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Rare Malformation Syndromes: Diagnosis and Management

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ABSTRACT: Birth defects have a major impact on neonatal, infant, and childhood mortality and morbidity. According to World Health Organization, about 240 000 newborns die worldwide within 28 days of birth every year due to birth defects. Also, birth defects cause a further 170 000 deaths of children between the ages of 1 month and 5 years. The main causes of birth defects are genetics, chromosomal abnormalities or single gene defects, exposures to medicines, chemicals, radiation, certain pollutants, maternal nutritional deficiencies or other toxic substances, environmental factors including infectionsduring pregnancy, and unknown causes.
The spectrum of severe birth defects may vary over time or with geographical area, reflecting the interaction between genetic and non-genetic factors. The focus of this study is to present our experience in the early prenatal diagnosis and management of rare malformation syndromes.
KEYWORDS: Down syndrome, Ebsteinanomaly**,** Chromosomal duplication.

I. INTRODUCTION

Congenital anomalies have a significant impact on neonatal, infant, and childhood mortality and morbidity. [1]

According to World Health Organization, about 240 000 newborns die worldwide within 28 days of birth every year due to birth defects. [2] Also, birth defects cause a further 170 000 deaths of children between the ages of 1 month and 5 years. [2]

The most common types of major congenital malformations are heart defects, neural tube defects, and Down syndrome. [1, 3]

The main causes of birth defects are genetics, chromosomal abnormalities or single gene defects, exposures to medicines (alcohol, phenytoin), chemicals, radiation, certain pollutants, maternal nutritional deficiencies (folate deficiency) or other toxic substances, environmental factors including infections during pregnancy (syphilis, rubella), and unknown causes. [4-7]

The spectrum and prevalence of severe birth defects may vary over time or with geographical area, reflecting the interaction between genetic and non-genetic factors. [1, 8-11]

The focus of this study is to present our experience in the early prenatal diagnosis and management of rare malformation syndromes.

II. DOWN SYNDROME ASSOCIATED WITH EBSTEIN ANOMALY

Ebstein anomaly is a rare congenital abnormality involving the tricuspid valve and the right ventricle.[12]

Down syndrome is associated with congenital cardiac malformations in almost 40-50% of the cases. [13]

The most common congenital heart malformations associated with Down syndrome are atrioventricular septal defects, ventricular septal defects, atrial septal defects, patent ductusarteriosus, and tetralogy of Fallot. [3, 14]

We present a rare case of Down syndrome associated withEbstein anomaly, diagnosed prenatally in a 25 weeks fetus.

The ultrasound examination, performed transabdominally, using a General Electric ultrasound machine, revealed the presence of a monofetal pregnancy, in evolution, with the fetus in a cephalic presentation.

Ultrasound examination of the viscerocranium indicated: cerebral ventriculomegaly, with the posterior horns of the cerebral ventricles 10.5 mm, compared to 6 mm, which is the normal value corresponding to intrauterine development (Fig. 1).

Ultrasound morphological examination of the fetal thorax indicated the following cardiac anomalies: increased fetal heart circumference (106 mm), enlarged right atrium, tricuspid valve

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displaced apically, and normal interventricular septum (Fig. 2). Also, pleural effusion was detected.

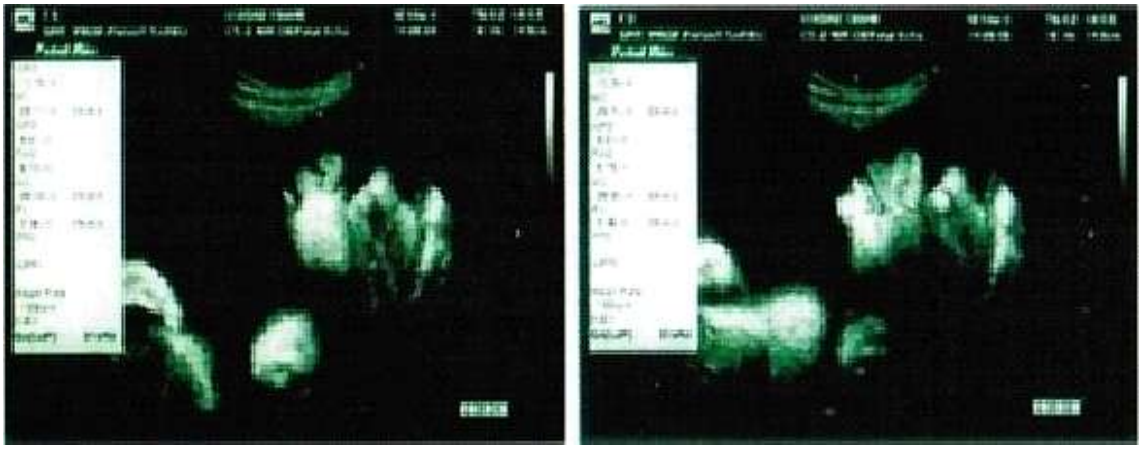

Figure 1.Ultrasound examination of the fetal head using two-dimensional ultrasound (2D) showing fetal facial profile

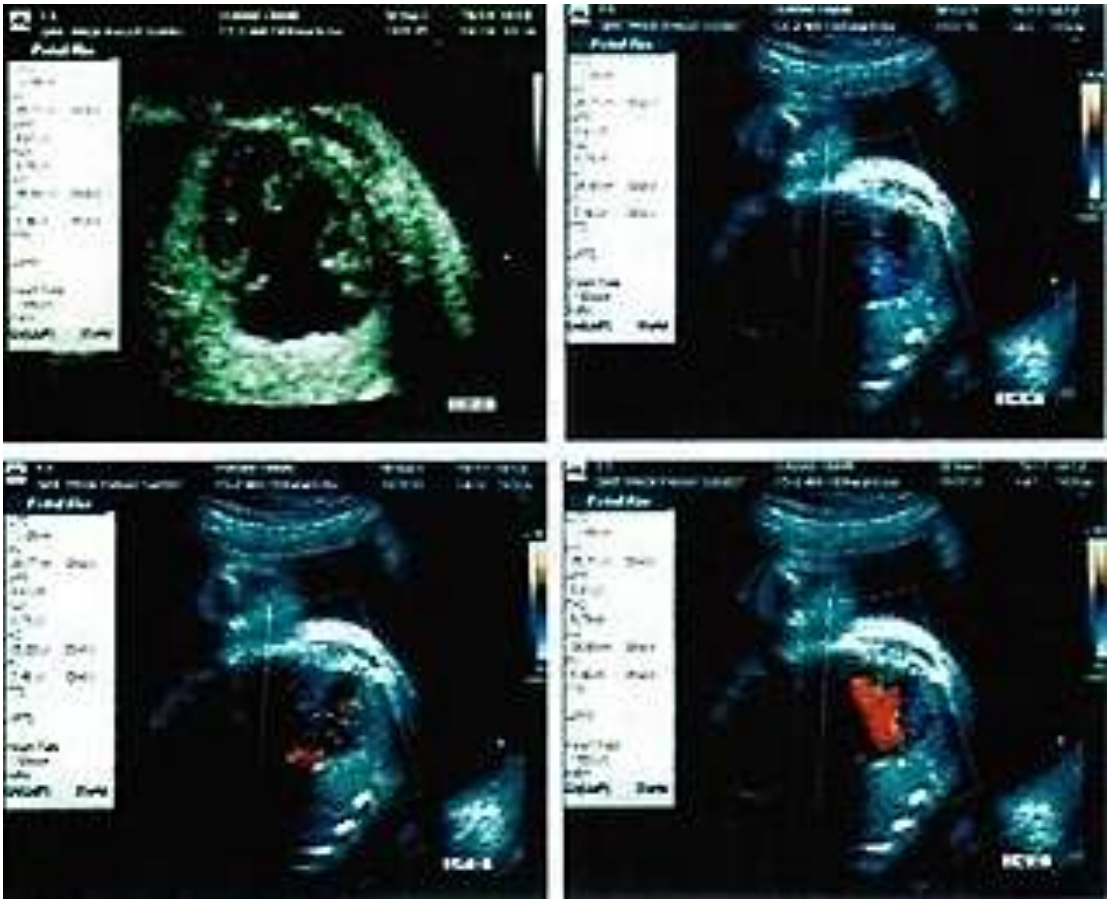

Figure 2.Ultrasound examination of the fetalcord using two-dimensional ultrasound (2D) and 2D power Doppler

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Considering the congenital malformations highlighted at the ultrasound scan, further prenatal investigations were recommended.

Amniocentesis and the analysis of fetal chromosomes revealed the presence of an abnormal fetal karyotype, respectively 47,XY,+21 (Fig. 3).

The results of non-invasive and invasive prenatal investigations, as well as the results of the cytogenetic examinations, confirmed the diagnosis of Down syndrome associated withEbstein anomaly, in a 25 weeks male fetus.

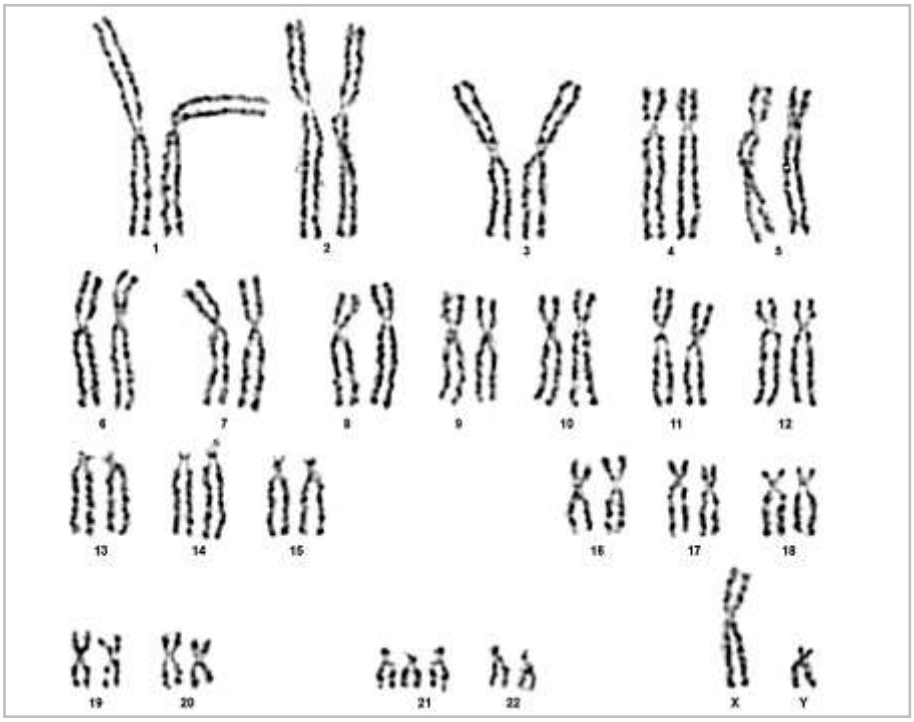

Figure 3.Fetal karyotype: 47,XY,+21

III. CHROMOSOMAL DUPLICATION: DUP(1)(Q32Q44)

Duplications of the long arm of chromosome 1 are rare and mostly the result of abnormal segregation of parental translocation chromosomes and their homologues. [15-19]

A 39-year-old Caucasian patient, pregnant for the first time, with no significant personal or family medical history, came to our clinic for a fetal morphology ultrasound examination.

Detailed ultrasound examinationrevealed a series of fetal anomalies were found, including cerebral ventriculomegaly and choroid plexus cysts (Fig. 4).

Considering the congenital malformations highlighted at the ultrasound scan, amniocentesis and the analysis of fetal karyotype were recommended.

The karyotype analysis of amniotic fluid cells detected fetal structural chromosomal changes, respectively chromosomal duplication, dup(1)(q32q44), and fetal karyotype 46,XY,dup(1)(q32q44).

The parental karyotype performed from peripheral blood did not register the presence of parental chromosomal abnormalities.

The child was born at 39 weeks and was underweight, with a weight of 2.350 grams, a body lengthof 45 cm, and a body circumference of 34.3 cm.

The newborn presented facial dysmorphia:

- receding forehead;
- rounded and weakly lobed ears;
- hypertelorism;
- oblique palpebral slits, directed upwards and backwards;
- ogival palate.

It was also noted that the soles of the feet were longer, with the second and trird toes shorter.

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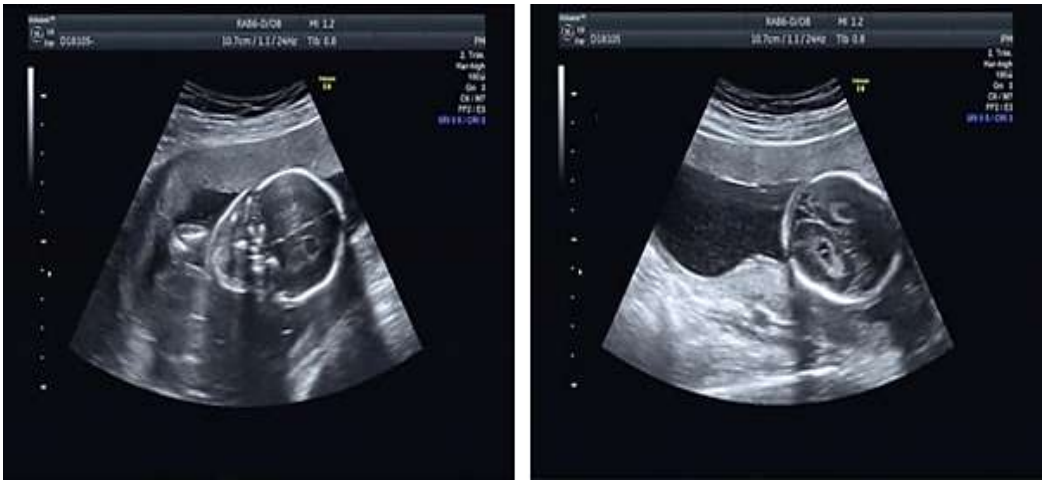

Figure 4. Ultrasound examination of the fetal head using two-dimensional ultrasound

The CT scan of the cephalic extremity indicated the prominence of the posterior horns of the lateral cerebral ventricles, and the X-ray examination of the skeleton indicated the presence of 11 pairs of ribs.

Sonographic evaluation of the abdomen revealed the presence of left renal hydronephrosis.

This is one of the very few cases of duplication dup(1)(q32q44) reported in the specialized literature.

IV. CONCLUSION

Global progress in reducing child mortality worldwide is remarkable, with significant declines in the mortality rate of children up to preschool age.

As a result, we believe that any isolated congenital defect must be thoroughly investigated, prenatal genetic investigations being crucial, for early diagnosis and effective case management to improve children's quality of life.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of informed consent

Informed consent was obtained from the patient included in the study.

Authors' contributions

Authors C.-C.A., D.-F.A. and Ş.-D.A. contributed to this work in conceptualization, methodology, software, and formal analysis.

Ş.-D.A. contributed in software, formal analysis, and data curation.

C.-C.A. and D.-F.A. contributed in validation, supervision, project administration.

All authors have read and agreed to the published version of the manuscript.

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