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Non-syndromic malformations of the central nervous system in twin pregnancies: diagnostic and other clinical features of importance

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ABSTRACT

Objective: The incidence of central nervous system malformations is higher among twins. Our aim was to summarize information about these malformations in twin pregnancies.
Study design: Based on a sample originating from the biggest genetic centre in Hungary between January 1990 and December 2008, we examined the data of 42 twin pregnancies associated with non-syndromic malformations of the central nervous system.
Results: The involvement of monozygotic fetuses and dizygotic ones of the same gender was found to be 62.5%. Usually only one of the fetuses was affected (57.1%), while the other one was healthy. The male-to-female ratio was 0.75. Identical and fraternal twins were found in 68.4% and 31.6% of the cases, respectively. In the pregnancies of our study the malformation was diagnosed before the 24th gestational week in 90% of the cases. Polyhydramnios (54.8%) was the most commonly associated non-central nervous system malformation.
Conclusion: Our findings suggest that, in addition to placentation and gestational age, the position of the affected fetus with relation to the uterine orifice is of great importance in determining whether selective abortion is an option in deciding about the outcome of pregnancies affected by craniospinal malformation.

1. Introduction

Owing to the risk of possible complications twin pregnancies are regarded as obstetric pathological conditions [1]. Due to the spread of assisted reproductive techniques, the incidence of multiple pregnancies has significantly increased. Approximately two thirds of twins are fraternal (dizygotic, DZ). Their prevalence is 7–11/1000 deliveries, which increases in parallel with increasing maternal age. Fraternal twins are the result of simultaneous ovulation of two egg cells fertilized by two sperm cells. The prevalence of identical (monozygotic, MZ) twins is 3–3.5/1000 deliveries [2]. MZ twins result from the separation of the zygote at different stages of development. If, after division, the two cells of the zygote separate, two placentas, two chorions and amnions develop (diplacental, dichorionic, diamnionic placentation, DDD). If the separation is only partial, the two placentas unite to result in monoplacental, dichorionic and diamnionic placentation (MDD). If embryonic division begins prior to the development of the chorion, it leads to the development of two amnions within a single chorion (monoplacental, monochorionic, diamnionic placentation MMD), but when the process starts after the formation of the amnions, it results in a single amnion (monoplacental, monochorionic and monoamnionic placentation, MMM) [3].

Congenital malformations in twin pregnancies, especially monozygotic ones, have been widely known to occur more commonly than in singleton pregnancies; moreover those malformations usually affect one of the fetuses alone [4,5]. There are several explanations for why the chances of genetic malformations in multiple pregnancies are higher [6]. Based on some studies, the risk of genetic disorders in twin pregnancies may be twice or three times as high as in singleton ones [7–9]. Certain malformations are associated with the process of twin formation itself (acardiacus, conjoined twins) [8], while the incidence of others exceeds the figures found in singleton pregnancies.

As in singleton pregnancies, craniospinal malformations appear to be the most common disorders in multiple pregnancies. In addition to neural tube defects, the prevalence of hydrocephalus is three times higher, while that of other central nervous system malformations is one and a half times higher in twin pregnancies [10]. Some publications report an even higher – as much as 10–15 times – increase in the prevalence of anencephaly [11].

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In this paper we summarize the knowledge about the association of twinning and malformations of the central nervous system, based on a sample originating from the biggest genetic centre in Hungary, and we highlight the significance of sonography in decision-making about the fate of an affected twin pregnancy.

2. Materials and methods

We undertook a descriptive study of all the 42 twin pregnancies associated with malformation of the central nervous system diagnosed at the Genetic Counseling Unit of the 1st Department of Obstetrics and Gynecology of the Faculty of General Medicine at Semmelweis University in the period of 1st January 1990 and 31st December 2008. Cases in which a fetal central nervous system malformation occurred as part of a syndrome were excluded from the study.

Hydrocephalus, spina bifida, spina bifida plus hydrocephalus, anencephaly and holoprosencephaly were the malformations occurring in the 42 twin pregnancies examined [12,13]. The fetopathological investigations were done at the Fetopathology Laboratory of the Department according to national and international protocols [14–16].

The computerized database containing the details of the individual cases served as the source of information. In addition to establishing the major demographic features, we had the opportunity to provide diagnostic details and a survey of the outcome of the pregnancies. We tried to pay special attention to the outcome because making a decision about the fate of twin pregnancies affected by malformation is one of the greatest challenges clinical genetics, and obstetrics and gynecology have to face. Together with providing the ultrasonographic diagnosis of the individual malformations we have attempted to reveal all the possible details of the associated non-central nervous system malformations as well.

For statistical analysis, differences between groups were evaluated with a 2-tailed Student's t test. For dichotomous parameters, the Fisher exact test was used. $P \leq 0.05$ was considered statistically significant. For the sake of simplicity the condition ventriculomegaly/hydrocephalus will simply be referred to as 'hydrocephalus' in the rest of the text.

3. Results

Among the 2178 craniospinal malformations, 42 (1.92%) occurred in multiple (twin) pregnancies. Maternal median age was found to be 28 ± 5.16 years.

Table 1 shows the distribution of the malformations in the examined twin pregnancies. Concerning the severity of the cases of hydrocephalus, in 11 pregnancies the diameter of the lateral ventricle was above 15 mm (severe hydrocephalus), while in 3 cases it was 12–13 mm (mild hydrocephalus). In the cases of spina bifida sacral localization occurred in 1 case, while the thoracolumbar or lumbar segment(s) were affected in the remaining 5 cases. In the 10 cases of associated spina bifida and hydrocephalus the diameter of the lateral ventricle was above 15 mm. Both cases of encephalocele were occipital. In each case the fetopathological or neonatological examination confirmed the prenatal diagnosis.

Table 1
Distribution of central nervous system malformations in twin pregnancies in the study.

Malformation	Number of cases (n)	Percentage (%)
Hydrocephalus	14	33.34
Spina bifida + hydrocephalus	10	23.81
Anencephaly	8	19.04
Spina bifida	6	14.29
Encephalocele	2	4.76
Holoprosencephaly	2	4.76
Total	42	100

Table 2
Placentation in twin pregnancies in the study.

Placentation	Number of cases (n)	Percentage (%)
Diplacental, dichorionic, diamnionic (DDD)	10	29.41
Monoplacental, dichorionic, diamnionic (MDD)	6	17.64
Monoplacental, monochorionic, diamnionic (MMD)	14	41.17
Monoplacental, monochorionic, monoamnionic (MMM)	4	11.76
Total	34	100

Note: Information about placentation was available in 34 cases.

Table 2 shows the placentation in the examined cases. Sex was known in 38 cases. In 26 cases (68.42%) the fetuses were of the same sex, while in 12 cases (31.58%) they were of different sex. The summarized male-to-female ratio was 0.75.

When we examined the effect of the individual malformations in the twin pregnancies we found that fetus A was affected in 24 cases (57.14%), and fetus B in 14 cases (33.34%). In 4 pregnancies both fetuses were affected by the same malformation (spina bifida with hydrocephalus). In 38 of the 42 cases (90.47%), the malformation(s) could be diagnosed before the 24th gestational week, and there were only 4 pregnancies (9.53%) with malformations diagnosed later than week 24.

As far as the outcome of the pregnancies was considered, abortion was induced in 30 cases (71.42%), while, with regard to the date of diagnosing the malformation, the pregnancy was terminated by induced premature delivery in 8 cases (19.04%). In 2 cases, the pregnancies were carried close to term and the mothers delivered a live, mature and healthy fetus A, together with the malformed fetus B in either case. In the remaining 2 cases (4.76%), fetuses B suffering from hydrocephalus were exposed to selective termination in the 22nd and 23rd gestational weeks (Table 3). In both cases, the intervention was possible due to the dichorionic placentation. These 2 pregnancies progressed uneventfully to the 37th and 39th gestational weeks and live, mature and healthy newborns were delivered.

The pregnancies were terminated at a mean gestational age of 23.3 weeks (the 2 pregnancies terminated via selective abortion were considered as 4 individual cases).

In 30 pregnancies with specific malformations, one of the twins was unaffected (71.42%), but in 2 cases in which one fetus suffered from hydrocephalus the other one was affected by further malformation such as anencephaly or encephalocele.

The results of our study showed a relatively wide range of associated malformations apart from of the central nervous system. Among the 8 cases of anencephaly, polyhydramnios was also diagnosed in six instances, in addition to which diaphragmatic hernia, esophageal atresia, pyelectasis and intestinal malrotation were also found individually. In the 2 twin pregnancies complicated with encephalocele, no other malformations of the central

Table 3
Outcome of twin pregnancies in the study.

Outcome of pregnancy	Number of cases (n)	Percentage (%)
Induced abortion	30	71.43
Induced premature delivery	8	19.05
Delivery	2	4.76
Selective abortion	2	4.76
Total	42	100