The Role of Periodontal Disease in Lymphatic Function

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Research Question
Does periodontal disease affect lymphatic function?

Abstract
Gingival lymphatic vessels drain interstitial fluid and transport immune cells to lymph nodes but despite this, it is unknown how the lymphatic system impacts periodontal disease in humans. In light of this, studies have been observed on animals with the vascular endothelial growth factor C (VEGFC), a growth factor known to be increased in periodontal patients. VEGFC is involved in lymphatic hyperplasia and lymphangiogenesis, the proliferation of lymphatic endothelial cells. This growth factor is believed to affect gingival lymphatic function in periodontitis patients.

When reviewing the literature, it is evident that the VEGFC receptor is of main interest when investigating lymphatics and periodontitis. One study found that inducing the overexpression of VEGFC in mice infected with P. gingivalis resulted in lymphatic hyperplasia and reduced lymphatic flow, meaning the invasive bacteria is not being cleared out as it should. Another study found that mice lacking gingival lymphatics experienced greater bone loss in periodontitis than mice with functional lymphatic systems.

Introduction
- The lymphatic system plays an important role in the body’s immune system to fight off infections like periodontitis.
- Periodontitis is a chronic inflammatory disease which destroys the periodontium due to the inflammatory response triggering generation of signaling molecules, recruitment of inflammatory cells, and activation of bone-resorbing osteoclasts.
- VEGFC growth factor levels are increased during inflammation, and it is believed that it impacts gingival lymphatic function in those with periodontitis.
- Studies on lymphatics and periodontitis have been conducted on mice, yet it is unknown how periodontitis affects lymphatic function in humans.

Review of Literature
- In these studies, K14 mice were used because they express the human VEGFC growth factor; the wild type mice who do not express VEGFC were the control.
- Both types of mice were infected with the bacteria P. gingivalis to induce periodontitis.
- Levels of VEGFC increase during inflammation, causing lymphatic endothelial cell proliferation which leads to hyperplasia of lymphatic vessels (Fig. 1) in K14 mice.
- Hyperplastic lymphatic vessels in K14 mice have slightly impaired lymph drainage because the vessel walls are enlarged.
- K14 mice had a more severe inflammatory response to the bacteria than the wild type mice who do not express VEGFC.
- K14 mice experienced more severe bone loss in periodontitis as compared to the wild type mice.
- Studies suggest impaired lymph drainage aggravates the periodontal disease process by reducing the ability to clear foreign invaders and bacteria.

Discussion
- Overexpression of VEGFC in inflammation leads to lymphatic vessel hyperplasia and impaired lymph drainage causing the lymphatic system to be at a disadvantage to fighting periodontal infections.

- Limitations:
  - These findings only revealed in mice
  - Unclear if human gingival lymphatic function is altered by periodontal disease
- Future studies:
  - Should be conducted on humans

Figure 1
Above, hyperplasia of lymphatics is shown in K14 mice compared to wild type mice.

Conclusion
These findings cannot confirm whether or not impaired gingival lymphatic function from worsens the periodontal disease process. Currently, there is no research on how periodontitis affects gingival lymphatics in humans. Although many speculate that VEGFC overexpression during periodontitis can cause impaired lymphatic function that leads to periodontal disease progression, future research is needed in order to further explore this field.

References