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ORIGINAL ARTICLE

Early clinical outcomes of congenital encephalocele and mortality risk factors: A tertiary center experience

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Abstract

Objective: To investigate the early clinical outcomes and prognostic factors of infants with congenital encephalocele.

Methods: We investigated newborns diagnosed with congenital encephalocele and treated in our hospital. We recorded data of the patients regarding the delivery history, anthropometric features, and clinical outcomes regarding mortality, shunt need, and hydrocephalus. We used conventional statistical methods (student's t test, Mann-Whitney u test) assuming a p significance at <0.05 and Bayesian models (Bayesian Kendall's tau test).

Results: We included 18 patients (%61.1 female, 38.9% male) in the study. The median birth week was 38 (36.3-39) weeks, and the mean birth weight was 2837+/-816 grams. 83.3% of the patients had undergone an operation with a median of 5 days. The defect diameter was more than 5 cm in 61.1% of the patients, and brain parenchyma was positive in the sac in half of the patients. 22.2% of the patients needed ventriculoperitoneal shunt insertion. The overall survival resulted in 61.1% in all patients and 73.3% in operated. There were statistically significant differences in terms of birth weight (p<0.001, 3150 v.s 2470 grams) and birth week (38.6 v.s 34.6 weeks, p=0.021), as deceased patients had lower birth weight and birth week.

In Bayesian Kendall's tau calculations, Neural tissue involvement, defect diameter more than 5 cm, birth weight (very strong evidence), operation within three days of life and birth week (strong evidence), and shunt need and seizures (moderate evidence) had an impact on mortality. There was no significant risk factor for hydrocephalus development, but there was a correlation between hydrocephalus and shunt need. Also, Dandy walker deformity correlated with shunt need (moderate evidence), but the birth week and neural tissue involvement were independent of shunt need (moderate evidence).

Conclusion: The poor prognostic factors for mortality were defect diameter larger than 5 cm, neural tissue involvement in the sac, lower birth week, lower birth weight, and seizures, and the good prognostic factor was operation before postnatal three days of life.

Keywords: Congenital encephalocele; infant; newborn; ventriculoperitoneal shunt; hydrocephalus

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Introduction

Congenital encephalocele is a type of bone defect on the calvarium resulting in protrusion of meningeal or brain tissue [1]. The terminology encephalocele refers to brain tissue herniation to the bone defect, and meningocele refers to the herniation that includes solely cerebrospinal fluid [2]. Congenital encephalocele is a variation of neural tube defect, like anencephaly and myelomeningocele [1]. This type is not a common neural tube defect variation, but it consists of 15-20% of all neural tube defects [3, 4], and congenital encephalocele prevalence is predicted as 0.8-5 in 10000 live births [5, 6].

The underlying pathology is a fusion defect in cranial neuropore closure at 24-26th days of embryogenesis [1,7]. The genetic and environmental factors also have an impact on congenital encephalocele development [8]. Approximately 60% of Congenital encephalocele-diagnosed patients have additional malformation or chromosomal defects [9, 10], 20% have microcephalus, Arnold-Chiari malformations type 2 or 3, craniosynostosis, and syringomyelia [11]. Also, associations are reported with congenital infections of toxoplasmosis, rubella, cytomegalovirus, and herpes simplex virus, as well as maternal history of children with neural tube defect and consanguineous marriages [12]. In general, neural tube defect recurrence in the following siblings is reported as 3.8%; however, this ratio is at an 8.9% rate for congenital encephalocele [13]. However, if the congenital encephalocele occurs as a part of an autosomal recessive syndrome like Meckel-Gruber, the recurrence rate will increase to 25% [14].

The differential diagnosis includes congenital cranial cysts, vascular malformations, and inflammatory lesions, which can mimic congenital encephalocele [15]. The prognosis is dependent on the mass of the herniated neural tube and the additional anomalies of the infant [15]. This study investigated the prognostic factors regarding mortality and the associated factors with complications in congenital encephalocele-diagnosed infants in this study who were treated in our 3rd-stage neonatal intensive care unit. The study aimed to help clinicians inform the families regarding prognosis and perform interventions in a timely fashion.

Materials and Methods

We included all patients diagnosed with encephalocele in Gungoren Hospital Neonatal Intensive Care Unit (NICU) between 2017-2023. We retrospectively recorded the perinatal history, anthropometric measurements at birth, birth week, and postnatal operation time. We also recorded the ventriculoperitoneal shunt need, hydrocephalus status, co-morbid diseases, and survival status. We investigated the mortality risk factors as well as the need for shunt and development of hydrocephalus. In addition, we assessed factors that are not correlated (in other words independent from) with mortality, shunt need, and hydrocephalus. We included all patients who underwent treatment in our NICU with congenital encephalocele and only excluded patients with concomitant anencephaly.

We obtained the study permission from Biruni University Ethical Committee with file number:2024-86-61.

In statistical calculations, we assessed the data distribution with the Kolmogorov-Smirnov test, skewness, kurtosis, and Q-Q plots. We used the student's t-test and Mann-Whitney test with normal and non-normal distributed data, respectively. We presented the data as mean+/-standard deviation, median (interquartile range), and % (n).

Also, we built H1 (correlation) and H0 (non-correlation, independence) hypotheses and assessed correlation coefficients with Bayesian Kendall's tau b test (stretched beta prior width was set at 1) and presented Bayes factors (BF). Bayes factors (BF10)>30 represent very-strong evidence, 10-30 strong, 3-10 moderate, and 1.1-3 anecdotal evidence, where <0.03 represent very-strong evidence for null (H0) hypothesis, 0.1-0.03 strong, 0.3-0.1 moderate, 0.3-09 anecdotal evidence. We

set alpha error rate significance at p<0.05. We used the Jamovi 2.3.18 package program with the jsq extension.

Results

We included 18 patients (61.1% (n=11) female) in the study. The median birth week at birth was 38 weeks (36.3-39), and the mean birth weight was 2837+/-816 grams. The perinatal features and anthropometric measurements are presented in Table 1.

All the congenital encephalocele cases were referred from surrounding cities and hospitals for delivery or after birth.

As we assessed prognostic factors regarding mortality, birth weight was 3150+/-516 in survivors, whereas it was 2470+/-760 in deceased patients (student's t-test, p=0.002). Also, the mean birth week was 38.6+/-1.3 in survivors, whereas it was 34.6+/-5.0 in deceased patients (student's t-test, p=0.021). The postnatal operation day was a median of 7 days in survivors, whereas it was 11 days in deceased patients (Mann-Whitney u test, p=0.072). None of the patients had a maternal folate replacement history or family history.

One patient had aortic coarctation, another patient had Meckel-Grubel syndrome, and one patient had both

Table 1. Descriptive features of the patient group

Birth week at delivery	38 weeks (36.3-39)
Gender	61.1% (n=11) Female 38.9% (n=7) Male
Delivery	72.2% (n=13) Cesarean Section 27.8% (n=5) Normal Spontaneous Delivery
Birth weight	2837+/-816 grams
Operated	83.3% (n=15)
Operation time	5 days (3-10)
Ventriculoperitoneal Shunt	22.2% (n=4)
Defect diameter >5 cm	61.1% (n=11)
Chiari type 3 malformation	5.6 % (n=1)
Operated within 3 days	27.8 (n=5)
Antenatal hydrocephalus	27.8% (n=5)
All hydrocephalus	33.3% (n=6)
Brain tissue involvement	50% (n=9)
Seizures	61.1% (n=11)
Operated	83.3% (n=15)
Survival	61.1% (n=11) in all patients 73.3% (n=11) in operated patients
Mortality causes	1 patient: Concomitant trakeoeosefageal fistula and anal atresia
	1 patient: Meckel Grubel syndrome+prematurity
	4 patients: Defect diameter >15 cm
	1 patient: Prematurity

anal atresia and trakeo-özefageal atresia. Two patients were born with prematurity, and four patients had big congenital encephalocele defects (more than 15 cm in diameter).

As we investigated factors that have an impact on survival were birth weight, neural tissue involvement, defect diameter >5 cm (very strong evidence), birth week and operation within 3 days of life (strong evidence), postnatal operation day, seizure, and shunt need (moderate evidence). We did not find any significant risk factor for hydrocephalus development except the correlation between hydrocephalus and shunt need. Delivery type was independent from survival and birth week, and Neural tissue involvement was independent from shunt need (moderate evidence), where Dandy Walker deformity was correlated with shunt need (moderate evidence). The results are presented in Table 2.

Discussion

Encephalocele has a female tendency in our patient group with 61.1%, whereas this ratio is reported as 48.7% [16], 49% [17], 58% [18], 58.8% [19], 69% [20], and up to 78.9% [21], and these results indicate

	Survival		Hydrocephalus		Shunt need	
	Kendall's tau	BF_{10}	Kendall's tau	BF_{10}	Kendall's tau	BF_{10}
Hydrocephalus	0.3223	1.538 A	—			
Shunt need	0.4264	5.21 M	0.4725	9.939 M	—	
Gender	0.0649	0.321	0.1612	0.452 AI	0.3959	3.522 M
Defect diameter >5 cm	-0.6364	165.4	-0.1612	0.452 AI	-0.1218	0.379 AI
Neural tissue involvement	-0.5698	48.0 VS	0	0.3 MI	0	0.3 MI
Antenatal hydrocephalus	0.2403	0.745	0.8771	>1000 VS	0.5635	43.0 VS
Dandy Walker deformity	0.1846	0.508	0.3385	1.649 A	0.4507	5.984 M
Seizures	-0.4545	5.176	-0.0348	0.322 MI	0.3892	2.466 A
Birth week	0.5187	20.3 S	0.0293	0.304 MI	-0.0442	0.309 MI
Birth weight	0.6008	84.104	0.1529	0.434 AI	0.2601	0.871 AI
Delivery type	-0.0141	0.301	-0.1754	0.487 AI	-0.3315	1.69 A
Postnatal operation day	-0.4401	3.637	-0.0737	0.35 AI	-0.2043	0.551 AI
Operation within 3 days	0.4947	13.9 S	0.0877	0.339 AI	-0.0331	0.305 AI

AI: Anecdotal evidence for independence hypothesis, MI: Moderate evidence for independence hypothesis, A: Anecdotal evidence for correlation hypothesis M: Moderate evidence for correlation hypothesis, S: Strong evidence for correlation hypothesis, VS: Very strong evidence for correlation hypothesis

that the female gender has a tendency for congenital encephalocele.

The median postnatal operation day in our study was 5 days, similar to a study reporting this duration as 8 days [18]. We could not find a study regarding mortality association with the operation time, but our results indicated that operation within 3 days was associated with lower mortality with strong evidence; however, this result should be proved with larger numbers of studies conducted with more patients.

Antenatal hydrocephalus was present in 27.8% of the patients, and a total of 33.3% of patients had hydrocephalus during the treatment in our study group. A study reported that 23.5 patients had hydrocephalus before surgery, 41.2% developed hydrocephalus after surgery, and 64.7% of patients suffered from antenatal or postnatal hydrocephalus [19], whereas other studies reported the total hydrocephalus ratio as 32.4% (ventriculomegaly) [17], 50% [18], and 73.5% [22].

Shunt operation was needed in 22.2% of the patients, but we did not include a patient who died due to prematurity to this ratio. Another study from our country reported this ratio as 26.3% [21], and other studies as 29.4% [17], 48% [18]. Another aspect is that two Chiari III needed shunt in the same study [18]. A patient with Chiari III malformation needed a shunt operation in our study. Shunt need is not rare in congenital encephalocele patients but clinicians should also be aware of Chiari III malformation.

Brain parenchymal involvement in the sac occurs in half of the patients in our patient group. A study reported that 47.4% of the patients had parenchyma inside the sac [21]. Also another study reported that 42.2% [17] and 58.8% [19] of patients had neural tissue in sac. Parenchymal involvement is a poor prognostic factor in congenital encephalocele diagnosed patients [17, 19], and according to the literature and our results roughly half of the patients suffer from neural defects in congenital encephalocele cases. Neural tissue involvement was associated with mortality in our study group with very strong evidence, where it did not affect shunt need with moderate evidence.

Encephalocele might occur in various regions, but is mostly seen in the occipital region at approximately 90% rate [23]. All of our encephalocele-diagnosed patients had occipital defects. Defect size is also another concern for clinicians as a study reported that 15.3% of the cases had a larger than 5 cm defect [16]. This rate was 61.1% in our study group. We think this high rate is higher than the literature as most of our cases were referred to our hospital from surrounding cities.

Seizure is also another concern for clinicians as a study reported a seizure rate of 25.5 rate [24] where 61.1% of our patients had seizures during hospitalization.

Mortality occurred in 38.9% of all patients and 26.7% in operated ones in our study, but other causes like prematurity or major congenital anomalies play significant roles. Studies reported mortality rates as 8%. [18], 28.2% [16], 29%. [23], and 32.1% (of the operated) [22], but these rates dropped from the 57% [20] rate, which was reported in the 80's. Trakeoeosefageal fistula, anal atresia, Meckel-Grubel syndrome, prematurity, and giant encephalocele sac were the causes of death in our study group. The prognostic factors for mortality resulted in defect diameter >5 cm, neural tissue involvement, birth weight, birth week, operation before 3 days (strong and very strong evidence), and seizures (moderate evidence) in our study group. Hydrocephalus did not affect mortality significantly (anecdotal evidence). A study reported that the presence of brain tissue in the sac and size were the main prognostic factors, but hydrocephalus was not [16], similar to our findings. Another study reported that cerebral tissue in the sac was a bad prognostic feature [20]. However, we still need more studies for prognostic features of congenital encephalocele.

Folic acid intake is a preventive factor for neural tube defects, and a study reported that 10.5% of the mothers used folic acid supplementation but was not effective [21]. None of the mothers used folic acid intake in our patient group. The daily adult folic acid need is 400 mcg [25], whereas the World Health Organization recommends 400 to 800 mcg doses to prevent neural tube defects [26].

Conclusion

The female gender has a tendency to encephalocele. Operation within postnatal 3 days of life was associated with lower mortality. Shunt operation need is not rare in congenital encephalocele patients, but clinicians should also be aware of Chiari III malformation. Neural tissue involvement was associated with mortality, where it did not affect shunt need. Seizures are not rare. The prognostic factors for mortality were defect diameter >5 cm, neural tissue involvement in the sac, birth week, birth weight, operation before 3 days, and seizures. Hydrocephalus did not affect mortality significantly.

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