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Verification of the main trends in gastroschisis incidence in the autopsy database

Gastroschisis is a life-threatening congenital malformation defined as a defect of full--thickness abdominal wall located mostly to the right of intact umbilical cord with herniation of abdominal viscera outside the abdominal cavity. The occurrence of gastroschisis is estimated at 0.47–4.9 per 10,000 live births (6). Gastroschisis was formerly considered as a relatively rare defect, however, initiation of birth defects register programmes in some countries revealed an increased occurrence of this malformation started at the 80s in some populations, e.g., in Scandinavian countries, France, Great Britain, Japan or Australia (6, 12, 14). The reason for this trend is unclear, however, the dynamics of changes indicates environmental rather than genetic factors. In fact, epidemiological and experimental studies revealed an association of gastroschisis with intrauterine exposure to some environmental agents including alcohol, cigarette smoke, zinc deficiency, carbon monoxide and variety of drugs (13,15,16). Furthermore, the correlation of the anomaly with young maternal age (<25 years) was also stressed (3, 12, 14, 15).

The pathogenesis of gastroschisis is unknown. According to the best known hypothesis, the malformation is a result of vascular abnormalities (interruption of the omphalomesenteric artery or premature involution of the right umbilical vein) in the first trimester of gestation (8). All factors interfering with these vessels formation in embryo could potentially induce the abdominal wall anomaly. The genetic predisposition for gastroschisis was also postulated (11).

The aim of the present study was to analyse the incidence of gastroschisis and its relation to the potential risk factors during two decades in the autopsy database.

MATERIAL AND METHODS

The autopsy database of the Clinical Pathomorphology Department, Medical University of Lublin from the period of 1981–2000 was reviewed. Out of 2,673 protocols concerning children aged up to 1 year, 1,062 cases with congenital malformations were found.

Information about age and sex of child, gestation age, birth weight, place of residence and detected malformations came from the autopsy protocols. Furthermore, for eight children with gastroschisis born after 1990, the case histories were also available, and the data on maternal and paternal age as well as diseases and drugs and chemicals exposure during pregnancy were also obtained. Data were analyzed by Chi-square Yates test. $\alpha=0.05$ ($p<0.05$) was considered significant.

RESULTS

Out of 1,062 autopsies of children with congenital malformations, 19 cases with gastroschisis have been found (1.8%). The incidence of gastroschisis has not significantly changed in the analysed

period of time (1981–1990 *vs.* 1991–2000; p=0.82) (Table 1). All children were live-born. The sex ratio was M:F=9:10. All but five children were premature and ten had birth weight below the value suitable for their gestational age (Table 2). In 5 cases (26.1%) gastroschisis was accompanied by other congenital malformations or variants, i.e. intestinal atresia – 4 cases, cardiac malformations – 2 cases and accessory spleen – 1 case. The surgical correction of the defect was performed in 14 children (73.8%). No familial history of gastroschisis or other congenital malformations were noted.

Table 1. Incidence of all the congenital malformations (CM) and gastroschisis in autopsies performed in the period of 1981–2000

Year	No. of CM	Percent of any CM corresponding to the decade	No. of gastroschisis	Percent of gastroschisis
1981	38	6.79	0	0.00
1982	29	5.18	0	0.00
1983	49	8.75	1	2.04
1984	63	11.25	1	1.59
1985	89	15.89	0	0.00
1986	57	10.18	2	3.51
1987	62	11.07	2	3.23
1988	55	9.82	2	3.64
1989	57	10.18	0	0.00
1990	61	10.89	3	4.92
Total	562	100.00	11	1.96
1991	81	16.14	1	1.23
1992	75	14.94	1	1.33
1993	51	10.16	0	0.00
1994	56	11.16	2	3.57
1995	36	7.17	1	2.78
1996	57	11.35	1	1.75
1997	54	10.76	1	1.85
1998	49	9.76	0	0.00
1999	21	4.18	0	0.00
2000	22	4.38	1	4.54
Total	502	100.00	8	1.59

The mean maternal age was 21.42 years. Two mothers were teenagers. The mean paternal age was 27.00 (Table 2). Eight mothers (42.0%) were from the urban areas. Two of the eight mothers for whom the information was available, suffered from common cold at the first trimester. However, no drugs administration or exposure to chemicals during pregnancy was revealed. Alcohol drinking and cigarette smoking were denied.

Table 2. Selected clinical data on children with gastroschisis autopsied in the period of 1981–2000

	n	Minimum	Maximum	M	Me	SD
Children age at autopsy (day)	19	1.00	91.00	14.00	2.00	27.643
Birth weight (g)	19	1100.00	3000.00	2325.00	2430.00	544.685
Gestational age (week)	19	33.00	40.00	36.58	37.00	1.575
Maternal age (year)	8	17.00	28.00	21.75	21.00	3.92
Paternal age (year)	8	18.00	34.00	27.00	28.00	5.21

M – mean, Me – median, SD – standard deviation

DISCUSSION

The results of the present study partly confirmed some general trends for gastroschisis, although the analysed group was highly selective and not representative for the whole population. The occurrence in offspring of young mothers is the feature typical of this anomaly and was also observed in the study group (3, 12, 14, 15). This coincidence is not clear. It could be excluded that protein, zinc and foliate deficiency are more common in young woman, especially in the light of nowadays style for the slim figure. The experimental data indicated that at least some of the above mentioned factors are associated with higher incidence of gastroschisis in the murine model (13). Deficiency of folic acid or other nutrients during pregnancy may result in disturbances in proliferation and differentiation of many kinds of cells including those participating in abdominal integument formation in the embryo (7). Furthermore, cigarette smoking and using some recreational drugs like cocaine, "ecstasy" or amphetamine is more common in younger persons (9, 15, 16). These agents can interfere with maternal uterine and placental vasculature and potentially participate in child vascular event that leads to gastroschisis. It can be partly supported by low birth weight of children with gastroschisis observed in the present study, which may indicate impaired transplacental nutrition due to abnormal placental function as well as maternal malnutrition, both being more likely in young mothers. More recently, changing in paternity among young mothers has been also considered as a risk factor of gastroschisis. Decreased immunologic tolerance to the antigens of a new partner associated with short time of cohabitation and usage of contraception barrier methods may alert vascular formation and cause gastroschisis development (3).

There is no direct evidence of drugs and chemicals exposure in the present study. However, in 11 cases first trimester of gestation came out in the autumn and winter when the infections, especially of the upper respiratory tract, are common. Therefore, either mild infections or administration of popular OTC (*over-the-counter*) medications cannot be completely excluded, despite their absence in medical records. So-called decongestant, e.g. pseudoephedrine or phenylpropanolamine as well as some cyclooxygenase inhibitors are associated with an increased risk of gastroschisis (1, 2, 10, 15, 16). The possible mechanism of the adverse foetal effect of decongestants is similar to other vasoconstrictors. The mechanism of cyclooxygenase inhibitors action is probably complex. They cross the placenta and interfere with conversion of arachnoid acid to prostaglandins, prostacyclin and thromboxanes that regulate various fetal physiological processes on the cellular and tissue levels (5). On the other hand, cyclooxygenase inhibition leads to increase of leukotrienes production (15). It seems that gastroschisis may be the consequence of prenatal cyclooxygenase-1 blockade (1, 2). Based on experimental animal and human observations, aspirin and ibuprofen are regarded as associated with the higher risk of gastroschisis formation (1, 2, 10).

The coincidence of gastroschisis with other congenital malformations is relatively low. The most common associated anomalies are similar to the present study, intestinal atresia as well as cryptorchismus (14).

Contrary to many world reports (6, 12, 14), there have not been significant differences in the incidence of gastroschisis in the last two decades in the presented group. It could be associated with better outcome of children with gastroschisis as a result of improvement of surgical treatment and intensive care (4), and therefore real prevalence of gastroschisis requires assessment of the whole affected population.

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SUMMARY

Gastroschisis is a rare congenital malformation defined as a defect of abdominal wall located mostly to the right of intact umbilical cord. Increased incidence of this anomaly in some populations has been recently reported. An association with young maternal age, protein-zinc deficiency and intrauterine exposure to vasoactive factors was also suggested. To verify some epidemiological findings on gastroschisis the autopsy database from the period of 1981–2000 was reviewed. Out of 1,062 children with congenital abnormalities 19 cases of gastroschisis have been found. The incidence has

not significantly changed in the analysed period (1981–1990 *vs.* 1991–2000, p>0.05). In 5 cases gastroschisis was accompanied by other malformations, i.e., intestinal atresia, cardiac defects and accessory spleen. The mean maternal age was 21.75 years. Two mothers suffered from common cold at the first trimester. However, no drugs administration or exposure to chemicals during pregnancy were revealed.

Weryfikacja głównych trendów występowania wytrzewienia w materiale autopsyjnym

Wytrzewienie (*gastroschisis*) jest rzadką wadą wrodzoną, polegającą na ubytku powłok brzucha najczęściej na prawo w stosunku do niezmienionego sznura pępowinowego. Ostatnio donoszono o wzroście częstości występowania tej wady w niektórych populacjach. Sugerowano także związek wytrzewienia z młodym wiekiem matek, niedoborami białek i cynku w diecie oraz wewnątrzmacicznym narażeniem na czynniki naczynioruchowe. W celu zweryfikowania niektórych informacji epidemiologicznych dotyczących wytrzewienia przeanalizowano dane z autopsji przeprowadzonych w latach 1981–2000. Na 1062 sekcje dzieci z wadami rozwojowymi w 19 przypadkach rozpoznano wytrzewienie. Częstość występowania wady nie uległa istotnym zmianom w badanym okresie (1981–1990 *vs.* 1991–2000, p>0.05). W pięciu przypadkach wytrzewieniu towarzyszyły inne zaburzenia rozwojowe, tj. atrezja jelit, wady serca oraz śledziona dodatkowa. Średni wiek matek wynosił 21,75 lat. Dwie matki przebyły infekcję górnych dróg oddechowych w pierwszym trymestrze. Żadna z kobiet nie przyjmowała leków ani nie była narażona na działanie środków chemicznych w czasie ciąży.