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Title of article: Encephalomeningocele cases reviewed over 10 years in Thailand:
a case series report

Authors:

Sitthiporn Agthong, M.D.

Department of Anatomy, Faculty of Medicine, Chulalongkorn University, Bangkok Thailand
10330

Email address: sitthipornagthong@hotmail.com

Viroj Wiwanitkit, M.D.

Department of Laboratory Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok
Thailand 10330

Email address: wviroj@pioneer.netserv.chula.ac.th

Corresponding authors:

Sitthiporn Agthong, M.D.

Department of Anatomy, Faculty of Medicine, Chulalongkorn University, Bangkok Thailand
10330

Email address: sitthipornagthong@hotmail.com

Abstract

Background: Encephalomeningocele, especially in the frontoethmoidal region, is a form of neural tube defects affecting patients in Southeast Asia more commonly than in Western countries. Its underlying cause is not known but teratogenic environmental agents are suspected. However, nutritional deficiency as in spina bifida cannot be excluded.

Methods: This study reports 21 cases of meningocele (without brain tissue in the lesion) and encephalomeningocele (with brain tissue) that were admitted to our hospital for surgical corrections in the period of ten years, from 1990 to 1999. Clinicopathological findings as well as occupations of family members and prenatal exposures to infectious agents or chemicals were reviewed and analyzed.

Results: Frontoethmoidal region was the most commonly involved area found in 20 cases. The combined pattern between nasoethmoidal and nasoorbital defects was the most frequently found (11 from 21 cases) and had more associated abnormalities. Encephalomeningocele had related abnormalities more than meningocele with proportions of 0.6 and 0.3, respectively.

Conclusions: Here, we confirmed that genetic defects are not likely to be a single primary cause of this malformation. However, we could not draw any conclusions on etiologic agents. We suggest that case control studies and further investigation on the role of nutritional deficiencies especially folic acid in pathogenesis of encephalomeningocele are necessary to clarify the underlying mechanisms.

Background

Encephalomeningocele is a congenital malformation characterized by protrusion of meninges and/or brain tissue due to a skull defect. It is one form of neural tube defects as the other two, anencephaly and spina bifida. There are mainly two types of encephalomeningocele, frontoethmoidal and occipital, according to different locations of the defect. The frontoethmoidal type which its defect locates in the area of frontal and ethmoidal bones, is exclusively common in Southeast Asia, including Thailand. Suwanwela and co-workers [1] have reported the incidence of 1:5,000.

Despite of the higher incidence of this congenital defect in this area, little is known about its etiology and pathogenesis. Some evidences from previous studies suggest environmental factors as potential causes [1,2,3,4]. So far, only aflatoxin has been proposed to be a teratogenic agent for this anomaly [2]. However, due to lack of more direct evidences, its role in the pathogenesis of frontoethmoidal encephalomeningocele is still uncertain. Indirect evidences from its closely related anomaly, spina bifida [5], may suggest the role of folate deficiency in encephalomeningocele. However, again, there were no studies on the relationship between maternal folate level and incidence of encephalomeningocele and some evidences have suggested different underlying mechanisms between these two forms of neural tube defects [6,7,8]. Therefore, studies in details of prenatal history, clinical presentation and pathological findings will be the first step to clarify the underlying cause.

Here, we report 21 cases of encephalomeningocele and meningocele admitted to the King Chulalongkorn Memorial Hospital, the biggest and most well-known center for corrective surgery in Thailand during 1990-1999. All accessible medical records of these patients have been extensively reviewed. For the first time, subtypes of meningocele and encephalomeningocele have been presented. Moreover, in order to investigate the role of environmental factors in the pathogenesis of encephalomeningocele, all relevant maternal histories during pregnancy have been reviewed and the attempt to relate these factors with the clinicopathological findings has been made.

Materials and methods

All data were retrospectively collected from the admission records of 21 patients diagnosed with meningocele or encephalomeningocele based on surgical findings in the period of ten years from 1990 to 1999. All these patients were admitted to have surgical corrections performed in the King Chulalongkorn Memorial Hospital, Bangkok, Thailand. The admission records contain histories of every admission of patients to the hospital including operative notes and pathological report forms. Environmental conditions, especially during pregnancy, were reviewed. These data were places of birth, parents' occupations, exposure to chemicals and/or drugs during pregnancy and prenatal infection.

It is noteworthy that we collected data from only this hospital because our center for corrective surgery of encephalomeningocele is the biggest center in the country. Additionally, with its offer of free operation to poor patients, this center has attracted most patients and probably has more cases underwent corrective surgery than any other centers in the country.

Results

Of 21 cases included in the study, 20 patients (95%) had lesions in the frontoethmoidal region and only one had in the occipital area. All patients were diagnosed at birth. They were 10 males and 11 females which make a male/female ratio 0.91. The patients' family histories revealed no siblings or known relatives diagnosed with meningocele or encephalomeningocele. The first surgical correction was performed at ages ranging from 2 months to 39 years. The main causes of delay were financial problems.

Considering surgical findings, the combined subtype (nasoorbital with nasoethmoidal lesions) was found in 11 patients. Six cases were affected with the nasoethmoidal subtype. Only one case had nasofrontal and occipital lesions each. No isolated nasoorbital subtype was found. The subtypes could not be identified in 2 cases due to previous surgeries at other hospitals and poor records of the surgical findings. In addition, the presence of brain tissue in the lesion has also been noted. The details are summarized in Table 1. The number of patients with meningocele was not significantly different from one of patients with encephalomeningocele (6 and 8, respectively).

Nine cases (42.9%) had complications or other associated anomalies as shown in Table 2. Most complications involved ipsilateral eyeballs. As comparing with surgical findings, 2 cases of meningocele and 5 cases of encephalomeningocele had associated abnormalities, as shown in Table 3. Four of those 5 cases with encephalomeningocele had the combined pattern of abnormality.

Apart from surgical and pathological findings, background information is also important especially in order to give some clues of possible causes of this congenital defect. For instance, people living in one region usually have unique customs and environment which might affect many aspects e.g. nutritional status, chemical exposure, infection, etc. If we see significantly higher incidence in one particular area, it may prompt us to look for unique characters of that area.

Regarding patients' geographic distribution, 10 cases were from the central region of Thailand. Of the remainings, 4, 5 and 2 were from the northern, northeastern and eastern regions, respectively. This distribution might be affected by the proportion of patients admitted to our hospital. As a result, we also compared the geographic distribution of encephalomeningocele patients with one of overall admitted patients in the same period of time (Table 4). No significant differences were seen between the distribution of these two groups.

Another factor analyzed was parents' occupations. This might suggest us of some common chemical exposure. Ten were peasants working on rice fields or farms. Six families worked in their own paddy fields. Other patients' parents which their jobs were not related to agriculture, worked for the government or government organizations and factories.

Furthermore, we also analyzed history of chemical contact during pregnancy and details are summarized in Table 5. Mothers of 4 patients had history of contact with chemicals or drugs. No maternal infections during pregnancy were found.

Discussion

There were 21 cases of meningocele and encephalomeningocele included in this study. This was all the cases admitted for surgery in the recent 10 years in the biggest center in Thailand. Neurosurgical department in our hospital is specialized and well-known among Thai patients and

physicians in corrective surgery for this anomaly. This probably implies that most cases of encephalomeningocele either first diagnosed by our hospital or other hospitals were sent to this center for further investigation and treatment regardless of financial status. It is also worth noting that admission records include all medical histories of patients from birth until the last admission. This means that we reviewed not only present illness but also past history including birth records. If there were newborns with masses suspected of encephalomeningocele, they must have been referred to the Neurosurgery department for further investigation. Thus, it is unlikely that the data we have are significantly affected by many missing cases. Although there were not many cases due to the nature of this congenital defect, we have attempted to analyze existing data in order to shed some light on this mysterious anomaly.

We found that the frontoethmoidal or sincipital region was the most frequent site of involvement in meningocele and encephalomeningocele which is consistent with the previous report [1]. Moreover, percentages of various associated abnormalities in this study were comparable with the above report. However, other studies reported higher frequencies of those abnormalities [3,9]. This disparity might come from different population included in the studies and different time-course before surgical corrections. Interestingly, lacrimal duct obstruction and agenesis of corpus callosum which have not been mentioned by previous studies, were found here. Anomalies of eyeball and lacrimal apparatus can be explained by the direct pressure generated from nasoorbital and nasoethmoidal masses to structures within and around the orbit. However, whether agenesis of corpus callosum in this case occurred in a sporadic manner or was associated with frontoethmoidal encephalomeningocele is unknown.

Meningocele and encephalomeningocele were found in a similar frequency with 4 and 3 cases, respectively. However, encephalomeningocele had a higher proportion of cases with associated anomalies than meningocele (0.6 and 0.3, respectively). Again, it might be explained by the hypothesis of larger size of mass and more direct pressure in encephalomeningocele due to additional presence of brain tissue in the lesion.

Concerning various subtypes of meningocele and encephalomeningocele, combined pattern which is composed of nasoethmoidal and nasoorbital subtypes, was the most frequently observed. The

nasoethmoidal subtype was the second most common and no isolated nasoorbital lesion was found. Combined subtype cases are likely to have the presence of brain tissue in the lesion more frequently as in Table 1 (6 and 3, respectively) since the defect was probably larger.

Several previous studies have found no difference between the number of male and female cases [2,9,10]. In addition, some studies have not found two cases in the same family or among close relatives [1,2,3]. As a result, those studies have proposed that encephalomeningocele is a multifactorial defect in which environmental factors play an important role. Our results support this hypothesis with a demonstration of a male/female ratio of 0.91 and no evidences of repeated involvement among close relatives. Then, we focus on history of prenatal exposure to chemicals and drugs. The positive history was found in only four cases. Therefore, a likely cause could not be identified.

It is interesting that all cases were in lower-middle or lower classes in term of income. This might suggest us of problems related to inappropriate self-care, for example, malnutrition. Therefore, we also reviewed the patients' geographic distribution. This is because some regions have unique culture and are at risk of some nutritional deficiencies. However, we could not demonstrate any predilection to a particular region because the distribution of encephalocele patients was almost identical to one of general patients admitted to the hospital except a slight increase toward encephalocele patients in the northern region. However, the number of cases is insufficient to achieve a strong conclusion.

We have further investigated patients' family occupations. 16 of 21 families worked in agricultural section. However, it is difficult to say that agricultural works are at risk of this congenital malformation because more than 50% of Thai people are still working in agricultural section. Case control study is needed to give more evidences regarding etiologic agents.

Conclusions

We reported 21 cases of the rare form of neural tube defects, encephalomeningocele. Most were involved in the frontoethmoidal region which is relatively common in Southeast Asia. Most frequently, nasoethmoidal and nasoorbital defects were concomitantly observed. With this pattern

of defect, brain tissue is likely to be present in the mass. Associated anomalies were mainly around orbits. Our data confirmed the previous findings that environmental factor is likely a main etiologic agent. Although, we could not identify any leads to more specific underlying causes, our findings suggest that the causes will not be easy to find and might be more complicated than we expected. Case control studies are needed to clarify the role of environment especially nutrition in encephalocele. Furthermore, more studies on relationship between folate and incidence of encephalomeningocele are also necessary.

Competing interests

Not declared.

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Table 1. Surgical findings classified by subtypes and pathology.

	Subtype			
	NF	O	NO	NE
	NO+NE			
	(Combined)			
Meningocele	-	1	-	2
Encephalomeningocele	3			
No record	1	-	-	1
	6			
	-	-	-	3
	2			

NO = Nasoorbital

NE = Nasoethmoidal

NF = Nasofrontal

O = Occipital

Table 2. Associated abnormalities and complications.

Abnormalities & Complications	No. of cases
Anophthalmia	
- unilateral	1
- bilateral	0
Microphthalmia	
- unilateral	2
- bilateral	0

Lacrimal duct obstruction	2
Amblyopia	
- unilateral	1
- bilateral	0
Corneal clouding	
- unilateral	2*
- bilateral	0
Microcephaly	1
Hydrocephalus	1**
Agenesis of corpus callosum	1
No abnormalities	12
<hr/>	
Total	21***

* One case was at contralateral side.

** Ipsilateral enlargement of lateral ventricle

*** One case had unilateral hydrocephalus with agenesis of corpus callosum.

One case had ipsilateral anophthalmia and contralateral corneal clouding.

Table 3. Associated abnormalities and subtypes.

Abnormalities & Complications	Subtype								No record	
	Meningocele				Encephalomeningocele					
	NE	Combined	NF	O	NE	Combined	NF	O		
Anophthalmia	-	-	-	-	-	-	-	-	-	1*
Microphthalmia	-	1 ^a	-	-	-	1	-	-	-	-
Lacrimal duct obstruction	-	-	-	-	-	2	-	-	-	-
Amblyopia	-	1 ^a	-	-	-	-	-	-	-	-
Corneal clouding	-	-	-	-	1	-	-	-	-	1*
Microcephaly	-	-	-	1	-	-	-	-	-	-
Hydrocephalus	-	-	-	-	-	1 ^b	-	-	-	-
Agenesis of corpus callosum	-	-	-	-	-	1 ^b	-	-	-	-
No abnormalities	2	2	-	-	-	2	1	-	-	6**
Total	6				8				8	

a,b Abnormalities in the same patients

* Combined subtype

** Three cases had nasoethmoidal lesions. One case had a lesion in combined subtype.

NE = Nasoethmoidal

NF = Nasofrontal

O = Occipital

Table 4. Comparison between the proportion of encephalomeningocele cases distributed in each region of Thailand and one of all admitted patients in the hospital in the same period.

Region of Thailand	Proportion*	
	Encephalomeningocele cases	All admitted patients
Central	0.5	
Northern	0.6	
Northeastern	0.2	
Eastern	0.05	

Southern	0.2
0.2	
	0.1
0.1	
	0
0.04	

* Number of cases in each region / total number of cases

Table 5. Drugs or chemicals contacted during pregnancy.

Drug or chemicals	No. of cases
Alcohol	2
Acetone	1
Medications	
- Aspirin	2
- Steroids	1
- Herbal	1
extracts	1
- Unidentified	
Total	4*

* One case ingested both alcohol and aspirin.

One case used aspirin, steroids, unidentified drugs and alcohol.