Capillary Malformation: Expression of Angiogenic and Vasculogenic Factors

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**Background:** Capillary malformations are associated with soft-tissue hypertrophy. The purpose of this study was to determine if angiogenesis or vasculogenesis is upregulated in this overgrowth condition.

**Methods:** Capillary malformation specimens were collected prospectively from nine patients after resection: lip (n=6), lower extremity (n=3). The average age of the cohort was 25.9 years (range 10-49 years). Neovascularization was compared to normal control tissue. Specimens were analyzed by immunohistochemistry for CD31 (microvascular density), CD31/H3 (proliferating endothelial cells), and CD34/CD133 (endothelial progenitor cells). Quantitative real-time reverse-transcriptase polymerase chain reaction (qRT-PCR) was used to determine mRNA expression of progenitor cells (CD133) and factors that recruit them: vascular endothelial growth factor (VEGF-A), hypoxia-inducible factor-1α (HIF-1α), matrix metalloproteinase-9 (MMP-9), and stromal cell–derived factor-1α (SDF-1α). Angiopoetin-1,-2 (ANG-1,-2) and VEGF receptors (VEGFR1,2 and neuropilin1,2) also were quantified using qRT-PCR.

**Results:** Microvascular density (6.2%) was greater in capillary malformations compared to normal specimens (2.8%) (p = 0.03). Endothelial proliferation was noted in capillary malformations (5.1/field), but not in normal tissue (p = 0.01). Endothelial progenitor cells were absent in both study and control tissues. ANG-2 (2.7-fold), neuropilin 1 (2.0-fold), and neuropilin 2 (3.3-fold) were increased in capillary malformations (p = 0.005), whereas VEGF-A (0.5-fold), VEGFR1 (0.8-fold), VEGFR2 (1.7-fold), ANG-1 (1.1-fold), HIF-1α (0.7-fold), MMP-9 (1.8-fold), SDF-1α (1.6-fold), and CD133 (0.4-fold) were not elevated (p = 0.6).

**Conclusions:** Capillary malformations exhibit elevated vasculature and proliferating endothelial cells; progenitor cells are not present. Neovascularization by angiogenesis may be involved in the evolution of capillary malformations. Further investigation may enable the prevention of soft-tissue overgrowth using pharmacotherapy.