Residência RP Pediátrica
Publicação Oficial da Sociedade Brasileira de Pediatria
ISSN-Online: 2236-6814

Submitted on: 09/21/2023
Approved on: 01/15/2024

CASE REPORT

Septo-optic dysplasia: a case report on Morsier Syndrome

Marina Bonagurio Julio[1], Brenna Marques Amorim Tenorio[1], Helen Vinco Secchin[2], Juliana Brizzante Ferreira[1], Marina Dall'Ara de Souza[1]

Keywords:
Case reports,
Optic nerve hypoplasia,
Neonatology,
Septo-optic dysplasia.

Abstract

Introduction: Septo-optic dysplasia, also known as Morsier Syndrome, is considered a rare congenital disease, with an estimated incidence of 1 in every 100,000 live births and is characterized by the triad: midline defects (corpus callosum agenesis and/or septum pellucidum), optic nerve hypoplasia and hormonal abnormalities of the hypophysis. The clinical changes of the disease are varied, which makes the diagnosis a challenging, but essential to reduce the high morbidity associated with the disease. **Goal:** Report a case of septo-optic dysplasia syndrome and how it came to be diagnosis. **Case report:** Male patient, born in a maternity hospital in city of São Paulo, with changes in the initial physical examination: micropenis, macrocrania and nystagmus. The neonatology team questioned the presence of any syndrome. As part investigation of malformations, requested an ophthalmological evaluation that identified bilateral optic nerve hypoplasia. Other findings were hormonal abnormalities of the pituitary glands and, therefore, two of the diagnostic criteria for Morsier Syndrome. **Final considerations:** The pediatrician must be capable of clinical diagnostic reasoning of rare syndromes, as he is the first professional who has contact with the patient, in order to initiate early intervention, reducing associated morbidities.

[1] Hospital São Luiz Gonzaga, Pediatria - São Paulo - São Paulo - Brazil.
[2] Instituto Nacional de Saúde da Mulher, da Criança e do Adolescente Fernades Figueira (IFF - FIOCRUZ), Neonatologia - São Paulo - São Paulo - Brazil.

Correspondence to:
Marina Bonagurio Julio.
Hospital São Luiz Gonzaga. R. Michel Ouchana, 94 - Jaçanã, São Paulo - SP, 02276-140. E-mail: m.arinabonaj@gmail.com; m.arinabona@hotmail.com

Resid Pediatr. 2024;14(4).
DOI: 10.25060/residpediatr-2024.v14n4-1168

This work is licensed under a Creative Commons Attribution 4.0 International License.

INTRODUCTION

Septo-optic dysplasia, also known as Morsier's syndrome, is a rare congenital disease with an estimated incidence of 1 in every 100,000 live births that equally affects both sexes. [1]

The disease features a triad of findings that includes midline abnormalities (agenesis of the corpus callosum and septum pellucidum), optic nerve hypoplasia, and pituitary hormone abnormalities. Diagnosis requires at least two of the three. It may be suspected and diagnosed based on clinical alterations at birth, as reported below, or later in children with short stature and other endocrine-metabolic and visual disorders. [1]

The main clinical alterations are dysgenesis of the corpus callosum, schizencephaly, microphthalmia, anophthalmia, strabismus, optic nerve hypoplasia, precocious or delayed puberty, micropenis, autism, and cardiac and skeletal malformations. Diagnosis can be confirmed by ophthalmological examination, magnetic resonance imaging of the skull, and pituitary hormone assessment. [2, 3, 4]

Clinical and imaging presentations vary and relate to the type and extent of associated abnormalities. Intrauterine diagnostic examination with transfontanellar ultrasound may be required to allow early intervention and decrease the morbidity associated with the disease. [5, 6]

CASE REPORT

The patient was a male infant born at full term at Hospital São Luiz Gonzaga (HSLG - SP) by cesarean section due to arrest of descent during the second stage of labor and macrosomia. His mother was a woman of advanced maternal age in her third pregnancy with no complications in past pregnancies. She had two healthy children from the same father. The mother and father were not related by blood. She started prenatal care at two months of pregnancy and went to nine consultations, with negative serologies for hepatitis B, hepatitis C, syphilis, and HIV. She had a urinary tract infection treated in the first trimester of pregnancy, with no history of alcohol or drug use. The infant was born with an APGAR score of 5/7, requiring neonatal resuscitation. He was referred to a neonatal intermediate care unit.

Early physical examination found the patient had a micropenis, macrocrania, and nystagmus. He was in respiratory distress in the delivery room and required CPAP for two days. He remained on oxygen therapy with a nasal catheter for 110 days. The patient also had prolonged jaundice and underwent phototherapy for seven days.

Evaluation for ophthalmic alterations identified bilateral optic nerve hypoplasia. Morsier's Syndrome was then considered a diagnostic possibility.

The neonatology team proceeded with the investigation:

1) Karyotype: 46, XY;
2) Laboratory tests were performed for the early detection of panhypopituitarism, as listed in Table 1:

Table 1. Laboratory tests performed during hospitalization in the neonatal unit.

	First week of life	2 months of age
Dehydroepiandrosterone	4.7 ng/mL (RV <3.5 ng/mL)	-
Dihydrotestosterone	269 pg/mL (RV 250 – 990 pg/mL)	-
T3	96 ng/dL (RV 100-470ng/dL)	-
Free T4	0.76 ng/dL (RV 0.65-2.4 ng/dL)	-
TSH	2.98 mIU/mL (VR 0.8-9.2 mIU/mL)	6.69 mIU/mL
T4	-	4.3 ng/dL
Thyroglobulin	-	25.43 ng/mL
LH	<0.07 mIU/mL (VR <0.3 mIU/mL)	<0.07 mIU/mL
FSH	<0.3 mIU/mL (VR <0.9 mIU/mL)	0.4 mIU/mL
Testosterone	<10 ng/dL (VR <60 ng/dL)	<10 ng/dL
Serum cortisol	1.2 mg/dL (VR 4-22 mg/dL)	13.2 mg/dL
GH	2.81 mg/L (VR <3mg/L)	3.74 mg/L
Adrenocorticotropic hormone	-	15.4pg/mL (5-46 pg/mL)

3) The patient was referred to Hospital Santa Marcelina for an ENT evaluation and was diagnosed with type I laryngomalacia, with no treatment prescribed;
4) Imaging tests performed: ultrasound of the kidneys and urinary tract without alterations; transthoracic echocardiogram found of a 4mm ostium secundum atrial septal defect, with flow directed from the left atrium to the right atrium and indirect signs of pulmonary hypertension; transfontanellar ultrasound without alterations; computed tomography of the skull and sella turcica without alterations; total abdominal ultrasound without alterations.
5) The patient required prolonged enteral nutrition, and a gastrostomy was performed at three months of age due to low weight gain and difficulty sucking.

The patient was discharged at four months of age (116 days) with a recommendation of ad libitum breastfeeding, a prescription of hydrolyzed protein formula, 2 drops/day of Adtil, 5 mcg/kg/day of levothyroxine, and 10 mg/m² of hydrocortisone. He was provided follow-up care at the pediatric hepatology, endocrinology, ophthalmology, and otolaryngology services.

The patient was hospitalized multiple times for recurrent respiratory conditions and wheezing and was lost to follow-up. At the age of six months, he was admitted to Hospital São Paulo with bronchiolitis, where he was evaluated by the genetics team and referred for outpatient follow-up, where he is currently being treated.

Figure 1 shows a magnetic resonance imaging scan of the skull without alterations, revealing the location and morphology of the pituitary gland, which is compared with a scan of the patient at nine months of age (Figure 2) without the typical T1 signal hyperintensity in the sella turcica, but with signal hyperintensity in the floor of the third ventricle, in the region of the median eminence, anterior to the mammillary bodies, measuring 0.3 cm, possibly an ectopic pituitary gland, with the corpus callosum, septum pellucidum, and optic nerves showing a typical morphology.

A recent physical examination showed the patient had delayed global development, plagiocephaly, a prominent forehead, bilateral nystagmus, limited pronation of the elbows, joint hypermobility (possibly secondary to hypotonia), and a micropenis. He is awaiting a follow-up visit with a geneticist to evaluate the possibility of performing a magnetic resonance imaging of the sella turcica with paramagnetic contrast. The patient remains on continuous use of medication. His family is having trouble keeping up with the follow-up visits with specialists.



Figure 1. RMagnetic resonance imaging scan of the skull without alterations. The arrow indicates the location of the pituitary gland. Image taken from https://doi.org/10.53347/rID-17529. Accessed on 09/29/2023. [5]

DISCUSSION

Morsier's syndrome, or septo-optic dysplasia, is a rare congenital disease first described in 1941 by Reeves and later studied by neurologist George de Morsier, receiving the name Morsier Syndrome. Information about this condition must be disseminated since individuals diagnosed with it may suffer significant developmental impairments. [7]



Figure 2. Sagittal T1 section of the patient's magnetic resonance imaging scan of the skull from 10/13/2022. Absence of the typical T1 signal hyperintensity in the sella turcica. Signal hyperintensity in the third ventricle floor, in the median eminence region, anterior to the mammillary bodies, measuring 0.3 cm, possibly an ectopic pituitary gland.)[5]

Diagnosis can be made based on suspicious clinical alterations and imaging exams with the presence of at least two of the three following signs: midline abnormalities (agenesis of the corpus callosum and septum pellucidum), optic nerve hypoplasia, and pituitary hormone abnormalities. The three components appear in 30% of cases, with hypopituitarism and absence of the septum pellucidum being the most common findings. [7]

Genes involved in the embryonic development of the optic nerves, eyes, and pituitary gland (HESX1, SOX2, SOX3, and OTX2) have been related to the emergence of septo-optic dysplasia. However, the etiology is likely multifactorial. Familial cases comprise less than 1% of the cases of the disease. [1, 2]

The prenatal risk factors associated with Morsier's syndrome include maternal alcohol and drug use during pregnancy, maternal viral infections, gestational diabetes, young maternal age, primiparity, and prematurity. [8]

Clinical manifestations can vary from absent to severe, which makes diagnosis difficult. They include hypoglycemia, jaundice, micropenis with or without cryptorchidism, nystagmus, hypotonia, spasticity, and midline abnormalities. Metabolic disorders, mainly hypoglycemia and hypernatremia, may cause seizures and developmental delay. In older children, short stature is a significant indication of disease. [4, 5, 9]

Midline abnormalities vary and include agenesis of the corpus callosum, absence of the septum pellucidum, cerebellar hypoplasia, fornix aplasia, and schizencephaly. These alterations are present in up to 75-80% of patients and in as many as 90% when associated with neurologic deficits. [9, 10, 11]

Having an ectopic posterior pituitary gland has been correlated with pituitary hormone deficiency. [9] Growth

hormone (GH) abnormalities are the most common, but central hypothyroidism is diagnosed earlier. These deficiencies can develop over time and might not manifest in the first days of life, which calls for lifelong monitoring. [12]

Optic nerve ophthalmoscopy is of great diagnostic importance. Patients with optic hypoplasia present with small, pale papillae, often with a double contour. [13]

Clinical, laboratory, and fundoscopy findings must be accompanied by magnetic resonance imaging of the skull, the gold standard test for the brain malformations that characterize the syndrome, to rule out other possible associated midline abnormalities. Karyotyping must also be ordered for patients with additional brain deformities or extraneural structures. An abnormal karyotype is a factor tied to a worse developmental prognosis. [14, 15]

Treatment of the syndrome is aimed at correcting hormone deficiencies that may cause hypoglycemia, adrenal crisis, and death. Given the varied nature of clinical manifestations, patients must be followed by a multidisciplinary care team that includes pediatric ophthalmologists, geneticists, neurologists, and endocrinologists. [2, 4]

CONCLUSION

Septo-optic dysplasia is a rare, difficult-to-diagnose congenital disease with diverse clinical alterations. Studies have demonstrated the importance of early diagnosis in the treatment of hormone deficiencies to improve prognosis and avoid delays in neurological development in children with visual impairment.

The patient described in this case report met two diagnostic criteria: optic nerve hypoplasia and pituitary hormone abnormality. Only 30-47% of patients present the complete triad. We could not find pregnancy or maternal risk factors that might predispose the development of the condition. The neonatology team suspected a syndrome based on the alterations seen in the patient's initial physical examination and initiated testing and early treatment.

Since pediatricians are the first to interact with potential patients, they must be equipped with the knowledge to diagnose rare syndromes clinically.

REFERÊNCIAS BIBLIOGRÁFICAS

1. Alt C, et al. Clinical and Radiologic Spectrum of Septo-optic Dysplasia: Review of 17 Cases. Journal of Child Neurology, 2017; 32(9):797–803;
2. Cemeroglu Ap, Coulas T, Kleis L. Spectrum of clinical presentations and endocrinological findings of patients with septo-optic dysplasia: a retrospective study. J Pediatri Endocrinol Metab [Internet]. 2015 Abr; [citado 2018 abr 20]; 28(9-10):1057-63. Disponível em: https://www.ncbi.nlm.nih.gov/pubmed/25879316;
3. Ganau M, et al. Neuro-Ophthalmological Manifestations Of Septo-Optic Dysplasia: Current Perspectives. Eye Brain, 2019; 11:37-47;
4. Ward Dj, et al. Review of the MRI brain findings of septo-optic dysplasia. Clinical Radiology, 2021; 76(2): 160.e1-160.e14.
5. Gaillard F, Pituitary MRI - normal study. Case study, Radiopaedia.org (Accessed on 29 Sep 2023) https://doi.org/10.53347/rID-17529;
6. Palorath A, Kharode I. Septo-Optic Dysplasia Diagnosed in a Newborn Infant with Normoglycemia: The Importance of Thorough Physical Examination. Case Rep Pediatr., 2021; 2021:4836030;
7. Matushita Junior Jpk, Tiel C, Batista Rr, Py M, Gasparetto El. Septo-optic dysplasia plus clinical presentation and magnetic resonance imaging findings. Arq Neuro-Psiquiatr [Internet]. 2010; [citado 2018 dez 17]; 68(2):315-6. Disponível em: http://www.scielo.br/pdf/anp/v68n2/32.pdf;
8. Reis P, Mourão J. Septo-optic dysplasia/de Morsier's syndrome. Saudi J Anaesth [Internet]. 2017 Jan/Mar; [citado 2018 abr 20]; 11(1):106-7. Disponível em: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5292831/;
9. Reeves DL. Congenital absence of septum pellucidum. Bull Johns Hopkins Hosp 1941;69:61-71. Disponível em: https://doi.org/10.1016/0002-9610(57)90095-8;
10. Ferran et al. Septo-optic dysplasia: five patients report. Arquivo Neuropsiquiatria 2010; 68 (3): 400-405. Disponível em: https://doi.org/10.1590/S0004-282X2010000300014;
11. de Morsier, G., Naville, F. Etudes sur les dysraphies crânio-encéphaliques. Acta Neurovegetativa 23, 443–453 (1962). Dispoível em: https://doi.org/10.1007/BF01227006;
12. Shinar S, et al. Long-term postnatal outcome of fetuses with prenatally suspected septo-optic dysplasia. Ultrasound Obstet Gynecol., 2020; 56(3):371-377;
13. Lobo Ar. Septo-Optic Dysplasia A Case Presentation for Revisiting this Intriguing and UncommonCondition. J Radiol Med Imaging. 2021: 4(1); 1044;
14. Nagasaki K, Kubota T, Kobayashi H, Sawada H, Numakura C, Harada S, et al. Clinical characteristics of septo-optic dysplasia accompanied by congenital central hypothyroidism in Japan. Clin Pediatr Endocrinol [Internet]. 2017 Set; [citado 2018 abr 20]; 26(4):207-13. Disponível em: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5627221/;
15. Maurya V, Ravikumar Br, Bhatia M, Rai Slcr. Septo-optic dysplasia: magnetic resonance imaging findings. Med J Armed Forces India [Internet]. 2015 Jul; [citado 2018 mai 30]; 71(3):287-9. Disponível em: https://www.researchgate.net/publication/279636229_Septo-optic_dysplasia_Magnetic_Resonance_Imaging_findings.