Ophthalmic association of De Morsier syndrome- A Case Report

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Abstract

Introduction : *De Morsier syndrome is a rare genetic disorder. Common presenting features are optic nerve hypoplasia, pituitary dysfunction and midline brain abnormality. Other features may include generalized growth retardation, short stature, microglossia, megalostomia, strabismus, visual field defect, hypothyroidism, hypoprolactinemia and mental retardation.*

Care report : *A 15 years old female presented with alternate exotropia since childhood and gradual blurred vision for the last five months. On examination unaided vision was 6/18p in each eye. Aided vision was 6/9p with -2.50 DS in right eye and 6/12 with -1.75 DS / -0.50 Dcyl x90® in left eye. Anterior segment reveals normal. Fundus showed double ring sign of optic disc in either eye. Intraocular pressure was 09 mm of Hg in right eye whereas 10 mm of Hg in left eye. She had alternate exotropia of 55prism diopter with spectacle .Ocular motility showed -1 restriction in adduction in each eyes. Stereopsis was absent. Colour vision was 11/24 in either eye by pseudo isochromatic ishihara test. Physical examination revealed megalostomia, microxanthia. She was mentally retardate and short stature. Height was 156 cm whereas weight was 119 kg which indicate that she was suffering from obesity. Besides she had menstrual abnormality, hearing defect, palpitation, cardiac problem and insomnia.*

Conclusion: *Out of three diagnostic criteria, the patient has optic nerve hypoplasia and pituitary dysfunction. It represents that it may be a case of De Morsier syndrome. To understand full spectrum of presentation is important for early diagnosis, management, genetic counseling and provide better visual future.*

Introduction

De Morsier syndrome is a rare genetic malformation syndrome featuring underdevelopment of the optic nerve, pituitary gland dysfunction and midline brain abnormality. Two of these features need to be present for a clinical diagnosis. Only 36% of patients have all three features.[1]

The first major feature, optic nerve hypoplasia, is the underdevelopment of the optic nerves, which carry visual information from the eyes to the brain. Underdevelopment of optic nerve is evident by smaller sized optic disc and double ring sign. In affected individuals, the optic nerves are abnormally small and make fewer connections than usual between the eyes and the brain. As a result, people with optic nerve hypoplasia have impaired vision in one or both eyes.[2] Vision ranges from normal vision to complete blindness. Optic nerve hypoplasia can also be associated with significant ophthalmic manifestation like

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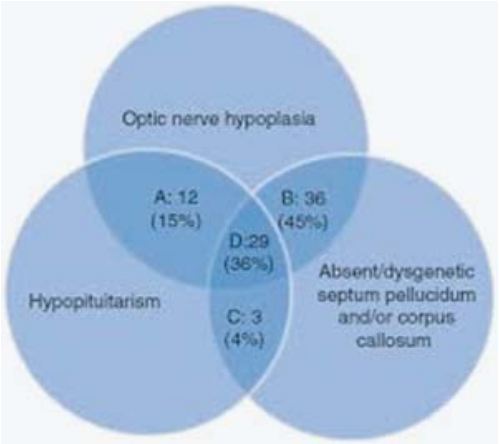
strabismus, refractive error and nystagmus which appears by 1-8 months of age.



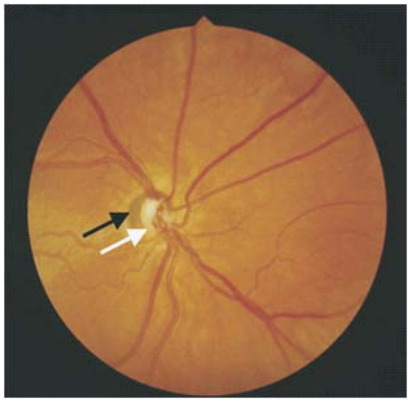


Fig: Double ring sign of optic disc

The second characteristic feature of De Morsier syndrome is the abnormal development of structures separating the right and left halves of the brain. These structures include the corpus callosum, which is a band of tissue that connects the two halves of the brain, and the septum pellucidum, which separates the fluid-filled spaces called ventricles in the brain. In the early stages of brain development, these structures may form abnormally or fail to develop at all.[3] Depending on which structures are affected; abnormal brain development can lead to intellectual disability and other neurological problems.

The third major feature of this disorder is pituitary hypoplasia. The pituitary is a gland at the base of the brain that produces several hormones. These hormones help control growth, reproduction, and other critical body functions. Underdevelopment of the pituitary can lead to a shortage (deficiency) of many essential hormones. Most commonly, pituitary hypoplasia causes growth hormone deficiency, which results in slow growth and unusually short stature. Severe cases cause panhypopituitarism, a condition in which the pituitary produces no hormones. 3 Panhypopituitarism is associated with slow growth, low blood sugar (hypoglycemia), genital abnormalities, and problems with sexual development.

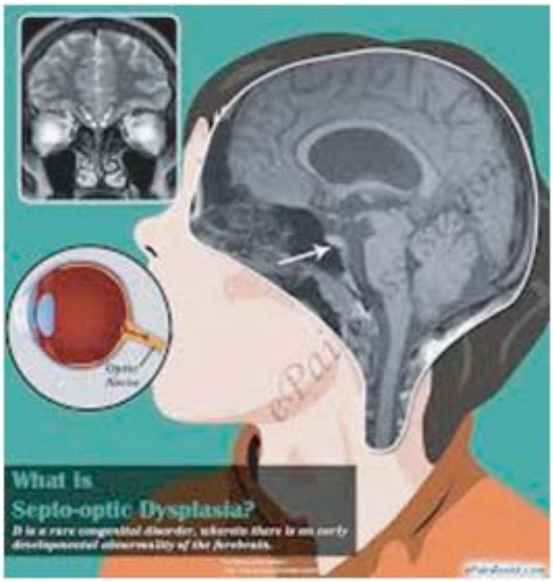


Fig: Features of De morsier syndrome

The signs and symptoms of De Morsier syndrome can vary significantly. Some researchers suggest that septo-optic dysplasia should actually be considered a group of related conditions rather than a single disorder. About one-third of people diagnosed with septo-optic dysplasia have all three major features; most affected individuals have two of the major features. In rare cases, septo-optic dysplasia is associated with additional signs and symptoms, including recurrent seizures (epilepsy), delayed development, and abnormal movements. Associated anomalies are cleft palate, neuro sensory hearing defect, congenital heart defect, digital defect, intestinal malformation, renal agenesis, colour blindness.

Case Report

A 15 years old female presented with alternate exotropia since childhood and gradual blurred vision for the last five months. On examination unaided vision was 6/18p in each eye. Aided vision was 6/9p with -2.50 DS in right eye and 6/12 with -1.75 DS / -0.50 Dcyl x90® in left eye. Anterior segment reveals normal. Fundus showed double ring sign of optic disc in either eye .Intraocular pressure was 09 mm of Hg in right eye whereas 10 mm of Hg in left eye. She had alternate exotropia of 55prism diopter with spectacle .Ocular motility showed -1 restriction in adduction in each eyes. Stereopsis was absent. Colour vision was 11/24 in either eye by pseudo isochromatic ishihara test. Physical examination revealed megalostomia, microxanthia. She was mentally retardate and short stature. Height was 156 cm whereas weight was 119 kg which indicate that she was suffering from obesity. Besides she had menstrual abnormality, hearing defect, palpitation, cardiac problem and insomnia.

Fig: Microxanthia & Megalostomia

Fig: Obesity

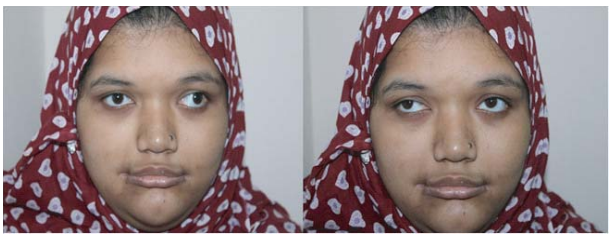


Fig: Alternate exo deviation

Investigation

The patient was investigated for serum hormonal level, Computerized tomography scan of brain, echocardiogram, ultrasonography of whole abdomen and Humphrey visual field analysis. The reports were following:

Serum thyroid stimulating hormone level: 0.25ng/ml (0.39-6.61 mg/ml)

Serum prolactin level: < 1.6 ng/ml (2-29 ng/ml)

Serum cortisol level: < 115 nmol/L (140-700 nmol/L)

Computerized tomography scan of brain reveals normal

Visual field of right eye is normal and left eye show superior altitudinal field defect.

Ultrasonography of whole abdomen show no renal agenesis and intestinal malformation.

Echocardiogram shows congenital heart disease.

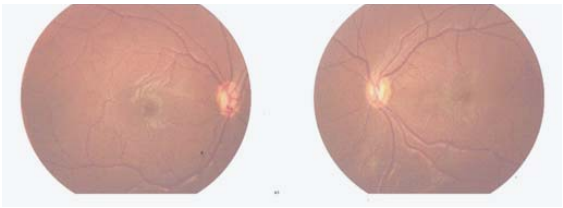


Fig: CFP showing optic disc hypoplasia with double ring sign

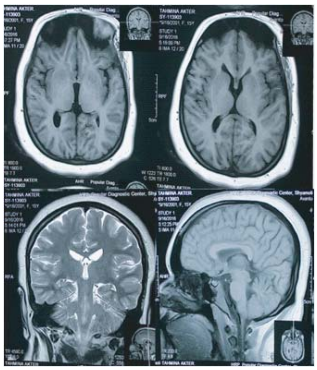


Fig: MRI of brain showing normal midline brain structures

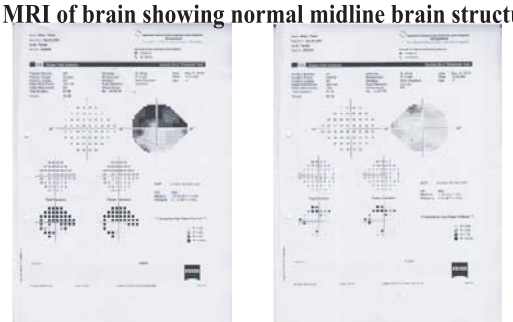


Fig: superior altitudinal field defect (Left)

Fig: Normal visual field (Right)

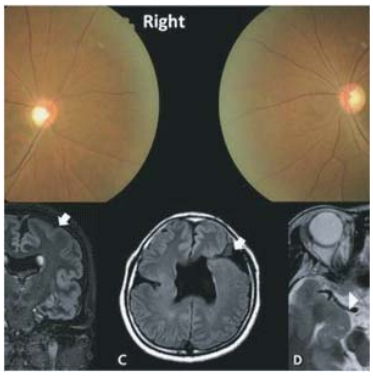
From above investigation it showed that the girl had optic nerve hypoplasia and pituitary dysfunction. Based on the characteristic systemic, ophthalmic finding and investigation reports it was revealed that it was a case of De Morsier Syndrome

Treatment

Refractive correction was given to the patient along with the advice for strabismus surgery. She was referred to retina specialist for evaluation of optic nerve hypoplasia. Consultation by neuro-ophthalmologist was done and referred to multi-disciplinary center for endocrine, gynecological and cardiac management.

Discussion

Septo-optic dysplasia is a rare phenotypically variable genetic malformation. Typical features of this rare syndrome are optic nerve hupoplasia, pituitary gland dysfunction and abnormality of the structures in the midline brain.



It is a sporadic birth defect of unknown etiology. It is commonly associated with young maternal age, valproate toxicity in utero. Genetic study shows mutation in HESX1, OTX2, SOX2 and PAX6 gene. It does not recur with subsequent pregnancy.[4]

Optic nerve hypoplasia is characterized by diminished number of nerve fibers. Predispositions include specific agents used by the mother during gestation such as excess alcohol, LSD, quinine, protamine zinc insulin, steroids, diuretics, cold remedies and anticonvulsant.[5] Less severe bilateral involvement may cause minor visual defects or squint at any time of childhood.

One of the important features of optic nerve hypoplasia is double ring sign; Small gray disc surrounded by a yellow halo of hypopigmentation caused by concentric chorioretinal atrophy; the outer ring represents what would have been the normal disc margin. The distance from the fovea to the temporal border of the optic disc often equal or exceed three times the disc diameter – this strongly suggest disc hypoplasia.[6] Other features include astigmatism, field defect, dyschromatopsia, foveal hypoplasia, strabismus, nystagmus.

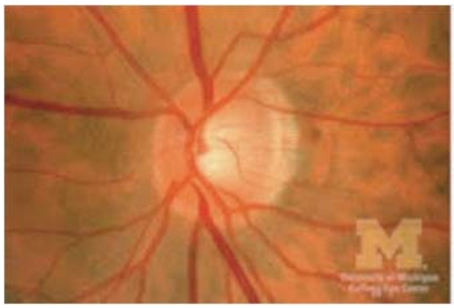


Fig: Double ring sign of optic disc

Midline brain abnormality includes absence of septum pallucidum, thinning or agenesis of the corpus callosum. Agenesis of septum pallucidum leads to holoprosencephaly, schizencephaly and seizure.

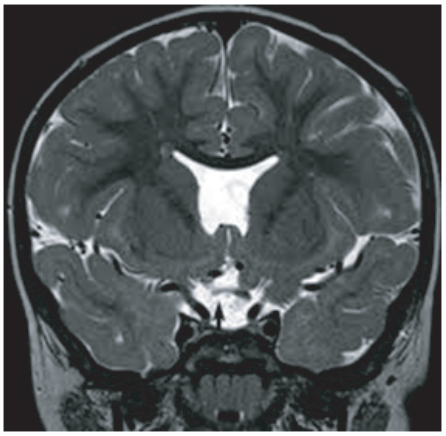


Fig: MRI of brain showing absence of septum pellucidum

Hypopituitarism with low growth hormone level is common. If recognized early; the hormone deficiency can be corrected and normal growth resumed. It has been suggested that retinal venous tortuosity in patients with bilateral optic nerve

hypoplasia may be a marker for potential endocrine dysfunction.[7]

A lifelong multidisciplinary approach is required to optimize growth and development and to lead as normal life as possible. Hormone replacement for hormone deficiency, spectacle correction for refractive problem, low visual aid for severe ocular morbidity, physical and occupational therapy are recommended for better life expectancy for this type of patient.

Conclusion

De Morsier syndrome remains a rare, heterogeneous and phenotypically variable disorder which can pose significant challenges due to delay in diagnosis, late development of hormonal deficiencies and the presence of other phenotypically features such as obesity and autism. Ophthalmic association makes the life critical along with other systemic manifestation. Early detection can provide better visual future.

Understanding the full spectrum of presentation is also important for early diagnosis and management of the patient. Genetic study of such a rare case is not only important to understand the etiology of the disease but also aids patient management, enabling accurate genetic counseling and early diagnosis. Careful longitudinal follow up of large patient cohort enable the development of more accurate diagnostic criteria and ongoing management plan.

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