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High Level Expression of Angiopoietin-2 in Human Abscesses

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Abscesses are common sequelae of infections which can occur in any organ or tissue. The cardinal feature of an abscess is central necrosis, surrounded by a highly inflamed pseudocapsule, which is responsible for the sensation of induration around the necrotic area. Clinically, abscesses are significant because they are resistant to antibiotics and require physical drainage in order to resolve.

While abscesses are common, the events leading to abscess formation are not fully understood. Recent advances in angiogenesis may account for the cardinal features of abscesses, namely central necrosis and pseudocapsule formation. We performed in situ hybridization on 5 paraffin fixed abscess tissues for two major angiogenesis factors, vascular endothelial growth factor (VEGF) and angiopoietin-2 (ANG-2).

We found high level expression of ANG-2 in abscess walls. High level expression of ANG-2 may account for the vascular leak of the pseudocapsule of an abscess. Overcoming this vascular leak may facilitate antibiotic treatment of abscesses.

Abscesses on 5 patients were incised and drained using a 4 mm punch. The specimens were fixed in formalin and subjected to in situ hybridization for VEGF and ANG-2 according to the method of McLaughlin et al. At least two of the drained abscesses were caused by methicillin resistant staphylococcus aureus (MRSA). All lesions (5) demonstrated high level expression of ANG-2 in the wall of the abscesses, especially in association with endothelium (Figure 1). VEGF expression was barely noticeable by ISH (data not shown).

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Discussion

Soft tissue infections are a major cause of morbidity and mortality in both the developed and developing world. The abscess wall is a barrier of inflamed tissue that gets its substance from vascular edema, which is a direct manifestation of vascular leak.

The major mediator of vascular leak is the peptide ANG-2. ANG-2 binds to the tie-2 receptor, which is expressed primarily on endothelial cells, activating multiple signaling pathways, including reactive oxygen generation. Interestingly, ANG-2 was originally thought to be an angiogenesis inhibitor, because under certain conditions, it was thought to cause regression of blood vessels. This view was challenged by the observation that high level expression of ANG-2 is present in both highly malignant tumors, such as glioblastoma multiforme, and inflammatory conditions such as psoriasis and hemangiomas. ANG-2 is never observed in normal skin. Treatment of cancers with angiogenesis inhibitors in humans is associated with normalization of blood vessels and enhanced delivery of antitumor agents. Virulence factors, such as nitric oxide, may play a role in ANG-2 activity in abscesses. ANG-2 has been shown to induce nitric oxide, and nitric oxide has been shown to cause resistance of common bacteria to antibiotic therapy, as well as impeding antibiotic delivery to these lesions. We propose that a similar phenomenon of leaky blood vessels may occur in infectious processes, and normalization of leaky blood vessels may aid antibiotic treatment.

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References

Figure 1.