Multiple minor congenital anomalies in autism
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ABSTRACT
The frequency of minor congenital anomalies and the mean number of these anomalies/person was examined in 76 patients with autism spectrum disorders and in unrelated control subjects matched by age and sex. The frequency of minor anomalies was not significantly different in the two groups, 14.47% in autistic children and teenagers, compared to 14.80% in healthy controls. The mean number of minor congenital anomalies was significantly higher in the autistic group, 3±0.70 minor anomalies/patient, compared to 1.43±0.36 minor anomalies/patient in controls. None of the control subjects had three or more minor anomalies. These results support the idea that minor anomalies, especially multiple ones may represent markers of early prenatal factors that contribute to the adverse outcome.

KEY WORDS multiple minor congenital anomalies, autism, predictive value

Introduction
Minor congenital anomalies are physical defects that, in themselves, do not have medical or cosmetic importance and they may occur in completely healthy individuals. Still, they represent indicators of altered morphogenesis and their recognition may alert the clinician to the possibility of the existence of a more serious defect. Several studies (1-3) revealed that multiple minor congenital anomalies correlate with disturbances of neurological development that occur during embryogenesis. The presence of these minor anomalies, especially more than three, may predict the future onset of a neuropsychic disorder.

Autism is a complex behavioral disorder of the brain that is of great concern to the pediatrician. It is a syndrome with multiple genetic and nongenetic causes. Autism refers to the wide spectrum of developmental disorders characterized by impairments of social interaction, language, communication, imaginative play; and of range of interests and activities. Twin studies reported 60% concordance for classic autism in monozygotic twins, attesting to genetic inheritance as the predominant causative agent. Reevaluation for a broader autistic phenotype, including communication and social disorders, increased concordance to 92% in MZ twins (4). This suggests that interactions between multiple genes cause autism but that epigenetic factors may contribute to its variable expression. The number of genes involved remains unknown. Pediatricians must diagnose the disorder, as soon as possible, because early intervention increases its effectiveness.

The purpose of the study was to see if patients with autism have more minor congenital anomalies than healthy individuals and if so, if this finding correlates with the history of the patients.

Material and Methods
The incidence and the mean number of minor congenital anomalies were investigated in 76 patients hospitalized in the Neuropsychiatry Center for children and Teenagers from Timisoara. Data were collected by performing multiple physical examinations and measurements where necessary for a greater accuracy (5). Minor anomalies studied are presented in table 1.

| Face        | Synophris, anteverted nostrils, bifid tip of nose, high arched palate, bifid uvula, micrognatia |
| Eyes        | Epicanthic folds, upslanting palpebral fissures, downsloping palpebral fissures, short palpebral fissures, hypertelorism, hypotelorism |
| Ears        | Malformed ears, asymmetric ears, low set ears, small ears, preauricular pits or tags, ear lobe creases |
| Head and Neck | Webbed neck, flat occiput |
| Hair        | Two or more parietal whorls, abnormal posterior whorl |
| Hands       | Clinodactily, partial cutaneous syndactily, simian crease, Sydney crease, |
| Trunk       | Accessory nipples, short stern, haemangioma, cafe-au-lait spots |
| Feet        | Broad hallux, partial syndactily |

A full history was taken, with questions about prenatal, perinatal and postnatal period. Data regarding the age of the parents, mother's age
being of special interest, regarding pregnancy including illnesses, drugs or use of alcohol during this time were collected. Other important data were those concerning length of pregnancy, child's weight at birth, the existence of twin pregnancies, as well as the existence of spontaneous abortion or stillbirth in the family. Perinatal history included data about labour, birth, presentation, Apgar score and the condition of the child during the first week of life. Data about postnatal history regarded the psycho-motor development of the child, existence of trauma, severe disorders during infancy or childhood or surgery (6, 7).

The control subjects consisted of children and teenagers corresponding as ages and sex, with no history of neurodevelopmental disorders. They were chosen randomly from kindergartens and schools.

Results and Discussions

Autistic syndrome represents a complex disorder with various etiology. It is a developmental disorder characterized by onset during infancy or childhood, social and communication deficiencies, different stereotypes. The wide phenotypic variability of the autistic spectrum disorders reflects the interaction of multiple genes within an individual's genome and the existence of distinct genes and gene combinations among those affected. Data from whole-genome screens in multiplex families suggest interactions of at least 10 genes in the causation of autism.

Establishing of a positive association with some markers could be useful for identification of the cause and the prenatal or postnatal onset of the disorder. These markers could be represented by minor congenital anomalies.

Sex ratio in autistic children was:

- Boys: 42.86%
- Girls: 57.14%

The age of the patients varied between 3 and 18 years, the mean age being 11.6 years.

The incidence of minor congenital anomalies in the autistic group was 14.47%, approximately equal to their incidence in the control group, 14.8%.

The mean number of minor congenital anomalies/patient in the autistic group was 3±0.70, significantly higher in the autistic group, compared to 1.43±0.36 minor anomalies/patient in controls (p<0.001). The incidence of minor congenital anomalies in the autistic group is presented in fig. 1.

Most autistic patients have at least 3 minor congenital anomalies.

About 85% of the minor congenital anomalies seen in these patients are anomalies of the mouth, eyes, and ears. The minor anomalies, most frequently found were:

- Regarding the anomalies of the hand, only clinodactily of the fifth digit was seen..
- Studying the histories of the patients, it was noticed that:
  - the mean age of the mothers at conception 24.7 years, varying between 21 and 33 years
  - 21.4% of the mothers had illnesses.
  - one of the pregnant women used alcohol during pregnancy, the child presenting signs of the fetal alcohol syndrome.

The mean birth weight of the children was 3115g. Low birth weight for gestational age was noticed only for the infant with fetal alcohol syndrome, in concordance with data from literature (8).

One of the cases is a girl from a dyzzygotic twin pregnancy, the other child being unaffected. Her mother was 33 years and her father 37. This affected daughter had 4 minor congenital anomalies and autism, but the unaffected brother, who was also examined had no congenital anomalies.

Another case had related parents, first degree cousins. The patient is the second child, the first one who had major congenital defects died soon after birth. Data about this couple reveal that both
parents are mentally retarded. Their son has 2 minor congenital anomalies.

Observations regarding this family are concordant with data from literature concerning a higher risk for congenital defects in consanguineous matings and also with data regarding the higher frequency of psychiatric disorders among the relatives of the autistic patients (9).

28.5 % from autistic patients also had a major congenital defect, represented by microcephaly.

Considering the clinical manifestations of the disorder, that requires a complex sustained and long duration treatment, establishing of an early diagnosis is absolutely necessary (10). The observations from this study, more than half of the patients having three or more minor congenital defects lead to the conclusion that a careful examination of the infant or child, for establishing the presence of multiple minor congenital defects in one patient, might represent a marker of a central nervous system developmental dysfunction. Detailed and accurate clinical examination may help establishing genotype-phenotype correlations.

References

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