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PIK3CA-related overgrowth spectrum (PROS): a case report and review of the literature

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Introduction

PROS encompasses a group of overgrowth syndromes associated with somatic mutations in the PIK3CA gene, resulting in abnormal tissue proliferation leading to variable phenotypes. Prenatal diagnosis of PROS is challenging due to the mosaic nature of the mutations and late appearance of signs. Prenatal Imaging, may reveal features like macrocephaly, limb asymmetry, and vascular malformations, but these are nonspecific and can overlap with other conditions. Next generation sequencing (NGS), may fail to detect low level mosaic mutations, particularly when the affected tissue does not exhibit enough mutated cells. PROS is often only confirmed postnatally, after genetic testing of skin biopsy or affected tissues.

Our case

In this case, a 32-year old Caucasian woman, with a medical history including type II diabetes, chronic hypertension, and hypothyroidism, had a pregnancy

complicated by **persistent left superior vena cava (PLSVC), hemiazygos vein dilation, polyhydramnios, macrocephaly, ventriculomegaly, and a femur length discrepancy** in the third trimester. Genetic testing, including karyotyping, array-CGH, and FGFR3 mutation analysis, was negative. Prenatal imaging raised the suspicion of a vascular anomaly. **NGS of the amniotic fluid was negative.** The baby was delivered at 37 weeks and presented macrocephaly, body asymmetry, telangiectasias, confirming the vascular component of the disorder. Postnatal skin biopsy revealed a pathogenic mosaic mutation in PIK3CA gene (c.1635G>TC) ,confirming the diagnosis of PROS.

Literature Review

Literature review on prenatal detection of PROS identified 18 cases with ultrasound findings. In 16, the diagnosis was confirmed prenatally on amniotic fluid, 8 were identified retrospectively.

Conclusion

Our case represents a postnatally diagnosed PROS, with a **negative retrospective NGS analysis on amniotic fluid**. Late appearance of clinical signs and limitations of prenatal genetic testing for mosaicism underscores the difficulty of prenatal diagnosis in PROS.