Expression of angiopoietin receptors TIE2 and TIE1 in equine exuberant granulation tissue

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Introduction: Exuberant granulation tissue (EGT) in horses is a frequent complication in second intention healing of limb wounds, that results in delayed wound healing and/or unacceptable wound cosmesis. Previous studies have shown that scar tissue is associated with an excessive angiogenic response characterized by an immature and leaky vascular network. The Angiopoietin-TIE pathway is a promising target for angiogenesis normalizing therapy, as this pathway plays an important role in vascular maturation. Recent data show that immune cells, such as macrophages and neutrophils may become activated by angiopoietins, and that these cells are also involved in the regulation of angiogenesis. Here, we aimed to investigate the expression of the angiopoietin receptors TIE2 and TIE1 in equine EGT.

Materials and Methods: Samples were obtained after routine excision of EGT from healing distal limb wounds in 4 equine patients. After fixation in 3.5% formaldehyde, the samples were embedded in paraffin. Immunohistochemical staining was performed using antibodies against the receptors TIE2 and TIE1, and calprotectin (MAC387, a marker for macrophages, monocytes and neutrophils). DAB was used as chromogen to visualize antibody binding. Horse corpus luteum samples were used as a positive control.

Results: Endothelial cells of blood vessels stained positive for TIE2 and TIE1. TIE2 and TIE1 staining was also observed in a large fraction of calprotectin positive cells, which stains monocytes, macrophages and neutrophils. Histological examination indicated that each of these cell types were represented by positive staining for the TIE receptors.

Conclusion: Our results indicate that the Angiopoietin-TIE pathway is important in EGT, not only in endothelial cells, but also in a subset of macrophages and neutrophils. Further research should investigate if these cell subsets play a role in regulating angiogenesis within EGT. In addition, this is the first time that the presence of the TIE1 receptor is reported on neutrophils.

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