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Research Paper: Neurodevelopmental Outcome of Patients With Agenesis of Corpus Callosum

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ABSTRACT

Background: Agenesis of Corpus Callosum (ACC) is a type of brain dysgenesis with various clinical manifestations.

Objectives: This study aimed to investigate the clinical and neurodevelopmental outcomes of patients with ACC.

Materials & Methods: In this cross-sectional study, the clinical and neurodevelopmental conditions of 62 patients with complete ACC referred to subspecialty clinics of pediatric neurology, Isfahan University of Medical Sciences, Isfahan, Iran, were investigated. Quantitative data were shown as Mean±SD, and qualitative data as frequency or percentage. In addition, the f Chi-square test was used to compare some data in SPSS version 22.

Results: In this study, 62 patients, including 29 boys and 33 girls with a Mean±SD age of 4.99±5.07 years, were included. Among the patients examined, 54.4% were born of consanguineous marriage, 82% had developmental delays, 80.4% had mental retardation, 89.1% had a speech delay, 23.7% had nutritional problems, 42.4% had facial dysmorphic features, and 27.6% had abnormalities of muscle tone. Among the associated problems stated by the patients, 15.5% of them had heart diseases, 22.4% visual disorders, 5.2% hearing deficit, 25.8% behavioral problems, 50% seizures, and 53.3% had abnormal electroencephalogram. Interestingly, 12.9% of the patients had normal or near-normal development.

Conclusion: The prevalence of developmental delays, speech and language disorders, mental retardation, facial deformities, seizures, and abnormal muscle tone were common in the patients with ACC.

Keywords: Agenesis of corpus callosum; Epilepsy; Brain

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Highlights

- Most of the patients with agenesis of the corpus callosum have developmental delay.
- A significant percentage of these patients have dysmorphic features.
- Epilepsy is common in patients with the agenesis of the corpus callosum.

Introduction

The Corpus Callosum (CC) is the most crucial interhemispheric commissure, responsible for transmitting motor, sensory, and cognitive information between the two hemispheres of the brain. Abnormalities of CC include complete and partial agenesis and hypoplasia. Agenesis of Corpus Callosum (ACC) is the most common central nervous system dysgenesis [1]. Moreover, ACC has been reported in 0.3% -0.7% of the general population and in 2% to 3% of patients with developmental delay [2].

Considering recent advances and the widespread use of prenatal ultrasound, prenatal diagnosis of ACC in pregnant women is common. Because of uncertainty regarding the long-term neurodevelopmental outcome of the patients with ACC, there is a significant concern on making decisions for both the families and physicians. Signs and symptoms of ACC vary greatly from person to person, but some signs and symptoms are prevalent in these patients, including developmental delay, seizure, visual disturbances, abnormal muscle tone, the decreased coordination of movements, and swallowing and chewing problems [2]. Currently, there is no specific treatment for ACC-related debilities; however, some medical and educational services can improve disabilities in patients with ACC.

A multidisciplinary team, including neurologists, psychiatrists, geneticists, occupational medicine specialists, speech and language pathologists, music therapists, and social workers, could be very helpful in this regard [3].

Materials and Methods

In this cross-sectional study, 62 patients with ACC referred to subspecialty clinics of pediatric neurology, Isfahan University of Medical Sciences, Isfahan City, Iran, were included from March 2016 to January 2019. The inclusion criteria included all patients with complete ACC. The patients with suspected or proven-acquired CNS damage were excluded. Written consent was taken from the patient's family for using their data in this study. At first, a pediatric neurologist examined all the included patients. For all the patients, a questionnaire related to the patient's data, including demographic and personal information, familial history, the presence of epilepsy, speech disorders, visual impairment, hearing deficit, swallowing difficulty, behavioral problem, and developmental status according to developmental screening test (Denver II), was completed. After information preparing, collecting, archiving, and entering into SPSS v. 22, the quantitative data were shown as Mean±SD and qualitative data as frequency or percentage. In addition, the f Chi-square test was used to compare some data.

Results

In this study, 62 patients, including 29 boys and 33 girls with a Mean±SD age of 4.99±5.07 years, were enrolled. Notably, two patients were identical twins, and four cases had a sibling with ACC. About 82% of the patients had a motor delay, 80.4% mental retardation, 89.1% speech delay, 23.7% nutritional problems, 42.4% facial dysmorphic features, and 27.6% abnormal muscle tone. Among the associated problems, 9.3% of the patients had cardiac anomaly, 23.3% visual impairment, 7% hearing deficits, 20.9% behavioral problems, and 46.5% seizure disorder.

According to the Chi-square test, there was no significant difference between the two sexes in terms of age, parental affiliation, developmental delays, mental retardation, speech delays, nutritional problems, dysmorphic features, abnormal muscle tone, congenital heart disease, visual problem, hearing deficit psychiatric disorders, epilepsy, and abnormal Electroencephalography (EEG) (P>0.05) (Table 1).

Discussion

In our study, the prevalence of ACC was more common in female subjects than the male ones. In a previous study, the prevalence rate of this disorder was about 52% in men [4]. In another study in 2011, out of 185486 live

Table 1. Demographic characteristics and neurodevelopmental outcome in the patients with agenesis of the corpus callosum

Variables		Mean±SD/No. (%)			P
		Male (n=29)	Female (n=33)	Total (n=62)	
Age (y)		4.47±3.64	5.49±6.17	4.99± 5.07	0.44
Delivery type	Normal delivery	8 (36.4)	10 (41.7)	18 (29.0)	0.47
	Cesarean section	14 (63.6)	14 (58.3)	28 (45.2)	
Parental consanguinity		13 (44.8)	18 (58.1)	31 (54.4)	0.36
Motor delay		24 (82.8)	26 (81.3)	50 (82.0)	0.57
Mental retardation		22 (84.6)	23 (76.7)	45 (80.4)	0.34
Speech delay		22 (88.0)	27 (90.0)	49 (89.1)	0.57
Nutritional problem		8 (27.6)	6 (20.0)	14 (23.7)	0.35
Facial dysmorphisms		17 (58.6)	21 (63.6)	38 (61.2)	0.17
Cardiac anomaly		3 (10.3)	6 (20.7)	9 (15.5)	0.23
Visual problem		7 (24.1)	6 (20.7)	13 (22.4)	0.50
Hearing deficit		0	3 (10.3)	3 (5.2)	0.11
Abnormal muscle tone		5 (17.2)	11 (37.9)	16 (27.6)	0.07
Behavioral problem		9 (31.0)	7 (21.0)	16 (25.8)	0.06
Seizure		14 (48.3)	16 (51.6)	30 (50.0)	0.50
EEG Abnormal		14 (48.3)	18 (58.1)	32 (53.3)	0.30
Normal development		3 (10.3)	5 (15.0)	8 (12.9)	0.26

births, 38 cases of ACC were reported, of whom 26 cases were boys, and 12 cases were girls [5].

More than half of the patients in our study had genetically related parents, and consanguineous marriage was common among them. Notably, two patients were identical twins. Moreover, in two families, two children had ACC. The results of our study show a significant role of the genetic anomaly as etiology of ACC, which is consistent with the results of previous studies that reported a significant role of genetic etiologies in patients with ACC [6-8].

In our study, motor developmental delay, mental retardation, and speech delay were recognized as the most common disabilities observed in patients with ACC. Developmental disabilities have been reported in previous studies. In previous studies, diverse intensities of behavioral and neurodevelopmental disorders and mental retardation have been reported in patients with ACC [9, 10]. In the study by Bedeschi et al. to examine the clinical and genetic findings of 63 patients with ACC, it was reported that 52 cases had some degrees of mental retardation [9].

In another study, among 40 patients with ACC, most patients had developmental delays [10]. In the study by Kim et al. performed on 31 patients with ACC, 4 cases were normal, and it was stated that the patients with more anomalies in the central nervous system are at a relatively higher risk of developmental problems [11]. There is no uniform prognosis for ACC because this disease is associated with a wide range of clinical manifestations. The degrees of behavioral and neurodevelopmental disorders in ACC vary, and evidence suggested that other accompanying anatomical changes in the Central Nervous System (CNS) associated with ACC have significant roles in the outcome.

In our study, 61.2% of the cases had facial dysmorphisms. In a previous study, the dysmorphic feature has been reported in more than half of the studied patients [9]. Furthermore, in our study, 15.5% of the patients had Congenital Heart Disease (CHD). In another study, the prevalence rate of CHD was reported as 27.6% [4]. Dysmorphic features and involvement of other organs in some patients with ACC indicated the syndromic nature of this disorder in this group of patients.

Abnormal muscle tone was relatively common in our study's subjects. Additionally, about one-third of the patients had axial hypotonia, accompanied by spasticity of the limbs in a few of them. In a study, the prevalence rate of abnormal muscle tone was 33.5%, which was close to the results of our study [4].

Seizures and abnormal EEG were relatively common in our patients. In another study, epileptic seizures were observed in 23% to 39% of patients with ACC. Of note, the most common type of seizure was infantile spasm [12].

In our study, behavioral problems were observed in 25% of the patients. One study found that one-third of patients with ACC also have psychiatric disorders [13]. Many psychiatric conditions are associated with ACC and callosal dysfunction, including schizophrenia, autism, and attention deficit hyperactivity disorders [8].

In our patients, 13% had normal mental development and cognitive function. Moreover, all the cases with normal or near-normal cognitive development had isolated ACC and no facial dimorphism or organ involvement suggestive of syndromic anomaly. In previous studies, normal or near-normal development has been reported in 7% to 25% of patients with ACC [1, 3, 11]. Patients with syndromic disorders have varying degrees of developmental abnormalities, but in isolated cases of the corpus callosum, a developmental function may be normal or relatively normal only in some patients.

Conclusion

ACC is a type of brain dysgenesis with diverse clinical manifestations. In this study, the prevalence of developmental delays, speech and language disorders, mental retardation, facial dysmorphisms, seizures, and abnormal muscle tone were common in the patients with agenesis of the corpus callosum. Notably, one of the limitations of this study was the impossibility of advanced genetic studies to determine the underlying genetic derangement.

Ethical Considerations

Compliance with ethical guidelines

All study procedures were done in compliance with the ethical guidelines of the Declaration of Helsinki for Medical Studies (2018).

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflicts of interest.

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