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| **Hemoglobin Bart hydrops fetalis: A model for studying placental hypoxia in stillbirth** |
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| **Introduction** Placental ischemia can be on a pre-placental (maternal), placental and post-placental (fetal) basis, and specific morphologic features of villous vascularization can reflect these different etiologies, particularly pre-placental and placental, whereas less is known about changes in post-placental causes. Vascular features can be accurately determined by morphometry.  We have previously shown that stillborn hydrops fetalis (HF) resulting from hemoglobin (Hb) Bart disease can serve as a model for intrauterine hypoxia, and placentas from such cases show a distinctive peripheral villous stromal myofibroblastic hyperplasia (PVSH). We hypothesized that Hb Bart disease, which results in profound fetal hypoxia, would lead to placental hypoxia on a post-placental basis before intrauterine fetal death.  **Material and Methods** We performed vascular morphometry on placental villous vessels, comparing placentas in 14 stillborn Hb Bart HF cases to 18 non-Hb Bart HF cases. Parameters measured included: total area of villous stroma included for vessel analysis; number of vessels; vessel density; perimeter (cross-sectional vascular boundary); vascular area; luminal area; endothelial thickness; and shape coefficient.  **Results** Villous vessels of Hb Bart HF showed increased numbers of vessels (*p*=0.001) and a thick vascular endothelial layer (*p*=0.002).  In addition, placental villi of Hb Bart HF containing PVSH showed a longer vascular perimeter (*p*=0.008) and narrower lumen (*p*=0.002), with a more branching pattern of vascular remodeling (*p*=0.03), in comparison to villi lacking PVSH.  **Conclusions** Contrary to our expectations, the overall pattern of vascular changes in stillborn Hb Bart HF corresponded most closely to pre-placental hypoxia, presumably on the basis of the marked placentomegaly seen in Hb Bart HF, distending the uterine cavity and compromising blood flow on a mechanical basis. Nonetheless, some of the vascular changes may reflect other sources of hypoxia, such as hydropic villi causing a generalized diminished intervillous space (placental hypoxia), and the greatly reduced capacity of Hb Bart to extract oxygen from the intervillous space (post-placental). |
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