Title: Reduction of noradrenergic nerve fibers in endometriosis and its influence on the chronic inflammation

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Context: The chronic inflammatory disease endometriosis (EM) is one of the most common causes for chronic pelvic pain. Recent studies have shown a reduction of noradrenergic nerve fibers (NAN), which act anti-inflammatory. The genesis of the reduction remains unclear though it has a potential role in the maintenance of the inflammation and emergence of pain. Specific semas represent potential elicitors, due to their known role as nerve repellent factors in different chronic inflammatory diseases, like rheumatoid arthritis.

Objective: To define the principle of the depletion of NAN in endometriotic peritoneal tissue (pEM). Therefore analyzing the role of semas in the neuroimmunomodulation of EM. Analyze potential interaction of semas with EM-associated and not EM-associated macrophages as well as activated fibroblasts in EM patients and healthy women.

Methods: IHC/IF staining and ELISA.

Patients: pEM, healthy peritoneal biopsies (pb), peritoneal fluid (PF) and serum of women with and without EM were analyzed. Further classification: pelvic pain yes or no, cycle phase, EM stage.

Interventions: laparoscopy

Main Outcome Measures: NAN in pEM express semas receptors, suggesting a possible repelling of these by semas. Macrophages and activated fibroblasts express semas only in pEM. EM patients with and without pain showed significant different expression levels.

Results: pEM and PF of EM patients show increased semas and receptors levels. pEM has higher density levels of macrophages and activated fibroblasts.

Conclusions: The inflammatory reaction in EM leads to a macrophage release and activation of fibroblasts, which express semas. Suggesting a potential role of semas in the reduction of the noradrenergic innervation and consequently of anti-inflammatory factors, thereby leading to the chronic inflammatory conditions in EM, potentially contributing to pain emergence.