genetic or traumatic insult effects the normal development of the optic nerves, septum pellucidum, corpus collosum and hypothalamus.[7,8] This occurs approximately six weeks into gestation which coincides with the active development of these structures.[7,8]

The "Destructive Theory" is presently favored. It suggests some type of intrauterine pathologic process that destroys the brain tissue, and occurs after the anatomy has already been established.[7,8] Lubinsky recently proposed a theory that the constellation of findings in septo-optic dysplasia is best explained by a vasculopathic event occurring early in embyrogenesis, and results in an interruption of the normal development of the optic nerves, and adjacent midline structures.[10]

Clinical Points

a. Risk Factors
   Septo-optic dysplasia has been associated with young mothers,[8,11] and is more prevalent in first born children.[11,12] Familial occurrence is rare, but may have the possibility of autosomal recessive inheritance.[11] Our patient's mother was under the age of 25 when the child, her first, was born. There was no family history of this syndrome.

b. Optic Nerve Hypoplasia
   Ophthalmospic findings are significant. Bilateral optic nerve hypoplasia (ONH) is a hallmark sign of this condition. A definite diagnoses of ONH can be made by the appearance of the disc. In ONH the disc is small, approximately one third to one half the normal size.[13] The nerve head is often pale and is usually surrounded by a grey to yellow peripapillary zone which may contain granular pigments.[13,14] This appearance is referred to as a "double ring sign".[13,14] Hypoplasia of the optic nerve is a developmental anomaly in which there is a subnormal number of axons.[13] Depending upon the degree of maldevelopment of the nerve fiber layer, visual acuity can vary from near normal to no light perception.[13,14]

c. Visual Sequelae:
   The majority of patients with bilateral ONH have severe visual impairment.[11] Depending on the severity, patients can have an absent pupillary light response,[11,14] nystagmus and strabismus.[9,11,14] Siatkowski and associates found significant visual problems in 35 patients with bilateral optic nerve hypoplasia: 86 % were legally blind, 85 % had nystagmus and 52% had strabismus.[6] Studies report variability among refractive error in children with septo-optic dysplasia. Weiss and Ross reported axial myopia greater than 4 di-

opters in 23% of children with bilateral ONH[15] and Zeki found astigmatism to be common.[16]

The study by Siatwaksi demonstrated 50% of the 35 patients to have no light perception; however, 19 of the 35 patients were also under 1 year of age.[6] The possibility of delayed maturation of vision with subsequent visual improvement must be considered.[6] For example, in a study of 11 patients who presented as blind in early infancy, eight demonstrated improved visually guided behavior and measurable grating acuity by age 5. Of the 11 patients in that study five had Leber's congenital amaurosis, four had ONH and two had macular colobomas.[17]

Our patient showed an improvement in visual awareness from the initial examination performed at 1 year of age to the last exam performed when the child was 3 years 11 months (47 months) of age. Although our patient still demonstrated very reduced visual acuity, the fact that some vision did exist is an important factor that will have an impact on the child's development and education. Our patient receives speech therapy, occupational therapy and physical therapy on a regular basis. Visual stimulation techniques have been attempted to be incorporated into the child's therapy. It is important to also remember that these children will do better with reduced stimuli and a controlled environment. They will have a slow response time and operate at near. Also important is the determination and correction of any significant refractive errors. Our patient was significantly hyperopic and the parent noted improvement in the child's visual awareness with the use of spectacles.

d. Neurological Sequelae

The neurological features of septo-optic dysplasia can include mental retardation, spasticity, abnormalities of taste and impaired olfaction; however, some individuals may exhibit only minor defects with normal intelligence.[9] A study by Margalith of 51 patients with severe bilateral ONH found a high prevalence of cerebral palsy 57%, mental retardation 71%, epilepsy 37% and behavioral problems 20%.[7] Brodsky and Glacier's study of 40 patients with severe bilateral ONH further supports the wide clinical spectrum seen with septo-optic dysplasia. Central nervous system abnormalities determined by MR imaging were seen in 75% of these patients.[5] Brodsky and Glacier further divided these patients into five subgroups. Group One (25%) was patients with isolated ONH, Group Two (53%) consisted of patients with ONH and absence of the septum pellucidum, Group Three (15%) was ONH with posterior pituitary ectopia, Group Four (20%) was ONH with hemispheric migrational abnormalities, and Group Five (25%) was ONH with intrauterine/perinatal hemispheric injury.[5] The patients in groups three, four and five were much more likely to have pituitary hormone deficiency and neurodevelopmental deficits ranging from developmental delays to mental retardation.[5] The isolated absence of the septum pellucidum was associated with normal neurodevelopment and endocrinologic function.[5] Brodsky and Glacier also concluded that thinning or agenesis of the corpus collosum was also predictive of neurodevelopmental delays due to its frequent association with cerebral hemispheric abnormalities.[5]

Our patient demonstrates severe developmental delays, and an agenesis of the corpus collosum. This correlates with the findings of Brodsky and Glacier that thinning or agenesis of the corpus collosum is predictive of neurodevelopmental delays. The corpus collosum is the major white matter tract concerned with interhemispheric transfer and integration of information.[5]

e. Endocrine Sequelae

Endocrine abnormalities can vary with the diagnoses of septo-optic dysplasia from no endocrine abnormalities to panhypopituitarism. Arlanian and associates found the most common pituitary abnormality to be a deficiency of growth hormone.[18] Other endocrine abnormalities found in patients with septo-optic dysplasia are a deficiency in adrenocortico hormone, anti-diuretic hormone with diabetes insipidus and/or thyroid stimulating hormone.[11]

Children with hypopituitarism can be symptomatic from birth by having severe hypoglycemia and seizures.[19] The neonate with septo-optic dysplasia may also exhibit prolonged jaundice and episodes of hypothermia associated with hypoglycemia.[19]

It has been noted by Brodsky that some children with septo-optic dysplasia and hypopituitarism are at a higher risk of premature death.[19] Brodsky reports five cases of children who died suddenly during a febrile illness. The deaths were primarily due to an inability of the children to increase corticotropin secretions in response to the stress on their bodies from the illness. This resulted in the children not being able to maintain adequate blood pressure and blood glucose levels.[19] The children with both malfunctioning anterior and posterior portions of the pituitary gland appear to be the most at risk.[19] Sherlock and McNicol have also noted that subclinical hypopituitarism can manifest as acute adrenal insufficiency following surgery with general anesthesia. This is another factor that must be considered in this population of children with septo-optic dysplasia, especially when considering strabismus surgery.[19,20]

Our patient had not presented with any endocrine deficiencies; however, it is important that his growth be monitored carefully. Several cases have documented that growth deficiencies can manifest in older children. One study followed a child from 18 months of age who manifested failure to grow at 6 years of age.[21] The other case followed from birth manifested growth retardation at the age of 9 years.[21] In both cases, the endocrine work-ups revealed a growth hormone deficiency.[21] Siatkowski, et al, have recommended that children 24 months or older, with bilateral ONH and normal growth and development, still be sent for a consult with a pediatric endocrinologist to ensure adrenal insufficiency, if present, does not go undiagnosed.[6]

CONCLUSION

The term septo-optic dysplasia is used to describe a wide variety of clinical conditions in patients with bilateral ONH, and a spectrum of midline anomalies that may or may not be accompanied by endocrine abnormalities. Our case exemplifies bilateral ONH and agenesis of the corpus collosum. This case is presented to demonstrate the significant findings associated with this syndrome. It is important to be aware of the blind child that presents with bilateral ONH, and the systemic anomalies that may accompany it. The cli-

nician must be able to make appropriate referrals, if necessary to determine the child's neurologic and endocrinolgic status.

The pediatric optometrist will most likely not be the first healthcare provider to examine the patient. Most of these patients will have already been seen by their pediatrician, and a neurologist. However, as in our case, the patient may present for a second opinion regarding the child's visual prognosis. Parents will want to know what their child sees, and if anything can be done to improve the vision. Information regarding the child's vision is an important factor in developing programs to aid in the education and therapy of the child. Therefore, an optometrist can be a valuable member of the child's rehabilitative team, which may include occupational therapists, physical therapists and speech therapists.

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