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Risk factors, presentations, associated anomalies, and outcomes of patients with encephalocele

Nawzhin Jange Jalyzada*
Ari Sami Hussain Nadhim**
Nabaz Muhamad Mustafa***

Abstract

Background and objectives: Encephalocele is a rare neural tube birth defect. Aim of this study was to find the risk factors and associated anomalies of patients with encephalocele, and its outcomes. **Methods:** We used a case-series study for 30 patients with encephalocele who were admitted to Shahid Dr. Aso Hospital from January 2017 to July 2018. The patients' clinical features and computed tomography findings were recorded and their outcomes classified into death, cerebral palsy, delayed mile stones, and good. **Results:** The genders of the patients were 11 (36.7%) male and 19 (63.3%) female with a female: male ratio of 1.7:1. There were significant associations between the site of the skull defect with microcephalus, seizure, and outcome and statistically significant association between the content of the sac and family history. The content of the sac was mostly mixed brain and cerebrospinal fluid (56.7%). The size of the sac was significantly associated with family history and hydrocephalus and all of encephaloceles were located in the midline mostly at occipital and occipito-cervical region. The outcomes were death (10%), poor (10%), delayed milestones (23.3%), and 56.7% good. There was also statistically significant association between outcome and other brain abnormality and microcephalus. **Conclusions:** Encephalocele was located in midline mostly at occipito-cervical region, the size of its sac is associated with hydrocephalus, the content was mixed brain and CSF, and its site was associated with seizure. Moreover, content and size of the sac was significantly associated with family history of neural tube defect.

Key words: Congenital brain anomaly, Congenital diseases, Encephalocele, Folic acid, Hydrocephalus, Microcephalus, Neural tube defect.

Introduction

The neural tube is a congenital narrow channel which closes during the third and fourth weeks of pregnancy to form the brain and spinal cord. Encephalocele, sometimes known as cranium bifidum, is a rare congenital neural tube birth defect and it occurs as a result of a defect in the skull[1-9]. It is a sac-like protrusion of brain tissue with its covering meninges through the defect[1-3, 5-10]. Moreover, it results from failure of closure of the neural tube; therefore, the defect is in the midline from nasion Figures (1) to occiput Figures (2)1, 3, 8, 11. The encephalocele can be pedunculated Figure (2) or sessile Figure (3) cystic lesion and it may contain herniated meninges and brain tissue which is called encephalocele or meningoencephalocele Figure (3) or only meninges which is called meningocele Figure (2) or meninges, brain tissue and part of ventricular system which is called encephalomeningocystocele or encephalomeningohydrocele and it is called encephalomyelocele if it contained both the brain and spinal cord tissues[12].

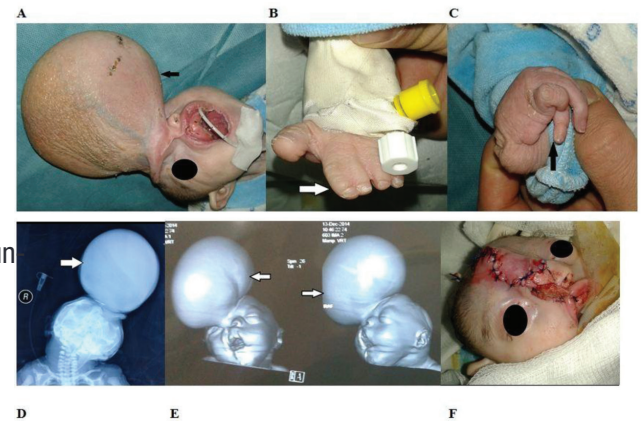

Figure (1): The images are for a 3-month-old female in-

*MBChB, KHCMS (Neurosurgery) trainee.
**MBChB, FRCS, FIBMS, Consultant Neurosurgeon.
***MBChB, FIBMS (Neurosurgery).
*,**,***Iraq, Kurdistan Region, Sulaimani City, Shar Hospital, Department of Neurosurgery.
Corresponding author: Nawzhin Jange Jalyzada, nawzhin9090@gmail.com

fant. (A) large encephalocele in nasion. (B) and (C) are polydactyly (left hand) and handicap (right hand). (D) Plain radiograph of head. (E) Intrauterine CT scan of the baby. (F) Post-operative image of the baby after resection of the encephalocele.

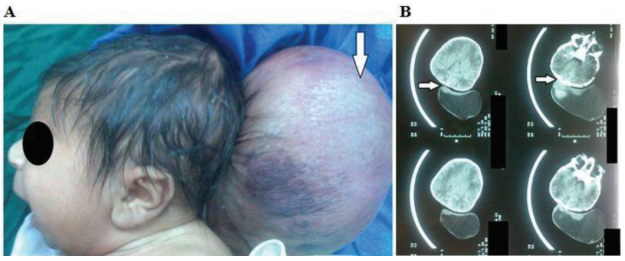

Figure (2): The images of 2-day-old male infant. (A) and (B) large pedunculated occipital encephalocele.

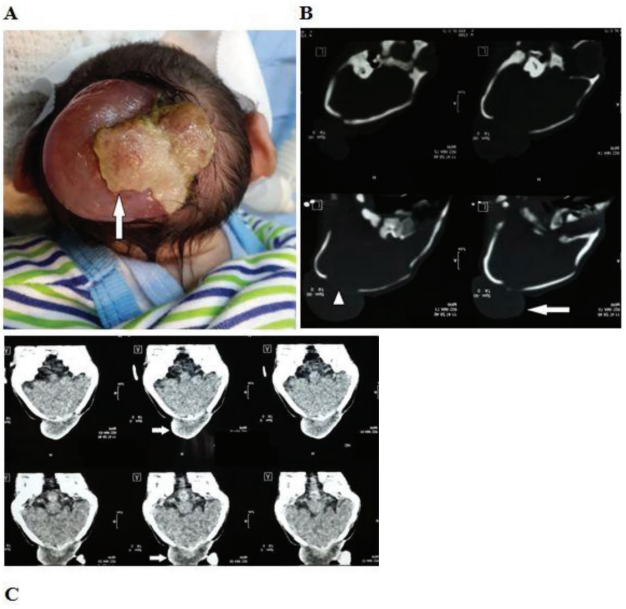

Figure (3): The images of 16-day-old male infant. (A) occipito-parietal encephalocele with scar. (B) CT scan of head (bone window) shows the bony defect (arrowhead). (C) Sessile encephalocele which contains brain tissue.

The incidence of encephalocele is 1:3000-10000[1-2, 7, 10, 13] and its prevalence is 0.08-0.5 per 1000 live birth[14].

The size of encephalocele is variable; it may be very small and just seen by naked eyes (Figure 4) or as large as the size of the skull or even larger (Figure 2). Furthermore, it usually associated with anomalies of cerebrum, cerebellum, and midbrain[1, 15].

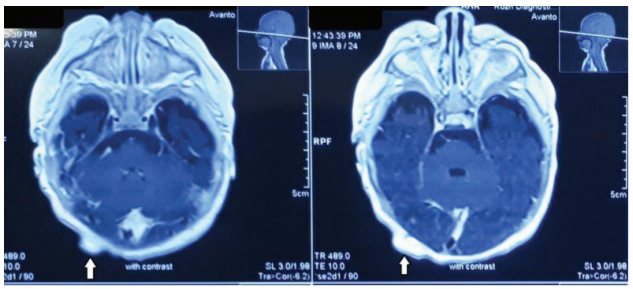

Figure (4):CT scan of a 2-month-old female infant which shows atretic encephalocele (arrows).

The cause of encephalocele is unknown, but many risk factors were postulated to be associated with neural tube defects; including encephalocele, such as genetic factor, environmental factors like exposure to radiation, viral infection, and some drugs like salicylic acid treatment during early period of pregnancy, hypervitaminosis, hypoxia, maternal nutrition deficiencies such as folic acid, aflatoxin exposure, advanced paternal age, and long intervals between pregnancies[1, 16].

Clinical features of encephalocele can vary from individual to another because they depend on many factors such as location, size of the encephalocele and the amount and type of neural tissue protruded[17].

The diagnosis is usually prenatally by ultrasonography and magnetic resonance imaging (MRI), but after birth it is usually apparent from the clinical features and imaging techniques such as MRI and computed tomography (CT) scan are used to find the associated anomalies[12]. Usually, CT scan is used because it can be performed rapidly and it's superior to MRI in showing details of bone defect, but MRI needs longer duration for its performance[12].

Generally, the sac is covered by healthy skin, but urgent surgical intervention is needed if cerebrospinal fluid (CSF) leak occured[1].

The treatment of choice is surgery; usually separating the sac and finding the bony defect edges, followed by cutting the sac and removal of the sequestrated brain tissues. Furthermore, the patients require long period follow up1.

In our study, we wanted to know risk factors for patients with encephalocele, its associated anomalies and outcomes.

Patients and methods

We used a case-series research design for our study and we collected 30 patients with encephalocele who were

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admitted to Shahid Dr. Aso Hospital during January 2017 to July 2018. They were 11 (36.7%) male and 19 (63.3%) female with a female: male ratio of 1.7:1. The patients were questioned and examined at one time. In addition, informed consents had been taken from the patients' parents for the inclusion of their children in this study and the study was accepted by the ethical committee of Kurdistan Higher Council of Medical Specialties (KHCMS).

The inclusion criterion was patients who presented with encephalocele.

The patients' age, gender, parental consanguinity, family history of neural tube defect, folic acid intake during the pregnancy, and seizure were asked. Clinical examinations, including trans-illumination test, were performed to specify the site, size (the size roughly was classified into atretic which is a small encephalocele that just can be seen by eyes Figure (4), large about the size of the head of the patients Figure (1) and (2), and medium in between these two sizes Figure (3) and the content of the sac. Due to the administrative and technical issues, we could not perform MRI for the patients and therefore, we solely depended on cranial CT scan to identify the exact content of the sac, hydrocephalus and other brain anomalies. The patients' outcomes classified into death, cerebral palsy (CP), delayed mile stones, and good.

The "IBM SPSS Statistics version 25" was used for the analysis of the data and both descriptive and inferential statistics were used. Furthermore, a p-values of ≤ 0.05 were considered as statistically significant, and highly significant associations, consecutively. In addition, Pearson Chi-Square was used to find out the significancy of association between independent and dependent variable pairs, and Pearson's R Correlation was used to calculate the direction of the correlation between the two variables

Results

There was zero percent history of radiation during the pregnancies. In addition, there were other associated congenital anomalies such as micrognathia (3.3%), cleft palate (3.3%), and 6.7% of the patients presented with cleft lip and palate and syndactyly.

There were statistically insignificant relationship between site of the defect and gender, parent consanguinity, family history, folic acid intake, drug history, hydrocephalus, but a statistically significant association of site of the defect with microcephaly, seizure, and outcome, Table (1).

Table (1) shows that microcephaly and seizure is more common in patients with frontal encephalocele while worse outcome and death is more common in patients with occipital and occipito-cervical encephalocele.

Table (1): The statistical relationships between variables with the site of the defect.

Variables		Site of the defect						p-value*
		Occipital (%)	Vertex (%)	Occipito-cervical (%)	Frontal (%)	Nasal (%)	Total (%)	
Gender	Male	5 (16.7)	3 (10)	2 (6.7)	1 (3.3)	0 (0)	11 (36.7)	0.8 (0.169)
	Female	7 (23.3)	3 (10)	6 (20)	2 (6.7)	1 (3.3)	19 (63.3)	
Parent consanguinity		8 (26.7)	3 (10)	4 (13.3)	2 (6.7)	1 (3.3)	18 (60)	0.82 (0.001)
Family history		2 (6.7)	0 (0)	0 (0)	0 (0)	0 (0)	2 (6.7)	0.52 (-0.269)
Folic acid intake		1 (3.3)	2 (6.7)	3 (10)	1 (3.3)	0 (0)	7 (23.3)	0.52 (0.193)
Drug history		2 (6.7)	0 (0)	1 (3.3)	0 (0)	0 (0)	3 (10)	0.78 (-0.144)
Microcephaly		0 (0)	1 (3.3)	1 (3.3)	3 (10)	0 (0)	5 (16.7)	0.001 (0.477)
Hydrocephalus		3 (10)	3 (10)	3 (10)	2 (6.7)	0 (0)	11 (36.7)	0.57 (0.130)
Seizure		0 (0)	1 (3.3)	1 (3.3)	3 (10)	0 (0)	5 (16.7)	0.001 (0.477)
Outcome	Died	0 (0)	0 (0)	2 (6.7)	1 (3.3)	0 (0)	3 (10)	0.046 (-0.327)
	Poor (CP)	0 (0)	2 (6.7)	0 (0)	1 (3.3)	0 (0)	3 (10)	
	Delayed mile stones	3 (10)	3 (10)	0 (0)	1 (3.3)	0 (0)	7 (23.3)	
	Good	9 (30)	1 (3.3)	6 (20)	0 (0)	1 (3.3)	17 (56.7)	

*Measured by Chi-Square test; CP = Cerebral palsy

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There were statistically insignificant association between the content of the sac and gender, parent consanguinity, folic acid intake, drug history, microcephaly, hydrocephalus, seizure, outcome, and a statistically significant association between the content of the sac and family history, Table (2).

Table (2): The statistical relationships between variables with the content of the defect.

Variables		Content of the sac			Total (%)	p-value*
		Brain (%)	CSF (%)	Brain and CSF (%)		
Gender	Male	5 (16.7)	1 (3.3)	5 (16.7)	11 (36.7)	0.19 (0.291)
	Female	3 (10)	4 (13.3)	12 (40)	19 (63.3)	
Parent consanguinity		5 (16.7)	4 (13.3)	9 (30)	18 (60)	0.55 (-0.085)
Family history		2 (6.7)	0 (0%)	0 (0%)	2 (6.7)	0.05 (-0.425)
Folic acid intake		2 (6.7)	0 (0%)	5 (16.7)	7 (23.3)	0.39 (0.047)
Drug history		1 (3.3)	0 (0%)	2 (6.7)	3 (10)	0.72 (-0.009)
Microcephaly		2 (6.7)	0 (0%)	3 (10)	5 (16.7)	0.49 (-0.082)
Hydrocephalus		3 (10)	1 (3.3)	7 (23.3)	11 (36.7)	0.69 (0.034)
Seizure		3 (10)	0 (0%)	2 (6.7)	5 (16.7)	0.15 (-0.292)
Outcome	Died	0 (0%)	1 (3.3)	2 (6.7)	3 (10)	
	Poor (CP)	2 (6.7)	0 (0%)	1 (3.3)	3 (10)	
	Delayed mile stones	2 (6.7)	1 (3.3)	4 (13.3)	7 (23.3)	0.67 (0.019)
	Good	4 (13.3)	3 (10)	10 (33.3)	17 (56.7)	

*Measured by Chi-Square test; CP = Cerebral palsy

There were statistically insignificant associations between sizes of the sac and gender, parent consanguinity, folic acid intake, drug history, microcephaly, seizure, and outcome, and statistically significant association between the size of the sac with family history and hydrocephalus,Table (3).

Table (3): The statistical relationships between variables with the size of the defect.

Variables		Size of the sac			Total (%)	p-value*
		Atretic (%)	Medium (%)	Large (%)		
Gender	Male	2 (6.7)	4 (13.3)	5 (16.7)	11 (36.7)	0.83 (0.066)
	Female	2 (6.7)	8 (26.7)	9 (30)	19 (63.3)	
Parent consanguinity		4 (13.3)	5 (16.7)	9 (30)	18 (60)	0.11 (-0.097)
Family history		2 (6.7)	0 (0)	0 (0)	2 (6.7)	0.001 (-0.510)
Folic acid intake		0 (0)	5 (16.7)	2 (6.7)	7 (23.3)	0.13 (-0.038)
Drug history		0 (0)	0 (0)	3 (10)	3 (10)	0.15 (0.318)
Microcephaly		0 (0)	2 (6.7)	3 (10)	5 (16.7)	0.6 (0.171)
Hydrocephalus		1 (3.3)	8 (26.7)	2 (6.7)	11 (36.7)	0.02 (-0.264)
Seizure		1 (3.3)	2 (6.7)	2 (6.7)	5 (16.7)	0.88 (-0.085)
Outcome	Died	0 (0)	0 (0)	3 (10)	3 (10)	0.07 (-0.127)
	Poor (CP)	1 (3.3)	1 (3.3)	1 (3.3)	3 (10)	
	Delayed mile stones	0 (0)	6 (20)	1 (3.3)	7 (23.3)	
	Good	3 (10)	5 (16.7)	9 (30)	17 (56.7)	

*Measured by Chi-Squared; CP = Cerebral palsy

There was a statistically negative significant association between the outcome of the patients with encephalocele and other associated congenital brain anomaly i.e. when a patient is present with more congenital anomalies, his/her outcome becomes worse (calculated by Pearson's R Correlation),Table (4).

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Table (4): Association of outcome with other brain abnormality.

Outcome	Other brain abnormality								p-value*
	No (%)	Dandy walker (%)	Right cerebellar agenesis (%)	Dandy walker and corpus calosum agenesis (%)	Arachnoid cyst (%)	Corpus calosum agenesis (%)	Hydrocephalus (%)	Total (%)	
Died	1 (3.3)	0 (0)	1 (3.3)	0 (0)	0 (0)	1 (3.3)	0 (0)	3 (10)	0.002 (-0.646)
Poor CP)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (6.7)	1 (3.3)	3 (10)	
Delayed mile stones	3 (10)	1 (3.3)	0 (0)	1 (3.3)	1 (3.3)	1 (3.3)	0 (0)	7 (23.3)	
Good	16 (53.3)	1 (3.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	17 (56.7)	
Total	20 (66.7)	2 (6.7)	1 (3.3)	1 (3.3)	1 (3.3)	4 (13.3)	1 (3.3)	30 (100)	

*Measured by Chi-Square test; CP = Cerebral palsy

There were statistically insignificant association between outcome and hydrocephalus and seizure, and statistically significant association between the outcome and microcephaly,Table (5).

Table (5): Association of some clinical features of encephalocele patients with their outcome.

Variables	Outcome					p-value*
	Died (%)	Poor (CP) (%)	Delayed mile stones (%)	Good	Total (%)	
Microcephaly	2 (6.7)	2 (6.7)	1 (3.3)	0 (0)	5 (16.7)	0.003 (-0.65
Hydrocephalus	0 (0)	2 (6.7)	4 (13.3)	5 (16.7)	11 (36.7)	0.21 (0.005
Seizure	1 (3.3)	2 (6.7)	1 (3.3)	1 (3.3)	5 (16.7)	0.06 (-0.38

*Measured by Chi-Square test; CP = Cerebral palsy

Discussion

Neural tube develops in the midline during embryonic stage. Therefore, almost all of the neural tube defects occur in the midline and mostly at lumbosacral and occipital regions[1, 2, 7-9, 13, 18]. But, there are some sporadic cases in which encephalocele occurred in other than midline such as anterioinferior region of temporal lobe[5, 7, 19].

The Matson and Ingraham classification of encephalocele is widely accepted and it is based on the location of the encephalocele and it includes: basal, sincipital, convexity (frontal, parietal, occipital, and cervico-occipital), and atretic[7]. According to this classification, the most common location is cervico-occipital region[7]. Out findings are compatible with the Matson and Ingraham classification; all of our patients presented with midline encephalocele and occipital area was predominant; 40% occipital, 26.7% occipito-cervical, 20% vertex, 10% frontal, and 3.3% nasal ,Table (1).

Most of encephaloceles are congenital in origin i.e. primary[1-4, 7, 10-11, 15, 18-20], but acquired or secondary encephalocele can occur as a result of increased intracranial pressure e.g. due to tumor, surgery, trauma, and infection[5-7]. Encephalocele can also be acquired from congenital meningocele[14]. Furthermore, all of our patients had congenital encephalocele and this may be the cause of the occurrence of encephalocele at midline especially occipital region in our patients.

The size of the encephalocele is not important predictor of outcome because the prognosis depends on the location and amount of neural tissue inside the sac and associated anomalies[2, 5]. Therefore, the size of the defect is not as important as the content of the sac; thence, a small sac may contain large amount of neural tissue and associated more with microcephaly than larger defect. In addition, hydrocephalus and microcephalus are most critical risk factors[2]. Contrary to that, our results showed a statistically significant association between the site of the encephalocele and its outcome; the sites were mostly occipital and occipito-cervical followed by vertex and this may have been caused more pressure on vital structures in posterior

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fossa, Table (1), and a statistically insignificant association between the content of the sac and outcome. This may be because of the small sample size of our study due to rarity of the condition, Table (2). Furthermore, the size of the sac had no statistically significant association with the outcome because a larger size may contain only CSF, Table (3). Encephalocele can contain CSF, brain tissue and CSF, and rarely brain tissue only[3, 8]. Furthermore, the content of the encephalocele sac in our patients were as follows: 56.7% brain tissue and CSF, 26.7% brain tissue only, and 16.6% CSF only, Table (2). This congenital neural tube defect; encephalocele, may coexist with other congenital anomalies such as transposition of great arteries, atrial defect, ocular malformation, and craniofacial defects[2, 5], in addition to other congenital brain anomalies like: corpus callosum and cerebellar agenesis, cortical dysplasia and agenesis, ventricular anomaly, Arnold Chiari and Dandy Walker malformation, microcephaly and hydrocephalus[2, 5]. In our study, we found a very significant association between the outcome and other brain anomalies; we found 13.3% of patients with corpus callosal agenesis, 6.7% with Dandy Walker, 3.3% with Dandy Walker and corpus callosal agenesis, 3.3% with right cerebellar agenesis, 3.3% with arachnoid cyst, and 3.3% with hydrocephalus, Table (4).

About one third of the patients with encephalocele die and half of the patients who live beyond the first day of birth have various degree of developmental delay2. Our study showed a 10% death, 10% poor outcome, 23.3% delay in milestones, and 56.7% good outcome, Tables (1-4). The cause of death in our study may be due to that, most of the died-babies were presented with large occipito-cervical encephalocele and they were associated with cerebellar and corpus callosum agenesis. In the literature we searched, 32% of the patients had hydrocephalus[10]. Hydrocephalus and microcephalus were considered as the two important risk factors for worst outcome[2]. Our study showed half agreement with these findings; we found that microcephalus is statistically associated significantly with the worst outcome but hydrocephalus did not have significant association with the outcome although it accounted for 36.7% of the patients, Table 5. It may be due to that; hydrocephalus per se has better outcome if managed well.

Conclusions

Encephalocele is located mostly at occipito-cervical region. The size of its sac is associated with hydrocephalus, the content is mixed brain and CSF, and its site is associated with seizure. Moreover, the content and size of the sac is significantly associated with family history of neural tube defect. In addition, the outcome of encephalocele is not so good and if associated with other congenital and brain anomalies, occipital encephalocele, and microcephaly, it has worst outcome. We do recommend doing more researches on the assessment of risk factors/causes and preventive methods of neural tube defects.

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Conflict of interest

Nothing to declare.

References

1. Yucetas SC, Uçler N. A Retrospective Analysis of Neonatal Encephalocele Predisposing Factors and Outcomes. Pediatr Neurosurg 2017; 52:73-6.

2. Inan C, Sayin NC, Gurkan H, et al. A large posterior encephalocele associated with severe ventriculomegaly, cerebellar atrophy and transposition of the great arteries. J Clin Ultrasound 2018;46(9):588-90.

3. Jeyaraj P. Management of the frontoethmoidal encephalomeningocele. Ann Maxillofac Surg 2018; 8:56-60.

4. Arifin M, Suryaningtyas W, Bajamal AH. Frontoethmoidal encephalocele: clinical presentation, diagnosis, treatment, and complications in 400 cases. Childs Nerv Syst. 2018; 34(6):1161-8.

5. Bannout F, Harder S, Lee M, et al. Epilepsy Surgery for Skull-Base Temporal Lobe Encephaloceles: Should We Spare the Hippocampus from Resection? Brain Sci. 2018; 8(3):42.

6. Baro V, D'Errico I, d'Avella D, Denaro L. Transethmoidal Encephalocele and High Intracranial Pressure. Pediatr Neurosurg. 2018; 53(4):286-7.

7. Shi C, Flores B, Fisher S, Barnett SL. Symptomatic Parietal Intradiploic Encephalocele—A Case Report and Literature Review. J Neurol Surg Rep. 2017; 78:e40–e45.

8. Satyarthee GD, Moscote-Salazar LR, Escobar-Hernandez N, et al. A Giant Occipital Encephalocele in Neonate with Spontaneous Hemorrhage into the Encephalocele Sac: Surgical Management. J Pediatr Neurosci. 2017; 12(3):268–70.

9. Yhoshu E, Dash V, Bawa M. Double encephalocele: An unusual pres-

https://doi.org/10.56056/amj.2019.91

entation. J Pediatr Neurosci 2018; 13:264-6.

10. Alshamrani A, Habalrih F, Altweijri I, Alsaleh S, Ajlan A. Endoscopic trans-nasal repair of basal encephalocele associated with morning glory syndrome. Br J Neurosurg. 2018; 10:1-3. Available from: https://www.tandfonline.com/doi/full/10.1080/02688697.2018.1494264

11. Horcajadas A, Palma A, Khalon BM. Frontoethmoidal encephalocele. Report of a case. Neurocirugia (Astur). Forthcoming 2018;30. Available from: http://dx.doi.org/10.1016/j.neucir.2018.02.006

12. Cortazar AZ, Martinez CM, Feliubadalo CD, Cueto MR, Serra L. Magnetic resonance imaging in the prenatal diagnosis of neural tube defects. Insights Imaging. 2013; 4(2):225–37.

13. Richardson S, Khandeparker R, Raghuvaram A, Mohan R. Modified two flap palatoplasty in asymptomatic transsphenoidal encephalocele: a case report. J Korean Assoc Oral Maxillofac Surg. 2018; 44(2):86-90.

14. Gandhoke G, Goldschmidt E, Kellogg R, Greene S. Encephalocele development from a congenital meningocele: case report. J Neurosurg Pediatr. 2017; 20(5):419-22.

15. Lau W, Yung W, Leung W, et al. A case of "familial atretic encephalocele". Ultrasound Obstet Gynecol. 2018; 27. doi: 10.1002/uog.20109.

16. Bear K, Solomon B, Roessler E, et al. Evidence for SHH as a candidate gene for encephalocele. Clin Dysmorphol. 2012; 21(3):148–51.

17. Greene ND, Copp AJ. Neural Tube Defects. Annu Rev Neurosci. 2014;37: 221–42.

18. Raeiq A. Posterior Fontanelle Encephalomeningocele in a Neonate: A Case Report. Cureus. 2018;10(3): e2315.

19. Wang ZI, McBride A, Grinenko O, et al. Utility of CISS sequence in detecting anteroinferior
temporal encephalocele. J Neurol Sci. 2017; 381:59–61.

20. Rehman L, Farooq G, Bukhari I. Neurosurgical interventions for occipital encephalocele. Asian J Neurosurg. 2018; 13:233-7.

https://doi.org/10.56056/amj.2019.91