

Lichen Sclerosus and Vulvar Squamous Cell Carcinoma

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Maria Lagerstedt, MD, specializing in Dermatology and Allergology, University of Tampere and Tampere University Hospital, Finland, defended her PhD thesis "Vulvar lichen sclerosus, Characterization of childhood lichen sclerosus and evaluation of novel biomarkers in the progression of lichen sclerosus to vulvar squamous cell carcinoma" on 2nd of February 2018. The opponent was Professor Kaisa Tasanen-Määttä from University of Oulu, Finland and custos was Professor Erna Snellman. The thesis was supervised by Dos. Satu-Leena Laasanen and Prof. Erna Snellman.

The theses is available at: <http://urn.fi/URN:ISBN:978-952-03-0640-3>

Lichen sclerosus (LS) is a chronic, scarring dermatosis typically affecting the genital area. It can occur in women and men, and at any age. Childhood LS is a rare entity with a few existing previous studies. LS includes a risk for cancer (vulvar squamous cell carcinoma [SCC]) in 3–5% of patients, but there are no biomarkers available in clinical practise for the evaluation for the risk of malignancy.

The aim of the dissertation study was to characterise the features of childhood-onset LS and to evaluate the role of biomarkers, estrogen related receptor α (ERR α) and Serpin A1 (also called alfa-1 antitrypsin), in LS and vSCC.

Childhood LS showed remarkable effects on the patients' quality of life. Our study found an association with LS and sleeping disorders. The risk of other autoimmune diseases was elevated and scarring occurred in as many as one fifth of the patients. The relief of signs and symptoms of LS was common in puberty, but a permanent cure of the disease was not. However, many patients dropped out of follow-up at the time of puberty. The study concluded that the effective treatment and surveillance in a professional unit can diminish the risk of complications in lichen sclerosus patients at all ages.

The study found two novel markers in vulvar lichen sclerosus and vulvar SCC, ERR α and Serpin A1. The prognostic value of these markers in lichen sclerosus was not established. A novel finding was that both of the markers seem to have a role in development and progression of vulvar cancer.

Summary and conclusion

The current work was designed to explore the prevalence, clinical picture, comorbidities and prognosis of childhood LS and to identify immunohistochemical markers in LS and vulvar SCC. The results of this study can be summarized as follows:



Fig. 1. From left to right: Prof. Kaisa Tasanen-Määttä (opponent), Prof. Erna Snellman (supervisor), Maria Lagerstedt (responder), Dos. Satu-Leena Laasanen (supervisor).

- Childhood-onset LS is rare and often misdiagnosed. LS has a significant effect on the quality of life (QoL) of the patients, and the 15D questionnaire seems a promising tool for measuring the QoL in childhood-onset LS. The high risk for other autoimmune diseases should be kept in mind during the follow-up. To prevent the complications, the initial therapy should be effective enough to cure clinical symptoms and signs. Maintenance therapy and long-term surveillance are important.
- Healthy vulvar skin expressed ERR α , ERR β and ERR γ independent of age or hormonal status. In LS, the expression of ERR α was decreased independently of the clinical features, and showed no prognostic value. ERR α staining intensity further reduced in premalignant vulvar lesions. In vulvar

SCC, $ERR\alpha$ expression was lost or substantially decreased in all samples. This reduction of $ERR\alpha$ in cancer progression may associate with the inflammation-induced nature of vulvar SCC.

- Overexpression of Serpin A1 was associated with the pathogenesis of LS and vSCC. Tumor-cell specific Serpin A1 expression was detected in both LS-dependent and HPV-dependent vulvar SCC, and the expression levels increased in a malignant progression. However, Serpin A1 immunohistochemistry or serum levels seem not to be useful as prognostic markers in LS or vSCC.

List of original publications

- I. Lagerstedt M, Karvinen K, Joki-Erkkilä M, Huotari-Orava R, Snellman E, Laasanen SL. Childhood lichen sclerosus- A challenge for clinicians. *Ped Dermatol* 2013; 30: 444–450.
- II. Lagerstedt M, Huotari-Orava R, Nyberg R, Mäenpää JU, Snellman E, Laasanen SL. Reduction in ERR is associated with lichen sclerosus and vulvar squamous cell carcinoma. *Gynecol Oncol* 2015; 139: 535–540.
- III. Lagerstedt M, Huotari-Orava R, Nyberg R, Nissinen L, Farshchian M, Laasanen S-L, Snellman E, et al. Tumor-cell specific Serpin A1 expression in vulvar squamous cell carcinoma. Submitted.