Identification of Treatments for Hemophilic Joint Disease through Evaluation of Vascular Defects via Optimization of Imaging Techniques

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Purpose Hemophilia A (FVIII deficiency) is characterized by spontaneous bleeding in weight-bearing joints, resulting in an orthopedic complication called hemophilic arthropathy (HA). Bleeding causes inflammation and hypoxia, inducing angiogenesis. Despite advances in treatment, HA still develops. The project goal was to identify treatment and treatment targets for hemophilia that prevent vascular abnormalities. Procedure The goal was approached by developing insight into abnormal blood vessel formation, identifying multiple angiogenic markers expressed in FVIII KO models to serve as treatment targets, and testing the efficacy of the most promising anti-angiogenic treatment candidate targeting Vascular Endothelial Growth Factor (VEGF). Results It was determined that anti-VEGF significantly reduced aSMA positive vessels at week 2, that abnormal blood vessels are specific to hemophilia as compared to other joint diseases, that new vessel formation and vascular remodeling was increased in FVIII KO mice after bleeding but not to the same extent in WT mice subjected to joint bleeding, and that lack of hemostasis drives excessive vascular changes. Furthermore, a microCT based 3D model was developed for the visualization of blood vessels and immunofluorescent staining was optimized to allow for the identification of multiple angiogenic targets in the mouse hemophilic joints after bleeding. Conclusions The cause of HA development was discovered and plausible antibody treatments were identified. Vascular changes were analyzed via the optimization of imaging techniques.