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Pathogenesis of Vaginal Dryness in Primary Sjögren's Syndrome: A Histopathological Case-control Study

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Background/Purpose: Women with primary Sjögren's syndrome (pSS) often experience vaginal dryness, but the pathogenesis of this symptom is unknown. Previously, we reported impaired vaginal health and presence of a subepithelial infiltrate in the vagina of women with pSS[1]. In the current analysis, we quantitatively studied changes in lymphocyte subsets, endothelial cells and soluble immune markers in the vagina and endocervix of women with pSS, compared to age-matched controls, which may explain vaginal dryness.

Methods: Gynaecological examinations were performed in 10 premenopausal women with pSS, fulfilling the ACR-EULAR criteria, with symptoms of vaginal dryness, and 10 premenopausal non-pSS controls scheduled for laparoscopic procedures. Participants with inflammatory or infectious gynaecological morbidity were excluded. Endocervical swab and cervicovaginal lavage samples were collected, in which levels of pro-inflammatory chemokines and cytokines were analyzed using a multiplex bead based immunoassay. Mid-vaginal biopsies and endocervical biopsies were collected and stained for leucocyte markers, caldesmon for smooth muscle cells, ERG for endothelial cells and anti-podoplanin (clone D2-40) for lymphatic endothelium. The number of positive pixels/μm^2 was calculated digitally using Aperio ImageScope v 12.1.

Results: One pSS patient was excluded due to chlamydia, and 2 controls due to discovery of endometriosis during their laparoscopy. In the remaining 9 patients and 8 controls, median age was 36 years (IQR 33-46) and 41 years (36-44), respectively (p=0.61). A higher level of CXCL10 was measured in endocervical swabs of pSS patients (median 37.1 pg/ml, IQR 19.4-66.1) compared to controls (median 12.6 pg/ml, IQR 5.9-31.1, p= 0.046). No differences were found in levels of APRIL, BAFF, RANKL, TNF-α, CCL2, CXCL11, CXCL13, IL6, IL7 or IL8. One vaginal biopsy from a control was excluded from analysis as it was too superficial, consisting for 98% of epithelium. Three pSS and two control cervix biopsies which did not show representative endocervical tissue were excluded from analysis. The number of CD45+ and CD3+ cells (expressed as number of positive pixels/μm^2) in vaginal biopsies was significantly higher in pSS patients (p=0.012 for CD45, p=0.008 for CD3). Lymphocytic infiltration was mainly located in the subepithelial layer, with aggregates in dermal papillae. Endocervical CD45+ leucocytic infiltrates were seen in patients as well as controls, but CD20+

positive pixels/µm2 were significantly higher in pSS patients (p=0.041). Importantly, there was a significantly lower number of vascular smooth muscle cells (caldesmon+ pixels/µm2) in the vagina of pSS (p=0.031). In the endocervix, no significant differences were seen in endothelial or smooth muscle cells.

Conclusion: Our findings indicate that in addition to chronic inflammation, vascular disturbances in the vaginal mucosa are likely to contribute to vaginal dryness in women with pSS.

Reference: [1]JF Van Nimwegen et al. Arthritis Rheumatol. 2017; 69 (suppl 10). https://acrabstracts.org/abstract/subepithelial-infiltrate-of-the-vagina-in-primary-sjogrens-syndrome-the-cause-of-vaginal-dryness/.

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