Very low sFlt-1/PlGF ratio in foetal growth restriction: clinical insights from a case study

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Objective. To investigate the relationship between an atypical angiogenic marker profile, specifically a very low sFlt-1/PlGF ratio, in a pregnant woman with foetal growth restriction (FGR) and the subsequent diagnosis of Coffin-Siris Syndrome (CSS), a rare genetic disorder, in the infant.

Materials and Methods. A 19-year-old primigravida at 38.4 weeks of gestation was admitted for reduced foetal movements and FGR, with normal Doppler indices. Angiogenic markers, Placental Growth Factor (PlGF) and soluble fms-like tyrosine kinase 1 (sFlt-1), were measured using the Cobas e601 platform (Roche Diagnostics). Genetic testing via Whole-Exome Sequencing (WES trio) was performed on the infant and his parents.

Results. A very low sFlt-1/PlGF ratio (0.67) was observed in the maternal serum, due to high PlGF levels (2,615 pg/mL), more than 4 times above the 90th percentile for an uncomplicated singleton term pregnancy. sFlt-1 levels were within the normal range. At birth, the newborn presented with facial dysmorphisms, severe laryngomalacia and corpus callosum hypoplasia. Growing, he showed mild hearing loss and a psychomotor delay. Genetic analysis revealed a de novo SMARCA4 mutation, confirming the diagnosis of CSS. This gene seems to be also involved in angiogenesis.

Conclusions. This case underscores the importance of incorporating angiogenic markers into routine obstetric care, especially in cases of FGR. Our findings highlight that even a very low sFlt-1/PlGF ratio warrants attention and emphasize the need to analyse both markers. In particular, elevated PlGF levels may be associated with neonatal complications, therefore further research into placental angiogenesis is necessary.