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Etiology, Prenatal Diagnostics and Outcome of Ventriculomegaly in 230 Cases

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Key Words
Ventriculomegaly · Lateral ventricle diameter · Occipitofrontal diameter · TORCH serological test

Abstract
Objective: The aim of this study was to review and summarize the information regarding the etiology, diagnostics and outcome of ventriculomegaly. ***Methods:*** The study included 230 cases of ventriculomegaly examined between 1979 and 2000. The main diagnostic criterion for ventriculomegaly was the transverse diameter of the ventricular atrium at the level of the glomus of the chorioid plexus measuring >10 mm, irrespective of gestational age. ***Results:*** Gender distribution (male:female ratio: 0.98) coincided with that of the general population. In 32% of the cases (72/230), the history was positive; 6% (12/230) had a positive genetic history, while 26% (60/230) were associated with pathological obstetric events. The incidence rate of ventriculomegaly in the patients' history was found to be 2.61% (6/230). In nearly 60% of the cases included in this study, ventriculomegaly was diagnosed before the 24th week of pregnancy. Fresh fetal infection confirmed by *Toxoplasma* PCR real-time examination was diagnosed only in cases of severe ventriculomegaly. Based on the measurement of the diameter of the atrium of the lateral ventricle, severe and mild ventriculomegaly was diagnosed in 142/230 (61.7%) and 88/230 cases (38.3%), respectively. Termination of pregnancy was significantly more frequent in cases of severe than of mild ventriculomegaly (92 vs. 66%). ***Conclusions:*** The importance of positive obstetric and/or genetic history should be emphasized as it is in direct relationship with the increased incidence of this malformation. Regarding the practice of ultrasonography, mild ventriculomegaly (transverse diameter of the lateral ventricle <15 mm) has a much better prognosis than the severe form (transverse diameter of the lateral ventricle >15 mm) of the malformation. Based on the ultrasonographic diagnosis of ventriculomegaly, TORCH serological examination is also recommended since treating toxoplasmosis by medication may have a promising prognosis for the pregnancy. In cases of isolated ventriculomegaly alone, intrauterine karyotyping is not necessarily indicated, but in cases where ventriculomegaly is associated with other genetic disorders karyotyping should definitely be performed. Since ventriculomegaly is not incompatible with postnatal life by itself, the decision about the fate of the pregnancy is largely dependent on the presence of other organic disorders.

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Introduction

In the first weeks of embryonic life, the brain consists of three parts known as the prosencephalon, mesencephalon and rhombencephalon. By the 5th gestational week, following the closure of the neural tube, the prosencephalon is converted into the telencephalon (hemispheres) and diencephalons (thalamus, hypothalamus), the mesencephalon becomes the midbrain, while the rhombencephalon gives rise to the formation of the metencephalon (pons and cerebellum) and myencephalon (medulla oblongata). The dilated portions of the cavity of the neural tube are referred to as the cerebral ventricles. The pair of cerebral ventricles situated in the telencephalon is called the lateral ventricles, and the cavities of the rhombencephalon are known as the 3rd and 4th cerebral ventricles. The portions of the neural tube cavity, which remain narrow in the mesencephalon and the spinal cord, are referred to as the cerebral aqueduct and central canal, respectively [1].

Ventriculomegaly is a condition in which the increased amount of cerebrospinal fluid (CSF) dilates the cavities of the brain [2–5]. The causes include overproduction of CSF and blockage of CSF flow. If ventriculomegaly progresses, the matrix of the brain becomes thinner and the condition is diagnosed as internal hydrocephalus. In the case when CSF accumulates in the subarachnoid space, the condition is referred to as external hydrocephalus. Except for some rare forms, the disorder is first detected in the posterior horns of the lateral ventricles, the anterior horn and the 3rd cerebral ventricle being affected later.

The prevalence of ventriculomegaly is found to be 0.3–1.5/1,000 live births [6–10].

The aim of this study was to review and summarize the information regarding the background of ventriculomegaly. We attempted to evaluate the role of anamnesis, the different etiological factors as well as the possibilities and difficulties of prenatal diagnostics regarding ventriculomegaly. We also tried to emphasize the important points of the clinical management of the malformation. At the same time, we did not aim to perform a long-term neurological follow-up of isolated cases of ventriculomegaly; this is the task of a next study.

Material and Methods

This study included 230 cases diagnosed according the diagnostic criteria of ventriculomegaly at the Department of Obstetrics and Gynecology of the Medical University School of Debrecen and Genetic Counselling Unit of the 1st Department of Obstetrics and Gynecology at Semmelweis University Medical School in the periods of 1979–1990, and 1990–2000, respectively. (The fragmentation of this time period is due to the moving of the Genetic Counselling Unit from Debrecen to Budapest.)

History taking and prenatal ultrasonography performed in the Ultrasound Laboratory of our Departments, and laboratory tests (TORCH serology – *T*oxoplasma *O*thers *R*ubella *C*ytomegalovirus *H*erpes, maternal serum alpha fetoprotein – AFP) done in the Laboratory of our Department served as main sources of information regarding the examined cases.

Ventriculomegaly was almost always diagnosed via ultrasonography, mainly between the 12th and 24th gestational week. The development of sonography has made it possible to make earlier and more reliable diagnosis. In Hungary, prenatal ultrasound examinations are standardized according to the protocol of the Hungarian National Society of Ultrasound in Gynecology and Obstetrics [3].

Earlier, the diagnosis of ventriculomegaly was based on old criteria such as lateral ventricle width of more than 8 mm and the lateral ventricle-hemisphere width ratio. At present, the transverse diameter of the ventricular atrium at the level of the glomus of the chorioid plexus measuring more than 10 mm, irrespective of gestational age is favored as the main diagnostic criteria for ventriculomegaly [11–13]. Mild ventriculomegaly is defined as a transverse diameter of the atrium of the lateral ventricle measuring between 10 and 15 mm, while in the case of severe ventriculomegaly this value is above 15 mm. In cases of mild ventriculomegaly, the postnatal prognosis is favorable [14–16].

Further parameters of ultrasonographic diagnosis included measurements of the spaciousness of the lateral cerebral ventricles, certain diameters of the cranium (biparietal diameter – BPD, occipitofrontal diameter – OFD), head circumference – HC [(BPD + OFD) × 1.57], and the definition of the cranial index (CI; BPD/OFD × 100). In spite of their smaller diagnostic significance, BPD, OFD and CI are also worth mentioning regarding the sonography of ventriculomegaly.

Ultrafast MRI produces detailed and reproducible images of fetal anatomy. MRI is the most useful in the evaluation of the fetal brain, neck, chest and abdomen. In spite of its advantages, MRI diagnostics is actually not the part of the daily practice of genetic counseling.

In many cases, the development of ventriculomegaly is due to an intrauterine infection. TORCH serological examination (indicated by sonographic findings) makes the verification of recent maternal infections possible. In the case of a recent *Toxoplasma* infection, the sequelae of congenital toxoplasmosis can be reduced by 50% with spiramycin therapy. The adequate diagnosis of fetal *Toxoplasma gondii* infection was given by the quantitative real-time PCR examination of the amniotic fluid [17].

AFP levels in maternal serum increase rather than decline from the 10th until the 30th–32nd weeks. The optimal time of AFP sampling is the 16th gestational week. In physiological single pregnancies, the value ranges between 0.9 and 2.5 multiple of median (MoM). In the case of ventriculomegaly, no elevated AFP level is expected.

Karyotyping was performed via genetic amniocentesis or chorionic villi sampling.

Table 1. Distribution of ventriculomegaly cases according to positive obstetric and genetic history

Patient's history	% (n)
No history	28.69 (66)
Obstetric history	
Mature delivery	32.19 (74)
Artificial abortion	7.83 (18)
Genetic history	
Premature delivery	4.35 (10)
Perinatal damage	0.43 (1)
Intrauterine death	3.04 (7)
Ectopic pregnancy	0.87 (2)
Molar pregnancy	0.87 (2)
Miscarriage	14.35 (33)
Missed abortion	2.17 (5)
Induced abortion	5.21 (12)
Due to ventriculomegaly	2.61 (6)
Due to neural tube closure defect	1.31 (3)
Due to cardiac malformation	0.43 (1)
Due to multiple malformation syndrome	0.86 (2)

Table 2. Distribution of etiological factors in cases of ventriculomegaly

Etiological factors	% (n)
Agenesis of the corpus callosum	8.63 (5)
Stenosis of the aqueduct of Sylvius	13.79 (8)
Arnold-Chiari's malformation	3.45 (2)
Chromosome aberration	6.89 (4)
Dandy-Walker syndrome	5.17 (3)
Infections	15.51 (9)
T. gondii	12.06 (7)
Rubella virus	1.72 (1)
Cytomegalovirus	1.72 (1)
Holoprosencephaly	1.72 (1)
Intracranial hemorrhage	1.72 (1)
Intracranial tumors	1.72 (1)
Porencephaly	0
Multiple malformation syndrome	41.38 (14)
Aneurysm of the vein of Galen	0
Total	100 (58)

All the available pieces of information in the investigation were collected and processed by way of a computerized database.

Where statistical analysis was performed, significant difference was accepted at $p < 0.05$.

Results

The gender distribution in the diagnosed cases corresponded to that of the general population; the male:female ratio was 0.98.

Maternal and paternal median ages were found to be 26 ± 4.2 and 31 ± 5.2 years, respectively.

The malformation occurred almost equally often in first and second pregnancies, at an incidence rate of approximately 30%.

Checking the pregnant women's histories in table 1, in 72 cases (32%) a positive history was to blame; positive genetic history and pathological obstetric events were found in 6 and 26% of them, respectively. In cases of severe ventriculomegaly, the ratio of pregnancies with positive history was 28.9%, while in cases of mild ventriculomegaly 35.2%. The difference was not significant ($p > 0.05$). In the group with positive genetic history, the 6 cases in which ventriculomegaly had been detected earlier are worth a special mention. Their incidence rate, compared to the total, is 2.61%.

As shown in table 2, almost 75% of the cases consisted of ventriculomegaly inherited monogenically (stenosis of the aqueduct of Sylvius, Dandy-Walker syndrome AR), developing due to infection or appearing as part of syndromes and associations. (The etiology was known in 58 cases.)

The incidence of the combination of ventriculomegaly and multiple pregnancy was 4.34% (10/230). Two of them turned out to be monozygous pregnancies. Considering all of the multiple pregnancies, in 6 of them, only one fetus while in 4 pregnancies both fetuses were affected. It may be of interest to note that in cases when one of the fetuses was affected it happened to be fetus 'B' in 5 of the 6 cases (83%).

As table 3 shows, in almost 60% of the pregnancies investigated by us, ventriculomegaly was diagnosed before the 24th gestational week.

Elevated maternal serum AFP values were found in almost 31% of the cases, while in 11%, AFP levels were below the lower physiological limit (table 4). The median value was: 1.48 ± 0.6 MoM.

As it was seen on examining the etiological background of ventriculomegaly, the disorder developed due to intrauterine infection in a significant number of cases (16%). In clinical practice, these infections are screened using the TORCH serological test. According to table 5, findings by the TORCH test were at our disposal in 42 cases, 9 of which confirmed fresh maternal infection,

Table 3. Time of making the diagnosis in the examined cases

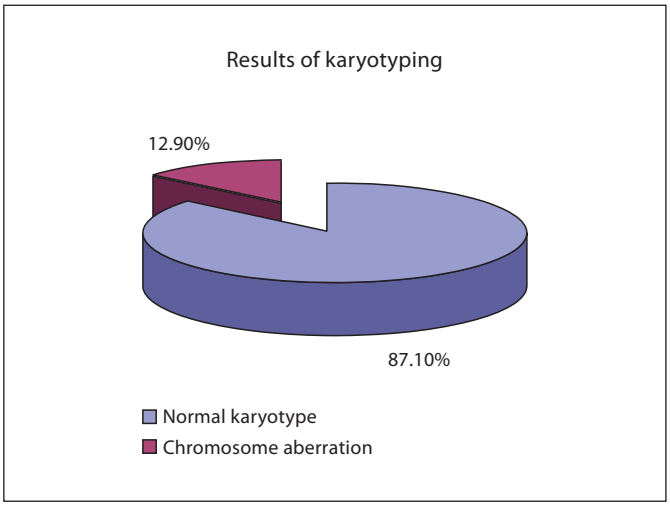
Gestational week	%	n
≤16	5.21	12
17–18	11.74	27
19–20	18.26	42
21–22	13.04	30
23–24	10.87	25
25–26	6.96	16
27–28	10.00	23
29–30	7.4	17
31–32	9.56	22
≥33	6.96	16
Total	100	230

Table 4. Maternal serum AFP in cases of ventriculomegaly

Maternal serum AFP level	%	n
Normal (0.9–2.5 MoM)	58.71	91
Elevated (>2.5 MoM)	30.32	47
Decreased (<0.9 MoM)	10.97	17
Total	100	155

Table 5. Results of TORCH serological screening in ventriculomegaly

Presence/absence of maternal infection	%	n
Fresh maternal infection excluded	78.57	33
Fresh maternal infection confirmed	21.43	9
T. gondii	16.67	7
Rubella virus	2.38	1
Cytomegalovirus	2.38	1
Total	100	42



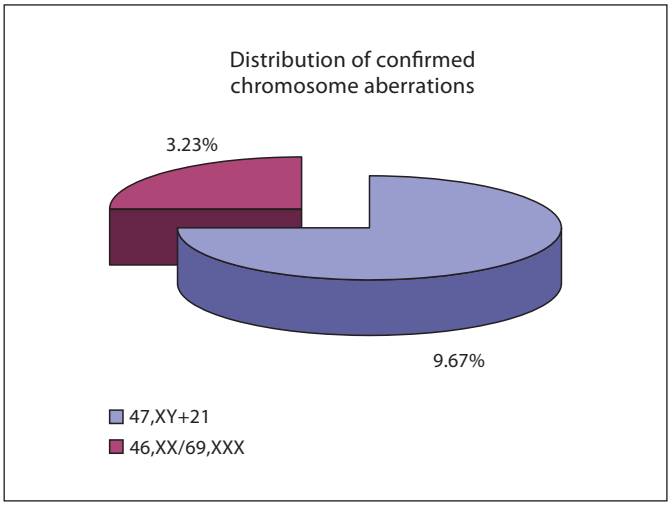


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Fig. 1. Distribution of karyotyping in ventriculomegaly.

their frequency being almost 22%. In 4 cases, the real-time PCR examination verified fetal *T. gondii* infection. In all cases of proven fetal *Toxoplasma* infection, a severe ventriculomegaly was verified. The incidence of viral infections was quite low.

Regarding the association of ventriculomegaly and chromosome aberrations, we had the data of 31 cases, including 4 pathological cases and 27 patients with healthy chromosomal structure (fig. 1). In the 3 cases of severe ventriculomegaly in which Down's syndrome was confirmed, the problem could be traced back to chromosome aberration due to higher maternal age. The fourth case of chromosome aberration (46,XX/69,XXX) occurred in a pregnancy with mild ventriculomegaly.

Based on the sonographic measurement of the diameter of the atrium of the lateral ventricle, severe and mild ventriculomegaly was diagnosed in 142 (61.7%) and 88 (38.3%) cases, respectively.

The measured BPD values were always interpreted in relation to the percentile figures for the age of pregnancy in question. BPD was found to be 75th percentile or higher in almost 50% of the cases, while 10th percentile or lower figures were found in just 17% of the cases.

In addition to BPD, the values for OFD were also checked, as shown in table 6. The percentile values at 75 or higher were found in nearly 70% of the cases and even percentile figures exceeding 90 were found in almost 52% of the cases.

HC (fig. 2) at 75th percentile or higher was found in nearly 45%, while findings of 50th percentile were also numerous at 24%. HC values of 10th percentile or lower were reported in approximately 15%.

CI can also be calculated (table 7) from the values of BPD and OFD. CI figures between 77 and 82 represented almost half of the sample; values above 87 and below 72 were equally rare.

In our sample of 230 cases, other craniospinal malformations were diagnosed in 35 patients, which corresponded to a rate of 15.21%. According to our expectations ventriculomegaly is most often associated with spina bifida, the prevalence of the sacral spine being the highest among the spinal regions.

Other disorders of the non-central nervous system occurred, or were detected by ultrasonography in a total of 151 cases (table 8), corresponding to a frequency rate of nearly 66%. Regarding the associating non-central nervous system malformations, no significant difference ($p > 0.05$) was noted between the cases of mild and severe ventriculomegaly. It was shown that disorders involving the quantity of amniotic fluid were the most frequent, whilst malformations involving the individual organs or systems were most commonly found in the urinary tract (13.25%). The 6.5% incidence of limb malformations should also be mentioned. Considering the most populous group of associated malformations, polyhydramnion of an approximately 22% incidence rate should definitely be mentioned. Of the other associated disorders, fetal pyelectasis, pes equinovarus and increased echodensity of the fetal bowels should be highlighted.

There were 2 cases in our sample, in which the examination results were suggestive of multiple malformation syndrome. In the first one, an 18-year-old primigravida was supposed to carry a fetus affected by Neu-Laxová syndrome: in addition to ventriculomegaly, corpus callosum agenesis, expressed microcephaly, micrognathia, flexion deformity of the leg and renal agenesis were detected in the 32nd gestational week. Following the diagnosis, the pregnancy was terminated by induced premature delivery, and the baby died shortly after birth. The autopsy confirmed the findings obtained by ultrasonography.

In the other case, ultrasonography performed in the 18th gestational week of a 24-year-old tertigravida re-

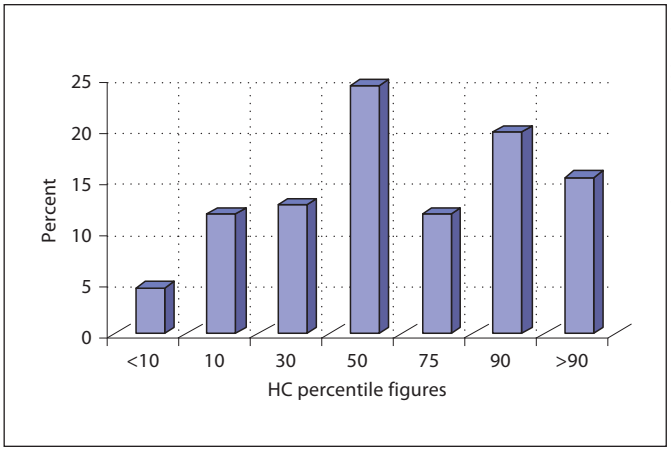

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Fig. 2. Values of HC in cases of ventriculomegaly.

Table 6. The values of the OFD in ventriculomegaly

Percentile values of the OFD	%	n
<10	3.84	4
10	7.69	8
30	6.74	7
50	13.47	14
75	7.69	8
90	8.65	9
>90	51.92	54
Total	100	104

Table 7. Values of CI in cases of ventriculomegaly (normal range in italics)

CI	%	n
<70	4.85	5
70–72	1.83	2
73–74	22.03	24
75–76	5.51	6
77–78	27.53	30
79–80	4.58	5
81–82	17.44	19
83–84	0.92	1
85–86	7.34	8
87–88	1.83	2
89–90	1.83	2
91–92	1.83	2
93–94	1.83	2
>94	0.92	1
Total	100	109

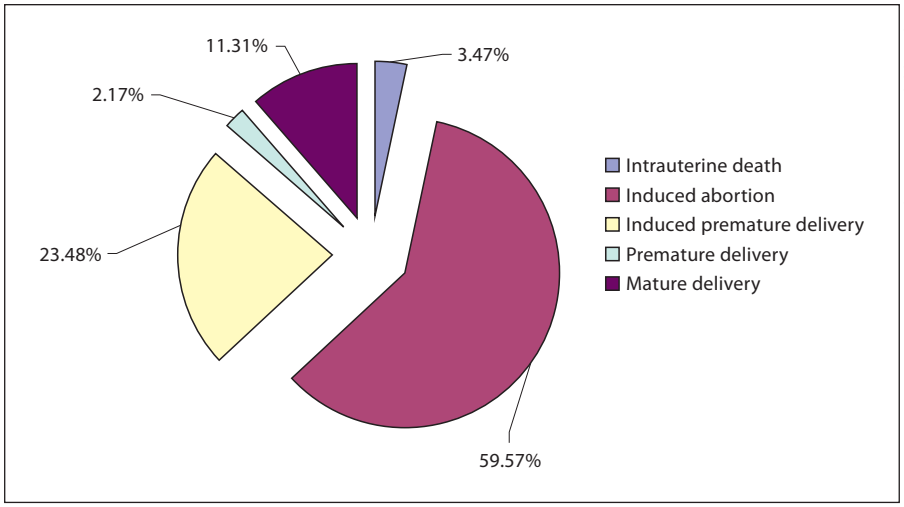

Fig. 3. Outcome of pregnancies in cases of ventriculomegaly.

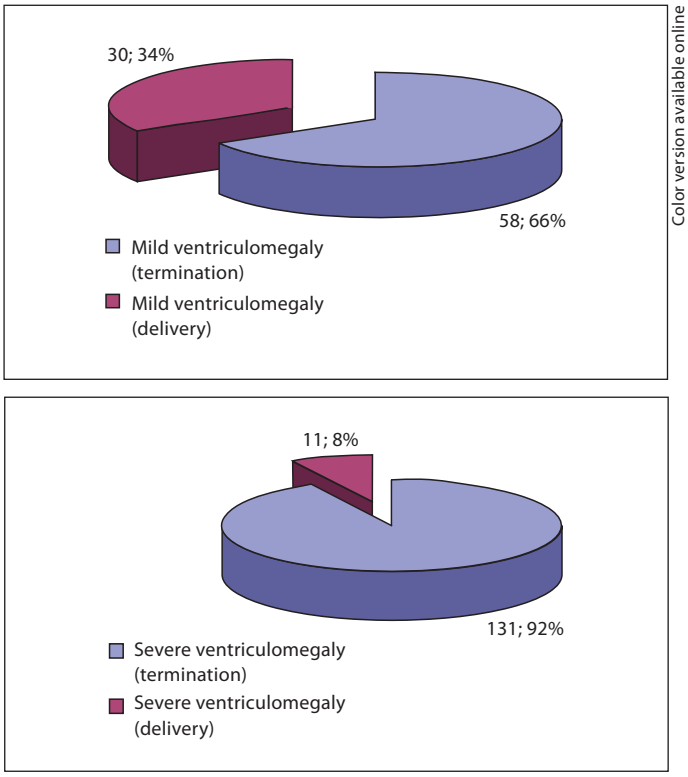

Fig. 4. Outcome of pregnancies in cases of mild and severe ventriculomegaly.

vealed grave facial dysmorphism (asymmetry of the halves of the face, micrognathia, severe cleft palate), vertebral malformation, diaphragmatic hernia, and dextrocardia in association with ventriculomegaly, the condition being suggestive of the Goldenhar complex. In the fetopathological investigation after induced abortion, additional malformations such as auricular deformity of the ear and microstomia – further symptoms of the Goldenhar complex – were also detected.

In our sample, pregnancies were terminated in 83% of the cases (induced abortion and induced premature delivery in 59 and 23%, respectively; fig. 3). Regarding the outcome of pregnancies associated with mild and severe ventriculomegaly, a significant difference ($p < 0.05$) was observed (fig. 4).

The outcome of pregnancies conceived after a diagnosed case of ventriculomegaly meant invaluable information for us. We examined a total of 64 such pregnancies: the data about which are summed up in table 9. In those cases, live, mature and healthy newborns overwhelmingly dominated (88%), but in 3 pregnancies (4.7%) ventriculomegaly was diagnosed again; in another case, a different malformation was detected.

Discussion

In the majority of the cases, ventriculomegaly is not dominantly associated with either sex (male:female ratio: 0.98).

Parental age is of great importance in genetic counseling. Maternal age around the median of 26 years is in close harmony with the 27 years median age published by Chervenak et al. [18], but somewhat lower than the 29 years median published by Vergani et al. [10]. Paternal age – considering social and conventional differences – is in agreement with the distribution of maternal age.

Table 8. Malformations of the non-central nervous system associated with ventriculomegaly

Malformations	%	n
Face	3.04	7
Facial dysmorphism	0.43	1
Facial hemangioma	0.43	1
Exophthalmos	0.43	1
Pierre Robin sequence	0.43	1
Cleft palate	1.31	3
Heart	3.47	8
Dilated chambers	0.43	1
Atrioventricular septal defect	0.43	1
Hypoplastic left heart syndrome	0.43	1
Dextrocardia	0.86	2
Three-chambered heart	0.43	1
Cardiomegaly	0.43	1
Atrial septal defect	0.43	1
Vascular system	1.73	4
Aortic dextroposition	0.43	1
Single umbilical artery	1.31	3
Gastrointestinal tract	4.78	11
Anal atresia	0.43	1
Esophageal atresia	0.43	1
Jejunal atresia	0.43	1
Intestinal dilatation	0.43	1
Echodense bowels	3.04	7
Urinary system	8.69	20
Renal agenesis	1.31	3
Ureteral agenesis	0.43	1
Fetal pyelectasia	3.04	7
Dysplasia of renal tubules	0.43	1
Posterior urethral valve	0.43	1
Polycystic renal dysplasia	1.73	4
Multicystic renal dysplasia	0.43	1
Dilated ureter	0.43	1
Soleiform kidney	0.43	1
Abdominal wall	1.73	4
Omphalocele	1.73	4
Limbs	6.52	15
Clubfoot	3.04	7
Hand malformation	1.31	3
Micromelia	1.73	4
Clinodactyly	0.43	1
Skeletal malformation	0.86	2
Quantitative differences of amniotic fluid	29.12	67
Polyhydramnion	21.73	50
Oligohydramnion/anhydramnion	7.39	17
Fixed posture	2.61	6
Fetal hydrops	2.17	5
Intrauterine growth retardation	0.86	2

Table 9. Outcome of subsequent pregnancies in cases of ventriculomegaly

Outcome of subsequent pregnancies	%	n
Mature delivery	87.51	56
Premature delivery	1.56	1
Intrauterine death	1.56	1
Miscarriage	1.56	1
Missed abortion	1.56	1
Ventriculomegaly	4.69	3
Other malformation	1.56	1
Total	100	64

Investigation into the obstetric-gynecological/genetic history of our patients was of special importance. On the basis of the results, it can be declared that the chances for ventriculomegaly to develop are higher if there is a positive genetic and/or obstetric-gynecological finding in the mother's history. Regarding positive history between the mild and severe cases of ventriculomegaly, no significant difference can be seen ($p > 0.05$).

Three large groups including the majority of etiological factors could be distinguished: monogenic cases, intrauterine infections, and cases occurring as part of syndromes and associations [16, 18, 19]. In addition to them, we should also mention cases associated with chromosomal defects. Tercanli et al. [9] came to similar conclusions about the distribution of etiological factors, while Jansen [20] found higher incidence rates for monogenicity and intrauterine infections (16 and 28%, respectively). According to Pilu et al. [19], chromosomal defects were fewer, at approximately 3.8%.

Considering the malformation and its association with multiple pregnancies, their incidence rate was found to be 4.34%. A publication by Den Hollander et al. [21] has reported a much higher incidence at 18%.

One of the most important tasks of genetic counseling is the earliest possible diagnosis of malformations [16]. Of course, the time when the malformation arises always has its influence on the chance of an early diagnosis, but it is still important to note that 60% of the diagnoses were made before the 24th gestational week. Vergani et al. [10] found that the mean time of diagnosing isolated malformations was in the 29th gestational week; in the cases with other complications it was in the 22nd gestational week that they could detect the malformations. According to the findings by Pilu et al. [19], diagnoses are most likely between gestational weeks 22 and 25. Benacerraf [6] found that, in addition to measuring the spaciousness of the lateral ventricle, the safest way of diagnosing a malformation before the 22nd gestational week was the determination of the lateral ventricle-hemisphere width ra-

tio. Tercanli et al. [9], however, thinks that the earliest time for detecting the malformation is in the 16–17th gestational weeks.

The maternal serum AFP values [22] above and below the physiological range were found in 31 and 11% of the cases, respectively. Csabay et al. [22] reported approximately 13% of serum AFP values above 2.5 MoM in isolated cases of ventriculomegaly.

Analyzing the TORCH serological findings, we found that in almost 22% of the cases a recent maternal infection was present. Jansen [20] found a 28% incidence rate for fresh maternal infections by *Toxoplasma*, rubella virus and cytomegalovirus, which means slightly higher figures compared to our sample. It is important to note that among the agents causing the infections, *T. gondii* was found most frequently in the background. This further emphasizes the indication of TORCH serological investigations in the case the ultrasonographic diagnosis of ventriculomegaly has been made, since treating toxoplasmosis by medication (spiramycin) may have a promising prognosis for the pregnancy. Though, for the safe diagnosis of fetal *T. gondii* infection a real-time PCR examination of the amniotic fluid is required. Based on our examinations it can be concluded that recent fetal *Toxoplasma* infection causes more frequently severe, rather than mild ventriculomegaly.

Of the 31 karyotypings, 4 were found pathological, which corresponded to a ratio of 12.90%. As far as the etiological role of chromosome aberrations is considered, in their publications, researchers such as Bronsteen and Comstock [23], Pilu et al. [19], Lipitz [24] and Vergani et al. [10] reported 8, 3.8, 3.6 and 2.8% incidence rates, respectively; by magnitude, these findings correspond to our value at 6.89%. Isolated ventriculomegaly alone is not necessarily indicative of intrauterine karyotyping, but in cases of a severe disorder, mainly when it is associated with other genetic disorders, it should definitely be performed.

Regarding the ratio of the cases of mild and severe ventriculomegaly of a big sample, only a few references are available. According to the investigations of Graham et al. [25], in 39 of the 64 examined cases (60.9%) a severe, and in 25 (30.1%) a mild ventriculomegaly was diagnosed. This ratio is quite similar to that of our sample.

Based on the 158 numerical data, BPD values were found to be or exceed 90th percentile in 34% of the cases. The same data were found at 50% in the sample of Chervenak et al. [26]. It is obvious that the values of BPD were significantly elevated only in the cases with expressed dilation of the lateral ventricles.

We had the opportunity to check OFD in 104 cases and found that it was or exceeded 90th percentile that of the relevant gestational age in 60%. If this parameter is examined in view of the BPD, the prognostic/diagnostic value of OFD should be regarded to be of greater importance than earlier.

Similarly to BPD, values of HC at or exceeding 90th percentile were found in 34% of the cases. Based on their own examinations, Den Hollander et al. [21] came to practically similar conclusions, but it should be remembered that HC values in the 50th percentile range were found to be the most common.

CI expresses the ratio of BPD and OFD with relation to each other (normal range: 73–83).

Making the prognosis of the disorder, in addition to the aforementioned points, other, possibly associated, neurological malformations are also of great importance. The 35 cases corresponded to 21% of the total sample, i.e. it could be regarded as the incidence rate of other associated neurological conditions for the given malformation. Within the 21%, spina bifida was found to be 10%; Isaksen et al. [27] reported 16% in his sample, while data by Csabay et al. [22] accounted for 17%. When associated spina bifida is detected, it is worth examining which anatomical region of the vertebral column is affected. The involvement of more caudally situated regions was negligible. Vintzileos et al. [28] found that the prognoses were the best and poorest in malformations of the sacral and thoracolumbar regions, respectively. Corpus callosum dysgenesis should also be mentioned among the associated malformations of the central nervous system [10]. Compared to the full sample, its incidence was found to be 2.17%, while Isaksen et al. [27] and Csabay et al. [22] reported 3 and 2.3%, respectively.

The disorders of the non-central nervous system in association with ventriculomegaly were found in 151 cases, which amounted to approximately 66%. In this large group, disorders of the highest incidence included disorders of the amount of the amniotic fluid (45%). In addition to that, the incidence of malformations affecting the urinary system and the limbs is also noteworthy. Vintzileos et al. [28] reported the quantitative differences in amniotic fluid at 30%, while Chervenak et al. [18] found the involvement of the urinary system and the incidence of cardiac malformations to be 18 and 15%, respectively (in our sample, the latter turned out to be 5.29%). Fetal pyelectasis turned out to be the most common disorder, but the incidence of pes equinovarus (clubfoot), cheilognathopalatoschisis (cleft lip, upper jaw and palate) single umbilical artery and echodense intestines should also be

mentioned. In the study by Chervenak et al. [18], renal agenesis, interventricular septal defect and cleft palate were mentioned as the most commonly associated non-central nervous system disorders.

Though ultrasound is the primary screening method for the evaluation of the fetal malformations, there are pitfalls in the diagnostics of the fetal brain and spine. The brain's appearance on ultrasound is based on the ability to obtain specific images of the cerebrum and spine. Maternal obesity or oligohydramnios may result in inadequate ultrasound images. Magnetic resonance imaging (MRI) is less affected by these factors. Ventriculomegaly [29–31] is the most common referral for MRI evaluation of the fetal central nervous system.

In the affected cases, nearly 60% of the pregnancies were terminated by induced abortion, while in 24% of them induced premature birth was chosen. According to a study by Tercanli et al. [9], induced abortion was used to terminate 33% of the pregnancies with ventriculomegaly, while in the study by Benacerraf and Birnholz [6] the relevant figure was close to 60%.

As far as further pregnancies are concerned, recurrence of ventriculomegaly was found to be 4.69%, which is in almost full agreement with the 5% risk generally found in the practice of genetic counseling.

It may be concluded that a positive history, including positive obstetric-gynecological and/or genetic history is important and should be emphasized as it is in direct relationship with the increased incidence of ventriculomegaly.

Regarding the practice of ultrasonography, mild ventriculomegaly (transverse diameter of the lateral ventricle <15 mm) has a much better prognosis than severe ventriculomegaly (transverse diameter of the lateral ventricle >15 mm). OFD values should be given even greater emphasis in the ultrasonography of severe ventriculomegaly and the evaluation of the findings.

In the case of ultrasonographic diagnosis of ventriculomegaly, a TORCH serological examination is also recommended since treating toxoplasmosis by medication may have a promising prognosis for the pregnancy.

It is also important to note that spina bifida, the most frequent malformation among the associated disorders of the central nervous system, occurred in the sacral region, which is the site with the best prognosis for this disease.

The assessment of associated malformations affecting the non-central nervous system is also of great significance since ventriculomegaly alone is not necessarily incompatible with postnatal life; therefore, the decision about the fate of the pregnancy and further prenatal care is greatly dependent on the presence of other organic anomalies [11–13, 32, 33].

In cases of isolated ventriculomegaly alone, intrauterine karyotyping is not necessarily indicated, but in the severe cases of the disorder, and/or when it is associated with other genetic disorders, karyotyping should definitely be performed.

In cases of severe ventriculomegaly diagnosed before the 24th gestational week and/or showing fast progression, the termination of pregnancy is recommended on a genetic indication, but if the diagnosis is made later, the solution lies in neurological surgery.

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