Placental microRNA, anti-angiogenesis, oxidative stress and mitochondrial dysfunction in selective FGR

Leung TY, Cheng YK, Meng M, Wang CC
Department of Obstetrics and Gynaecology, The Chinese University of Hong Kong, Hong Kong, Hong Kong

Objective

To investigate epigenetic mechanism and associated pathophysiology of sIUGR in the placenta of MCDA twin pregnancies.

Methods

This is a multicentre cohort study. Placentae from MCDA twin pregnancies complicated with sIUGR were recruited from various obstetric units of public hospitals in Hong Kong at birth. sIUGR was defined as EFW of small fetus below the 10th percentile, and fetal weight discordance was defined as discordance between the EFW of two fetuses >25%. sIUGR was further classified as type I if normal UA EDF, type II if persistently AREDF and type III if intermittent AREDF. MicroRNA expression profile of each twin's placenta was carried out by microarray and validated by qPCR. Angiogenesis and oxidative stress were determined by endothelial marker CD31, vascular endothelial growth factor (VEGF) and prostaglandin-endoperoxide synthase 2 (PTGS2) immunostaining. Relative mitochondria DNA (mtDNA) copy number was quantified by qPCR. Ultrastructure of mitochondria was examined by TEM. Mitochondrial activities were determined by citrate synthase (CS) and respiratory chain complex IV (COX4) immunostaining.

Results

Placental microRNA 199a (miR-199a) was significantly up-regulated in smaller twins than larger twins. MiR-199a inhibits the angiogenesis by targeting HIF-1α/VEGF pathway. Placental CD31 and VEGF protein expression was significantly lower and associated with higher PTGS2 protein expression in sIUGR twins. Placental mtDNA copy number was significantly increased also in placental mitochondrial swelling and rupture of the inner membrane, and CS and COX4 protein expression was significantly higher in sIUGR twins.

Conclusion

This study identified an epigenetic mechanism by miR-199a which may underline the anti-angiogenesis, oxidative stress and mitochondrial dysfunction in the placenta of sIUGR twin pregnancies.