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## Phenotype-genotype discordance in congenital malformations with communication disorders resembling trisomy 18 (Edwards syndrome)

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Statistical Analysis C  
Data Interpretation D  
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**Patient:** Female, 6  
**Final Diagnosis:** Phenotype-genotype discordance in congenital malformations with communication disorders resembling trisomy 18 (Edwards syndrome)  
**Symptoms:** —  
**Medication:** —  
**Clinical Procedure:** —  
**Specialty:** Otolaryngology

**Objective:** Congenital defects  
**Background:** Communication process disorders are very frequent in rare cases of chromosomal aberrations (deletions, insertions, and trisomies) such as Down syndrome (trisomy 21), Turner syndrome, Edwards syndrome (trisomy 18), or Patau syndrome (trisomy 13). Sometimes phenotype may delusively correspond to the characteristic features of a given syndrome, but genotype tests do not confirm its presence.  
**Case Report:** We present the case of a 6-year-old girl admitted to the Clinic of Phoniatrics and Audiology for the assessment of communication in the course of congenital malformations with phenotype characteristic for trisomy 18 (Edwards syndrome). Immediately upon birth, dysmorphic changes suggesting trisomy 18 (Edwards syndrome) were observed, but trisomy 18 was excluded after karyotype test results were normal (46, XX).  
**Conclusions:** Disturbed articulation was diagnosed: deformed linguo-dental and palatal sounds, interdental realization with flat tongue of the /s/, /z/, /c/, /dz/, /š/, /ž/, /č/, /dž/ sounds (sigmatismus interdentalis). Hearing loss was confirmed.

**MeSH Keywords:** trisomy 18 (Edwards syndrome) • phenotype-genotype discordance • Communication Disorders

**Full-text PDF:** <http://www.amjcaserep.com/download/index/idArt/884033>

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## Background

Communication disorders, especially hearing and speech impairment, are diagnosed in about 500 different genetic disorders that are accompanied by symptoms from the nervous, circulatory, urinary, osseous, and endocrine systems, the eyes, and the skin (Gorlin 1995). The condition may be difficult to diagnose, especially when it is rare or in cases when the following occur:

- Pleiotropy (i.e., the mutation of a single gene may trigger symptoms from other systems);
- Heterogeneity (ie, one phenotype is caused by mutation of different genes);
- The change of the expression may be observed in numerous syndromes.

Communication disorders are very common in cases of particularly rare chromosomal aberrations (deletions, insertions, and trisomies) such as Down syndrome (trisomy 21), Turner syndrome, Edwards syndrome (trisomy 18), or Patau syndrome (trisomy 13). Sometimes the phenotype may seemingly correspond to the characteristic features of a given syndrome, but is not confirmed in genotype testing [1,2].

## Case Report

A 6-year-old girl, E.W., was admitted to the Clinic of Phoniatics and Audiology (No. 6767/2009) for the assessment of communication development impairment.



Figure 1. Lower right limb.



Figure 2. Upper right limb.



Figure 3. Soft and hard palate proportion.

The child was born after spontaneous labor (birth weight 3150 g, Apgar 10) at 41 weeks gestation to closely related parents (primipara; uncomplicated pregnancy). Upon birth, dysmorphic changes suggesting trisomy 18 (Edwards syndrome) were observed, but the karyotype analysis result (46,XX) did not confirm the diagnosis and trisomy was excluded. The test was performed at the Institute of Medical Genetics, K. Marcinkowski University of Medical Science.

Upon admission to hospital, tests revealed facial dysmorphism: droopy and slanting eyelids (currently after 2 corrective plastic surgeries), low-set ears, and lower and upper limb malformations (deformed toes and horizontal skin crease of a hand).

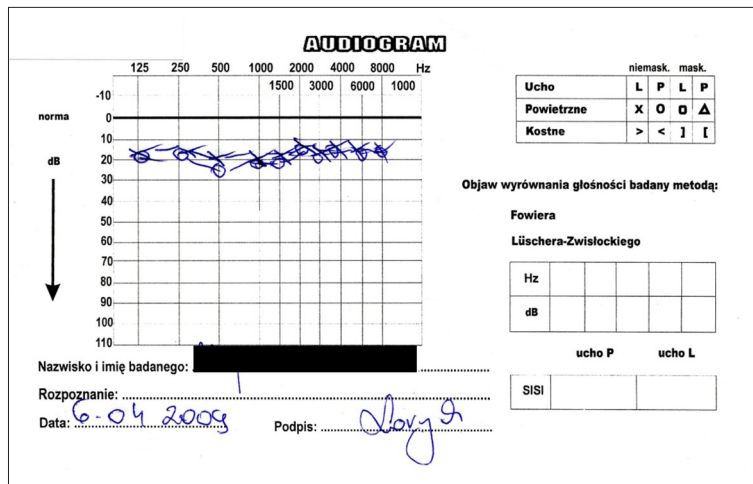


Figure 4. Tonal audiometry results.

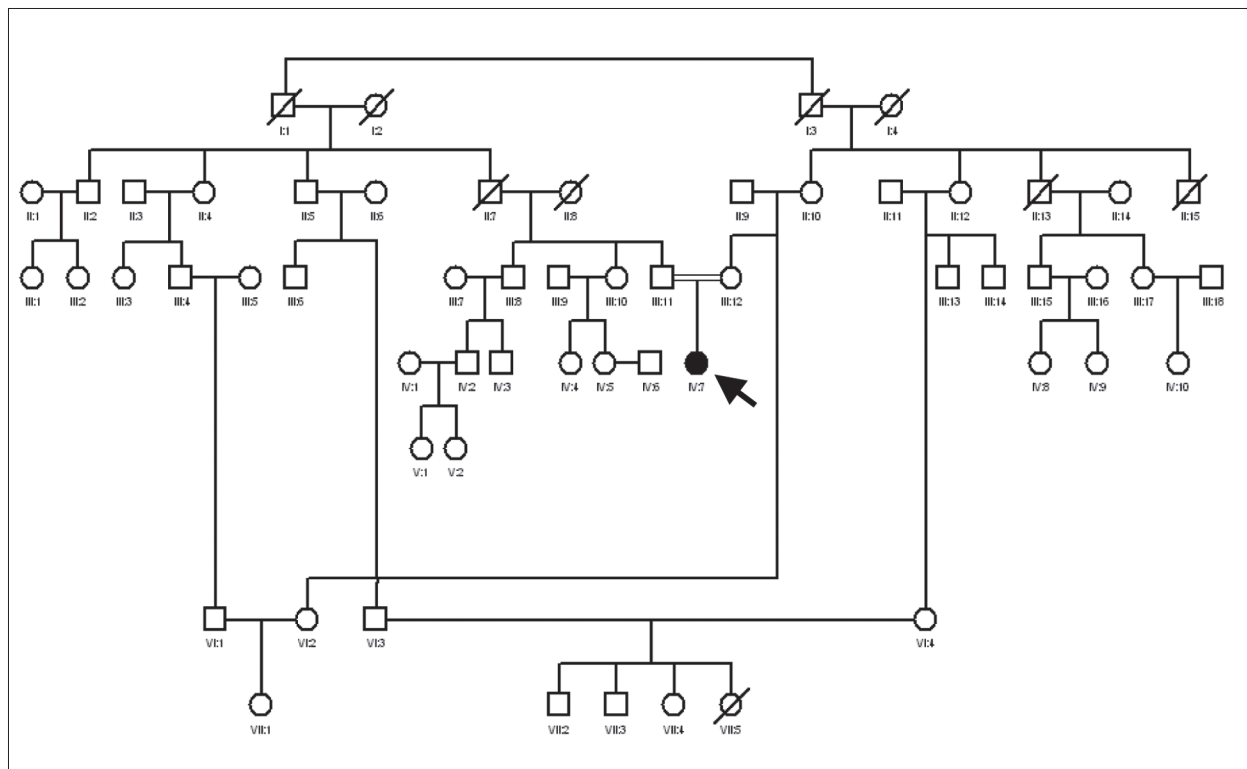


Figure 5. Family tree.

Phoniatric examination revealed a disproportion between the soft and the hard palate 1:1, and scarring of the soft palate. The development of the dentition did not correspond to the biological age of the child and buccal occlusion was diagnosed (Figures 1–3).

Audiological diagnostic evaluation was carried out at our Clinic. Pure-tone audiometry (tonal audiometry) revealed normal hearing in both ears (Figure 4). Impedance audiometry test (tympanometry) was performed twice and resulted in type B abnormal tympanogram, with no stapedius reflex. Hearing threshold was assessed on the basis of wave V and the BERA

test (Brainstem Electric Responses Audiometry) showed a response at 20 dB in both ears. Radiological examination of the head and the ears revealed low pneumatization of the mastoid bones and enlarged sella turcica.

Psychological evaluation (Leiter P-93) confirmed normal development in all cognitive areas: perceptive, intellectual, and executive functions.

Logopedic examination revealed disturbance of articulation apparatus (i.e., oral praxis), which included flat tongue mass,

difficulties with maintaining vertical position of the tongue, tendency for the jaw to move left during articulation, and buccal occlusion.

Lip and tongue motor activity was normal (assessed by means of oral praxis test by E. Stecko). Articulatory problems included deformed linguo-dental sounds and palatals, and interdental realization of the /s/, /z/, /c/, /dz/, /š/, /ž/, /č/, /dž/ sounds with flat tongue position (sigmatismus interdentalis). Denti-alveolar sounds /sz/, /ž/, /cz/, /dž/ and liquid sound /r/ were produced and realized correctly.

Central auditory test results were normal and the child willingly and eagerly engaged in the tasks of sound repetition (with elements of correction). Naming, active spontaneous speech (naming objects, people, phenomena, and activities), tempo, and phonematic hearing were also developed sufficiently for a child of this age.

To summarize, audiologic testing did not reveal significant anomalies that might hinder proper development of communication in the child.

Due to the fact that the phenotype corresponded to the fatal Edwards syndrome, the diagnostics also included genetic studies. Genealogical history was collected and a family tree of the child was compiled (Figure 5). The analysis of the pedigree of the child revealed there were cases of marriages between closely related family members that increase the possibility of genetic disorders. In our case the relatives are classified as the fifth degree. Classical karyotyping did not confirm chromosome 18 trisomy.

## Discussion

It is common knowledge that Edwards syndrome is fatal. We have presented our case because its phenotype was typical

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of Edwards syndrome, but genetic testing did not confirm it. This discrepancy was probably the reason why the patient survived, and it was also the incentive for us to analyze and investigate the case further.

Genes do not have representative resources to determine phenotypic features. Only primary protein structure is genetically encoded [3,4]. Features are located in the combination of numerous genes or in singular ones that may apply to other features (e.g., pleiotropy) [5]. The appearance of phenotypic features, even the so-called monogenetic ones, is the result of interaction of multiple genes (Waters) [2–6].

An interdisciplinary conference on differences between genotype and phenotype in cases of some genetically conditioned diseases was held in the 1990s at the Welshpool Conference.

In 1998 Courtens and Grossman described discrepancies between phenotype and genotype, using the example of twins with Noonan syndrome, which did not correspond to the changes found in the genotype. The authors noted that in some cases genetic *loci* that trigger the changes typical for the syndrome may in fact be located elsewhere.

In 2008 Cyril Gitiaux et al. described the case of 2 sisters with autistic features, mental retardation, and hypotony, in whom the phenotypic features were not confirmed in genotype – ADSL (Adenylosuccinate lyase) deficiency [2,7].

## Conclusions

In our case there was also a discrepancy between the genotype and the phenotype. The phenotypic features, visible since birth, suggested the presence of the Edwards syndrome. However, classical cytogenetic testing did not confirm the diagnosis (lack of trisomy of chromosome 18). Thus, the genotype-phenotype discrepancy requires further investigation.

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