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A CASE OF TWIN GROWTH DISCORDANCE DUE TO MUTATION IN THE CACNAID GENE

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OBJECTIVE

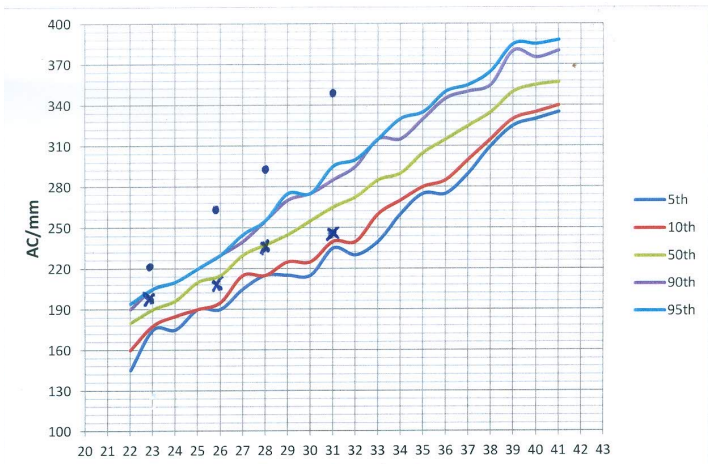
We report a case of a dichorionic diamniotic (DCDA) twin pregnancy with one twin presenting clinical features related to the extremely rare mutation in the **CACNAID gene**.

METHODS

This is a case report. The data were collected from the patient's medical chart, and a consent form was signed.

CASE REPORT

A 34-year-old primigravida with a DCDA twin pregnancy was admitted to the Department of Gynaecology and Obstetrics, at 26 weeks' gestation. It was decided to hospitalize the patient due to *discordant growth of the twins* for ultrasound monitoring. The discordant growth was first suspected in the 18th week of pregnancy.
Twin A (TA), male, had all of its fetal biometric measurements over the **99th percentile for GA**, as well as a thicker and hyperechoic stomach wall, a hydronephrotic right kidney, and an polyhidramnios. In the umbilical artery (UA), CD showed high pulsatile index. The second twin (TB), female, developed normally and the fetoplacental circulation was normal for the GA. While both of the twins' aCGH and karyotypes were normal, *one of the twins' NIPT results indicated an elevated risk for T13*. During hospitalization, greater discordant growth was observed, mostly at the expense of the TA. The amount of amniotic fluid of the TA progressed in **severe polyhydramnios**. In the case of the TB, there was an orderly increase in fetal weight.
The patient reported right hemiabdominal pain in the **31st week of pregnancy** as a result of polyhydramnios. The amnioreduction (1650 ml) was done. During that day, the reverse diastolic flow in the UA of TA was detected. Corticosteroid prophylaxis and magnesium sulphate neuroprotection were administered, and *the pregnancy was completed by caesarean section*.



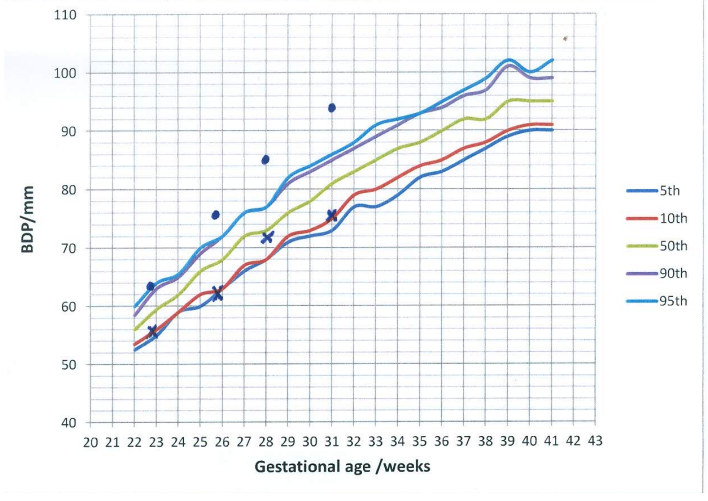


Figure 1. Fetal biometry showing discordant growth of the TA (▪) and TB (x)

*The first neonate (TA) was a male, 3230g, 51cm, with an APGAR score of 3 and 4, in the 1st and 5th minutes. The second infant (TB) was a female, 1330g, 39cm, and had an APGAR score of 6 and 7 in the 1st and 5th minutes, respectively. The NICU received admission for both twins, and **blood samples from the parents and twins were sent for genetic testing**.*
*TA was generally macrosomatic, had lower frontal and occipital hair growth, neck pterygium, and pronounced hairiness of the shoulders, arms, and legs. He also had a wide root of the nose, gothic palate, coarse facial features, and poorly formed head and ears. Moreover, left ventricular hypertrophy, hyperinsulinemic hypoglycemia and convulsions were detected. A fast progression of organ system malfunction occurred during his stay in the NICU, and despite intense therapy, **he had cardiorespiratory arrest on the fifth day of life**. TB was clinically monitored during the stay in the NICU, received all necessary therapy and was released home after 34 days in good general condition with a weight of 2070g.*

In male neonate (TA), genetic analysis revealed a heterozygous de novo, likely pathogenic variant in the CACNAID gene (c.2018T>C). This variant has not yet been reported in association with human diseases in biomedical literature. This variant was not identified in the patient's twin sister. Analysis of the parents determined a *de novo* origin.

CONCLUSION

THE CLINICAL PICTURE OF OUR PATIENT CAN FIT INTO THE CACNAID GENE MUTATION. IT IS ASSOCIATED WITH A POOR PROGNOSIS ONCE THIS CONGENITAL MALFORMATION MAKES NO FEASIBLE SURVIVAL. CONSIDERING THAT IT IS A DE NOVO MUTATION, THE RISK OF REPEATING THE MUTATION IN SUBSEQUENT PREGNANCIES IS EQUAL TO THE RISK IN GENERAL POPULATION