

Genetic insight in vein of Galen aneurysmal malformation

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Objective. The vein of Galen aneurysmal malformation (VGAM) is a rare alteration of the cerebrovascular development resulting from fistulous communication between Markowski's vein and deep choroidal arteries. The deriving aneurysmal formation is the most common non-cardiac cause of high-output heart failure in newborns. Despite the advances in interventional neuroradiology designed for embolization procedures, infant mortality remains high.

An obstacle in the improvement of care is the limited understanding of the pathophysiological and genetic basis of VGAM.

The aim of our study is to analyze genetic mutations to drive appropriate genotype-phenotype correlations that may impact on the therapeutic approach.

Materials and Methods. From April 2020 to April 2022 at the Bambino Gesù Pediatric Hospital in Rome we observed

11 newborns diagnosed with VGAM, 9 identified during the prenatal period. All the neonates had chorioid morphology, 9 underwent embolization, 3 died during the first month of life. Genetic investigations were obtained in 8 out of 10 patients.

Results. In our cohort, 2 patients showed a heterozygosis mutation in the family of NOTCH genes (NOTCH3 and NOTCH4) with maternal segregation pattern. These genes are known in the literature as signal regulators in morphogenesis and vascular remodelling process during the embryonic period. The NOTCH genes mutations in murine models are associated with cerebral arteriovenous malformations.

Conclusions. The identification of a VGAM could represent a recommendation for postnatal genetic study and counseling for future pregnancies, even if the genes that might be involved show incomplete penetrance and variable expressivity.