Neural Tube Defects: A Retrospective Study of 69 Cases

Abstract

Objective: Neural tube defects (NTDs) are congenital disorders that significantly increase the risk of death and disability in the 1st year of life. The aim of this study was to retrospectively evaluate the patients admitted to our neonatal intensive care unit because of NTD. Materials and Methods: We retrospectively examined the demographic features, familial risk factors, physical examination and radiological findings, and accompanying diseases of 69 patients with NTD. Results: Of the 69 patients hospitalized in a 5-year period, 38 were female and 31 were male. The median birth weight was 3150 g and the median delivery week was 38 weeks. Forty-nine of the patients (71%) had meningomyelocele, 11 patients (16%) had encephalocele, and nine patients (13%) had meningocele. Forty-five of the patients (65.2%) had Arnold–Chiari type 2 malformation. Twenty-five percent of the mothers had a history of periconceptional use of folic acid. The median time of making a diagnosis of NTD by prenatal ultrasonography was 20 (16–24) weeks. Thirty-nine of the patients (56.5%) had other organ disorders, some with multiple systemic disorders. Conclusion: The use of periconceptional folic acid in mothers and a decision for termination in selected cases may be effective in reducing the frequency of NTD.

Keywords: Meningomyelocele, neonate, neural tube defect

Introduction

Neural tube defects (NTDs) are a heterogeneous and complex group of congenital central nervous system (CNS) anomalies. Anencephaly, spina bifida, and encephalocele are included in this group. Inadequate cranial extension of the notochord which is constituted by the midline mesoderm, inadequate neurulation, lack of separation of the skin, and neural ectoderm after neurulation is completed and problems occurring during the process which constitutes filum terminale all cause open or closed spinal dysraphism. Encephalocele forms after the neural tube are closed. Neural malformations and malformations of the other organ systems frequently accompany NTDs.

In patients with lumbosacral spina bifida, problems including motor and sensory dysfunction in the lower extremities, anal and urethral sphincter failure, and neurogenic bladder may be observed. Especially, most patients with thoracic and lumbosacral spina bifida have an increased probability of hydrocephaly and Arnold–Chiari type 2 (hydrocephaly in association with meningomyelocele) malformation. Treatment and follow-up of patients with NTD require collaboration of many branches of health care and cause significant healthcare expenses. Generally, these congenital malformations significantly increase the rate of mortality and disability in the neonatal period and the 1st year of life.

This study was performed to retrospectively examine the clinical courses in patients hospitalized in the neonatal intensive care unit (NICU) in our hospital because of NTD.

Materials and Methods

Babies with NTD were specified by examining the records of the babies hospitalized in Baskent University Istanbul hospital in the last 5 years (October 2013–August 2018). File records of all 69 babies who were found to have NTD could be reached. Gender, birth weight, gestational age at the time of birth, maternal age, use of folic acid and medication during pregnancy, hypertension, diabetes and other maternal diseases, prenatal ultrasonography findings, time of prenatal diagnosis of NTD, familial history of morbidity, consanguinity between the mother and father, localization of spina bifida, and Arnold–Chiari type 2 malformation were evaluated.
bifida, if the sac was perforated, lower extremity examination findings, accompanying anomalies and comorbidities, ultrasonography findings, computed tomography findings or magnetic resonance imaging (MRI) findings, treatments applied, follow-up times, and reasons for mortality in the ones who died were recorded. SPSS statistical software (SPSS 11.5, SPSS Science, Chicago, IL, USA) program was used for statistical analyses. This study was approved by Baskent University Medicine and Health Sciences Research Committee (Project Number: KA18/297).

**Results**

The clinical characteristics of the subjects are summarized in Table 1. Thirty-eight (55.1%) of the babies were female and 31 (44.9%) were male. The median birth weight was 3150 (2640–3450) g, the median gestational week at the time of birth was 38 (37–39) weeks, and the median maternal age was 27 (22–33) years.

While a history of periconceptional use of folic acid was found in 10 (25%) mothers, 30 (75%) mothers did never use folic acid during pregnancy. Only two of the mothers (5%) used Vitamin B12. Information related to use of folic acid and Vitamin B12 could not be reached for 29 mothers. Four mothers (5.7%) were found to have a history of drug usage during pregnancy. One mother used selective serotonin reuptake inhibitor because of depression from the first trimester, one mother used alpha methyldopa because of gestational hypertension and three mothers had gestational diabetes. In these patients who were all followed up in external centers, the median time of making a diagnosis of NTD by ultrasonography in the prenatal period was 20 (16–24) weeks. Among 33 patients (47.8%) who were diagnosed prenatally, 27 (81.8%) were diagnosed as having meningomyelecele and six patients (18.2%) were diagnosed as having encephalocele. Thirty-six patients (52.2%) could be diagnosed in the postnatal period.

In the morbidity history of the mothers, one mother had gestational hypertension and three mothers had gestational diabetes. When familial history of similar disease was investigated, it was found that eight families (11.6%) had a history of NTD. Consanguineous marriage was found in 11 of the cases (15.9%); eight of these were second-degree consanguinity, while one was third-degree consanguinity. Consanguineous marriage was not found in any of the cases in which familial history of similar disease was positive.

Thirty-nine (56.6%) of the patients had other organ disorders including disorders involving multiple systems in some cases. Various orthopedic deformities (pes equinovarus, scoliosis) were found in 17 patients, various cardiac disorders (atrial septal defect, ventricular septal defect, patent ductus arteriosus, situs inversus totalis, double-outlet right ventricle, and arcus aorta hypoplasia) were found in 19 patients, urinary system disorders (hydronephrosis, renal agenesis, hypospadias, ectopic kidney) were found in seven patients, and cataract was found in one patient.

As a result of physical examination and imaging studies (cranial ultrasonography and cranial and/or spinal MRI), 49 (71%) of the patients were diagnosed as having meningomyelecele, 11 (16%) were diagnosed as having encephalocele, and 9 (13%) were diagnosed as having meningocele. Arnold–Chiari type 2 malformation was found in 45 (65.2%) of these patients and findings related to corpus callosum dysgenesis were found in nine.

Sac excision was performed in 16 of the patients, ventriculoperitoneal (VP) shunt operation in association with sac excision was performed in 49 patients, and operation could not be performed in three patients because of exitus or accompanying comorbidities (one patient had giant encephalocele, one patient had trisomy 18 [this patient who had multiple organ anomaly could not be intubated because of micrognathia and tracheotomy was performed], one patient had diaphragm hernia). Antibiotic treatment was initiated immediately in eight of the patients because cerebrospinal fluid leakage in the sac was observed after delivery; clinical sepsis developed in the postoperative period in two of these patients, but VP shunt infection did not develop, and they were discharged after treatment with appropriate antibiotics. Five of the patients who were operated died. The reasons for mortality included sepsis following intrauterine gastrointestinal tract (GIS) perforation secondary to malrotation (one patient) and multiple congenital anomaly (four patients).

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**Table 1: Clinical characteristics of the subjects**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (g), median (25%-75%)</td>
<td>3150 (2640–3450)</td>
</tr>
<tr>
<td>Gestational age (weeks), median (25%-75%)</td>
<td>38 (37-39)</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>11 (44)</td>
</tr>
<tr>
<td>Female</td>
<td>14 (56)</td>
</tr>
<tr>
<td>Maternal age (years), median (25%-75%)</td>
<td>27 (22-33)</td>
</tr>
<tr>
<td>Length of stay in hospital (days), median (25%-75%)</td>
<td>22 (18.5-37.5)</td>
</tr>
<tr>
<td>Folic acid use, n (%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>59 (75)</td>
</tr>
<tr>
<td>Yes</td>
<td>10 (25)</td>
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<tr>
<td>Vitamin B12 use, n (%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>67 (95)</td>
</tr>
<tr>
<td>Yes</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Prenatal diagnosis, n (%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>36 (52.2)</td>
</tr>
<tr>
<td>Yes</td>
<td>33 (47.8)</td>
</tr>
<tr>
<td>Frequency of cases, n (%)</td>
<td></td>
</tr>
<tr>
<td>Meningocele</td>
<td>9 (13)</td>
</tr>
<tr>
<td>Meningomyelocele</td>
<td>49 (71)</td>
</tr>
<tr>
<td>Encephalocele</td>
<td>11 (16)</td>
</tr>
</tbody>
</table>
The median time of hospitalization was 22 days (18.5–37.5) excluding the patients who died.

Discussion

The incidence of NTDs is specified by genetic and environmental factors and may vary depending on factors including the country’s developmental status, race, baby’s gender, and family’s socioeconomic and education status.\(^9,10\)

The incidence of NTDs has been reported to be 0.89–0.93 in 1000 live births in the European countries,\(^11\) 0.53 in the USA,\(^12\) 0.2–9.6 in Latin America,\(^13\) and 0.62–13.8 in the Arab countries.\(^14\) In our country, the incidence of NTD has been reported to be 5.6\(^15\) and 22.6\(^16\) in 1000 live births in various studies. Inadequate follow-up of pregnant women, high rates of consanguineous marriage, and lack of preference for prenatal termination because of religious beliefs may be the reasons for a higher incidence of NTD in our country compared to the European countries.

A history of consanguineous marriage was found in 11 of the cases, but they did not have a familial history of spina bifida. However, a history of spina bifida was found in the relatives of the parents.

Early prenatal diagnosis in NTDs (especially before the 24–26\(^\text{th}\) week) plays an important role in terms of therapeutic termination of pregnancy, when necessary.\(^17\) The time of prenatal diagnosis was the 24\(^\text{th}\) gestational week and earlier in 29 patients (42%). In our country, the legal borderline for medical termination is the 24\(^\text{th}\) gestational week. The file records revealed that medical termination was offered to the parents for the cases diagnosed prenatally before the 24\(^\text{th}\) gestational week, but the families did not accept this. This contributes to the higher incidence of NTD in our hospital and country compared to developed countries.

Arnold–Chiari type 2 malformation accompanies meningomyelocele at a high rate.\(^6\) In our study, Arnold–Chiari type 2 malformation was found with a rate of 65% (45 patients). Similarly, this rate was found to be 71.4% in the study conducted by Çelik et al.\(^18\) Hydrocephaly requiring surgical intervention was found in 71% of the cases which was an expectedly high rate.

NTDs may also affect the organs outside the nervous system depending on the time they form in the fetal period.\(^19\) We found anomaly in at least one of the organs including heart, eye, kidney, and skeletal system with a rate of 58%. It has been reported that accompanying anomalies develop as a result of mechanical action of the disorder in the neural tube and surrounding tissues and these increase the mortality risk to a significant extent.\(^7\)

Folic acid is a substance which is essential for synthesis of intracellular nucleotides used in DNA synthesis and for the methylation reactions taking place in the cell. Since the neural tube draft is formed in the early stages of pregnancy, sufficient folic acid should be available in the environment in the periconceptional period. It has been shown that folic acid deficiency causes NTDs and use of periconceptional folic acid decreases NTD recurrence by 50%–70%. Considering that 75% of the mothers of our patients had never used folic acid, families should be explained that they should use folic acid in the periconceptional period to decrease NTD recurrence in subsequent pregnancies. It has been reported that low Vitamin B12 levels during pregnancy independently increase the risk for NTD.\(^19\) Only two of the mothers of our patients had used Vitamin B12. Similarly, mothers who have not used Vitamin B12 during pregnancy should be informed that they should use Vitamin B12 in association with periconceptional folic acid in subsequent pregnancies.

Conclusion

It is possible to make the diagnosis in babies with NTDs by ultrasonography from the early stages of pregnancy. Prenatal diagnosis is delayed in an important portion of the cases. In cases where the diagnosis is made in time, it is observed that families decide to continue pregnancy because of sociocultural factors. In NTDs, morbidity or disorders in other organ systems accompany beside CNS disorders. The patients need long-term follow-up and collaboration of different clinical branches including pediatrics, neurosurgery, physical therapy and rehabilitation, and pediatric surgery and the follow-up process may also be backbreaking for families. Raising awareness of the families of babies who are diagnosed in the early prenatal period about the prognosis in addition to studies directed to periconceptional use of folic acid and Vitamin B12 may contribute to a reduction in sociocultural pressure.

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Conflicts of interest

There are no conflicts of interest.

References

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