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## Case Report

# Suprasellar choristoma associated with congenital hydrocephalus, anophthalmia, cleft lip and palate, and clinodactyly: a proposed variant of a unique new syndrome

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## ABSTRACT

A male infant was born with a bilateral cleft lip and/or palate, absent nasal structures, left anophthalmos, right coloboma, and bilateral fifth digit clinodactyly. Brain magnetic resonance imaging revealed severe asymmetric hydrocephalus, absent corpus callosum, a suprasellar mass with a high riding third ventricle, and no pituitary gland. He had a normal male karyotype and normal prenatal laboratory testing. He had no significant family history and no renal, vertebral, gastrointestinal, or cardiac malformations. This combination of central nervous system findings, ocular and craniofacial abnormalities, a normal karyotype, and limited skeletal abnormalities to our knowledge has only been previously described once in the literature in association with a disruption in Pax and Sonic Hedgehog protein pathways, and we conclude this patient represents a variant of this described syndrome.

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## Introduction

Each year, approximately 3% of all newborns in the United States are affected by major genetic or structural birth defects [1]. These malformations are a large contributor to neonatal mortality and health care costs. With the advancements in imaging and genetic testing, the medical community has an

improved understanding of the etiology and diagnosis of birth defects, which allows for better care and management. However, not all newborns with congenital anomalies have an etiology and diagnosis that is known or understood. In this case report, we present a patient with macrocephaly, a bilateral cleft lip and palate, left anophthalmia, coloboma of the right eye, clinodactyly, severe asymmetric hydrocephalus, and

Informed consent was obtained by the patient's parents.

Conflict of Interest: The authors declare that they have no conflict of interest

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**Table 1 – Prenatal testing results.**

Prenatal test	Results
Direct anti-globulin test	Negative
Group B <i>Streptococcus</i>	Negative
MaterniT21 cell-free DNA	Negative for 13, 18, or 21 chromosome
Maternal serum alpha-fetoprotein	Within normal limits
Amniocentesis	Untested

a likely suprasellar choristoma seen on prenatal and postnatal imaging. This unique combination of clinical and radiologic features is not associated with any known syndrome and is similar to only 1 previously described case in the literature.

### Case report

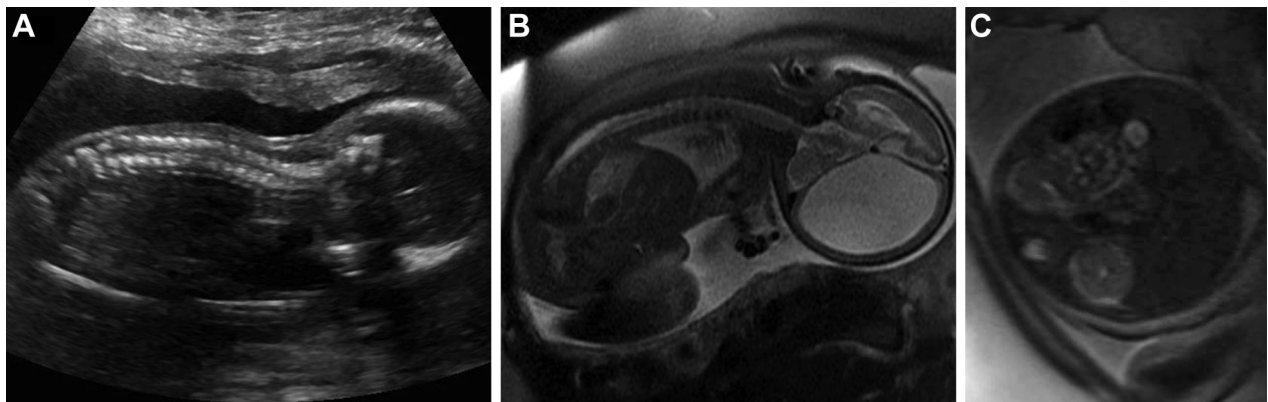
The male patient was the third child of a healthy 25-year-old gravida 5, para 2 Hispanic mother and nonconsanguineous father. The pregnancy was uncomplicated except for maternal otalgia and infection at 3-month gestation requiring a computed tomography scan. Medications taken during pregnancy included amoxicillin-clavulanate, acetaminophen with codeine, vitamin D, and prenatal vitamins. No smoking, alcohol, or other teratogen exposures were identified. All prenatal laboratory studies were unremarkable with the normal prenatal testing results presented in Table 1. Antenatal ultrasound at 21 weeks followed by antenatal magnetic resonance imaging revealed multiple congenital anomalies consisting of corpus collusum agenesis with no cavum septum pellucidum, marked dilatation of the right greater than left lateral ventricle with a thin rim of surrounding brain parenchyma, and an absent nasal cavity and left orbit with an unremarkable spine (Figs. 1A and B) and kidneys (Fig. 1C) and a 3-vessel cord with mid placental insertion.

The baby was born via an uncomplicated low transverse cesarean section at 39 weeks because of the known congenital anomalies. Birth weight was 3674 g and Apgar scores were 5 and 8 at 1 and 5 minutes, respectively. On inspection, he was found to have multiple congenital anomalies on physical examination consisting of macrocephaly measuring 40.5 cm,

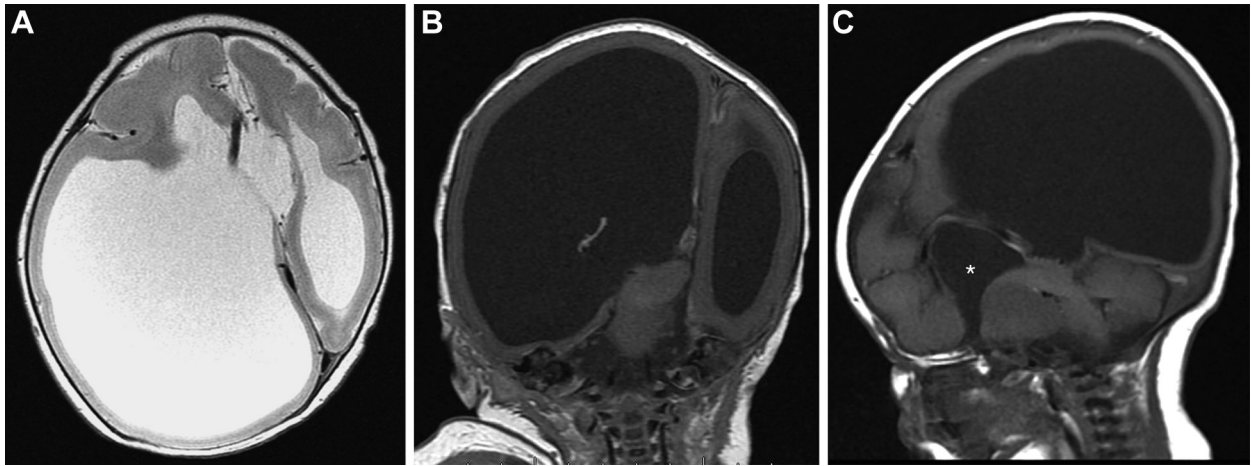


**Fig. 2 – Physical examination findings. Clinodactyly of right little finger.**

a bilateral cleft lip and palate, absent nasal structures, absent left orbit, malformed ears with absent ear canals, normal but small appearing genitalia, and bilateral clinodactyly (Fig. 2). A 24-hour genetic newborn screen was normal. The genetics consult preformed further testing which showed a normal 46 XY karyotype without abnormalities. CHARGE syndrome testing was not preformed because of lack of insurance reimbursement. Cardiac echocardiography performed 1 day after birth demonstrated a small cleft in the anterior leaflet of the mitral valve with an otherwise normal heart. Coloboma of the right eye was noted on ophthalmologic examination. On day 3 of life, magnetic resonance imaging of the brain again demonstrated multiple abnormalities including marked dilatation of the right lateral ventricle particularly at the atrium (Fig. 3A), right-to-left midline shift secondary to right lateral ventricle dilation (Fig. 3B), complete callosal agenesis and a high riding third ventricle (Fig. 3C), a suprasellar mass consistent with choristoma causing mass effect (Fig. 4A), absent left globe and orbit (Fig. 4B), diffuse bilateral pachygyria (Fig. 4C), absent midline craniofacial structures (Fig. 5A), and no normal sella or pituitary gland (Fig. 5B). Repeat ultrasound on day 8 of life confirmed these findings (Fig. 6). The infant was intubated on day 2 of life for respiratory acidosis. The infant's hospital course was also complicated by hypotension,



**Fig. 1 – Antenatal imaging findings. (A) Antenatal ultrasound findings of an unremarkable spine. (B) Antenatal T2 single shot fast spin echo magnetic resonance imaging finding of unremarkable spine (C) and kidneys.**



**Fig. 3 – Magnetic resonance imaging (MRI) findings of hydrocephalus. (A) T2 fast spin echo MRI image demonstrating agenesis of corpus callosum, colpocephaly, and ventricular dilatation. (B) T1 MRI finding of right to left midline shift and mild left ventricle dilatation. (C) T1 postcontrast MRI findings of callosal agenesis, high riding third ventricle (\*).**

bradycardia, gram positive sepsis, and oliguria requiring fluid resuscitation, empiric antibiotics, and dopamine. Metabolic complications of hypoglycemia, hypocalcemia, and hyponatremia were medically managed. Seizure activity was noted hours after birth and was confirmed with electroencephalogram, and seizures continued despite a maximum regimen of 3 anticonvulsants. Because of multiple congenital anomalies of the brain resulting in a poor prognosis, the parents decided to withdraw support. An autopsy was declined.

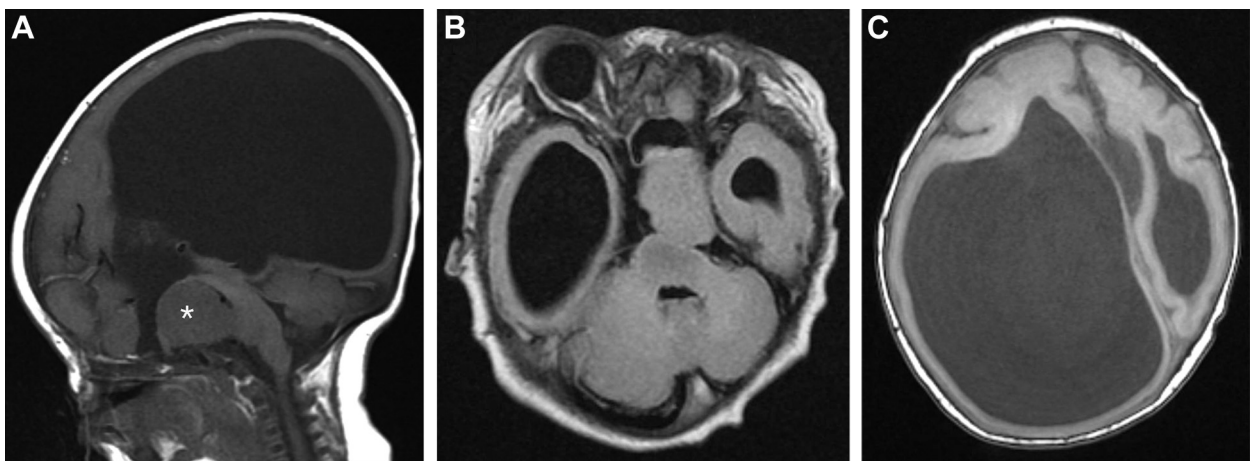
## Discussion

The combination of this patient's radiologic findings, normal karyotype, and limited skeletal abnormalities is unusual, and to our knowledge, has only once been previously described in

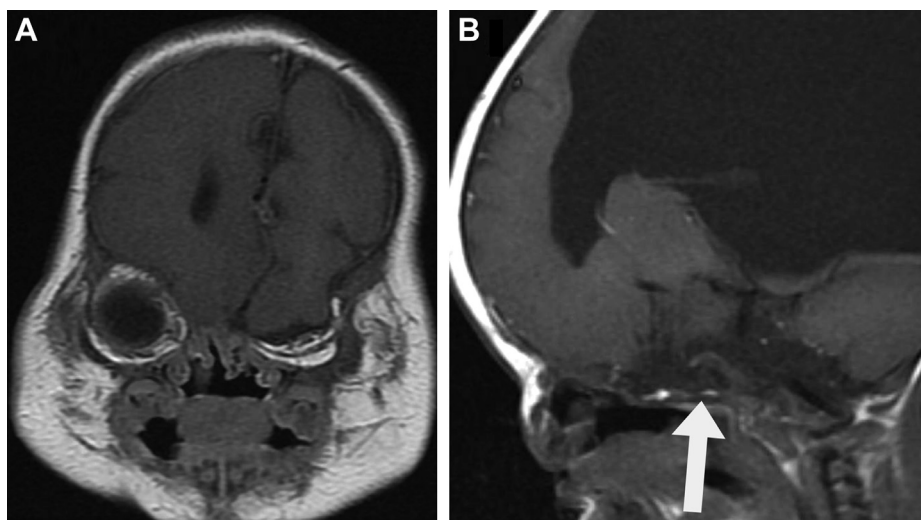
the literature. A 1999 case report [2] described a 7-year old with neuronal hamartoma associated with congenital obstructive hydrocephalus, anophthalmia, and cleft lip and palate similar to the patient presented here. Yet, other syndromes and etiologies of the findings described in the patient previously mentioned must be explored.

Hypothalamic hamartomas similar to the choristoma found in the presented patient are often a component of several congenital syndromes involving midline malformations. Two of these, Pallister-Hall syndrome and Smith-Lemli-Opitz syndrome, also demonstrate cardiac, pulmonary, genitourinary, and multiple skeletal abnormalities [3,4]. The lack of these features in our patient implies that these processes are likely not the etiology of the malformations.

The pattern of findings in this case is also suspicious for CHARGE syndrome. This syndrome includes coloboma, congenital heart defects, choanal atresia, delayed growth, and



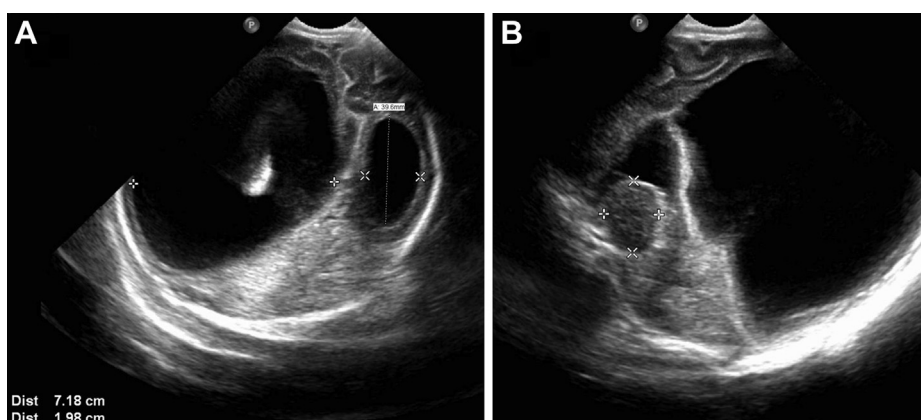
**Fig. 4 – Magnetic resonance imaging findings of congenital malformations. (A) T1 postcontrast MRI finding of the choristoma (\*) causing mass effect on the hypothalamus and floor of the third ventricle and demonstrating no contrast enhancement. (B) Fluid-attenuated inversion recovery MRI findings of absent left globe and orbit. (C) T1 MRI finding of diffuse bilateral pachygyria.**



**Fig. 5 – Magnetic resonance imaging findings of absent midline structures. (A) T1 MRI findings of absent midline craniofacial structures and nasal bone. (B) T1 MRI findings of lack of sella or pituitary gland (arrow).**

genital and ear abnormalities [5]. Our patient demonstrates some of these features except a significant heart or genital defect and cleft lip and palate in place of choanal atresia. However, each of the major features is not required for diagnosis of the syndrome. Clinical suspicion and genetic testing are used in forming a diagnosis. Over 90% of CHARGE syndromes are due to CHD7 mutations. This gene is responsible for creating a protein involved in gene regulation through chromatin remodeling [6]. CHD7 genetic testing was not completed in this case due to lack of insurance coverage. In addition, our patient's central nervous system findings consisting of severe hydrocephalus, choristoma, and pachygyria are not features of CHARGE syndrome, making this a less likely etiology for the congenital abnormalities observed in our patient.

It is difficult to categorize the clinical and radiologic findings of this case into a particular congenital syndrome. However, after an extensive literature review, we believe the 1999 case report initially referenced above shares the most similarities with our patient [2]. The respective cases each have findings of a hypothalamic hamartoma with severe hydrocephalus, complete corpus callosal agenesis, bilateral cleft lip and palate, anophthalmia, and microphthalmos. In addition, both patients had a normal 46 XY karyotype. The authors proposed a potential new syndrome with a mechanism based on disruption in Pax and Sonic Hedgehog protein pathways resulting in craniofacial, ocular, and cerebral malformations, and we conclude the patient in this case report is a variant of this described syndrome. Normal Pax proteins have been shown necessary for regulation of cell proliferation in the



**Fig. 6 – Postnatal ultrasound findings. (A) Ultrasound finding of dilatation of right lateral ventricle. (B) The large rounded, lobular mass seen on magnetic resonance imaging in the suprasellar region is redemonstrated causing mass effect on the third ventricle and measuring 1.8 × 2 × 2.3 cm. The mass demonstrated no internal vascular flow, demonstrated similar echogenicity to the brain parenchyma, was slightly asymmetrically displaced to the right, and represents the ultrasound finding of the choristoma. The symbols (+ and ×) reflect the sizing of the mass.**



developing diencephalon [7], whereas the Sonic hedgehog protein plays an important role in the induction of ventral midline cells of the rostral diencephalon [8], leading to the development of the prospective hypothalamus and splitting of the optic anlage into two lateral domains [7]. We speculate that the features seen in this case likely arose secondary to the disruption of molecular differentiation pathways involving Pax and Sonic Hedgehog proteins or closely related molecules.

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