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# 35186 Exploring the association between frontal fibrosing alopecia sunscreen and moisturizers

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**Exploring temporal disease progression and comorbidities in psoriatic disease**

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Psoriasis is associated with multiple systemic comorbid conditions. Most registry studies fail to recapitulate correlations between psoriasis and the temporal progression of broader diseases. Here, a holistic overview of the correlations of disease characteristics with temporal disease progression and long-term disease trajectories of psoriatic patients is explored. This observational, retrospective, noninterventional study identified psoriatic patients in the Danish National Patient Registry with an International Statistical Classification of Diseases and Related Health Problems-10th edition (ICD-10) code for psoriasis (L40.0 or L40.9) from 1999−2013. Relative risk (RR) measured strength of association between psoriasis and frequent disease co-occurrences to create disease trajectory clusters. All significant disease pairs (D1>D2) with an RR>1 and P D2 (D1 = psoriasis, D2 = any other ICD-10). 38/121 achieved RR>1; P D2 (median time range = 3-7 years). Crohn's disease (ICD-10 = K50) had a significant association to and from psoriasis diagnosis: RR = 1.36 [CI:1.34; 1.39] P K50) and RR = 1.56 [CI:1.53; 1.59] P psoriasis). The highest RR in both directions of psoriasis was enteropathic arthropathies (ICD-10 = M07): RR = 32.28 ([95% CI 32.16-32.41]; P M07 and RR = 39.35 [95% CI 39.22-39.47]; P psoriasis). 4/5 disease trajectories with 3 diagnoses had a significant direction from psoriasis>D2>D3 and an RR>1; $P < .001$. Disease trajectory clusters may facilitate clinicians in planning risk stratification of patients to identify optimal treatment options and prevent future comorbidities.

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**Expression of interleukin 36 receptor antagonist in a patient with generalized pustular psoriasis harboring the p.Pro82Leu variant in the IL36RN gene**

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Background: Mutation of the IL36RN gene contributes to the development of generalized pustular psoriasis (GPP). The IL36RN gene encodes interleukin (IL)-36 receptor antagonist (IL-36Ra), which has antagonistic roles against IL-36. Li et al. performed sanger sequencing to identify IL36RN mutations in 62 Chinese GPP patients, and reported a new variant, c.245C>T (p.Pro82Leu) in a patient with GPP. Since this p.Pro82Leu variant was not found in the psoriasis vulgaris and control groups in their study, they speculated that this variant might lead to exacerbated inflammatory responses. Meanwhile, SIFT and PolyPhen-2, pathogenicity prediction tools, predict this variant as tolerated and benign. To date, its pathogenicity was unknown.

Objective: To investigate the mRNA and protein expressions of IL-36Ra in a patient with GPP harboring the p.Pro82Leu variant.

Methods: To investigate mRNA expression of IL36RN, polymerase chain reaction was conducted on hair samples obtained from the patient and a healthy control using primers to detect mRNA of exons 2 and 5 in IL36RN. Immunohistochemical staining for IL-36Ra was performed to detect its protein expression.

Results: Gene analysis on blood obtained from a 76-year-old Japanese man with GPP demonstrated a mutation in IL36RN (c.245C>T). In the patient, mRNA expression of IL36RN was observed. Immunohistochemical staining revealed that IL-36Ra was expressed in the keratinocytes of the patient with GPP harboring the p.Pro82Leu as in those of the GPP patient without the mutation.

Conclusion: Our results indicate no aberrant splicing nor pathogenicity in this variant. This variant is not associated with the development of GPP.

*Commercial Disclosure: None identified.*

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**Exploring the association between frontal fibrosing alopecia sunscreen and moisturizers**

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Frontal fibrosing alopecia (FFA) is an immune-mediated cicatricial alopecia. Skin care products including sunscreen were suggested to influence disease pathogenesis. Given the conflicting data, the aim of this study is to provide a quantitative summary on this topic. A systematic search surveying PubMed database was conducted in August 2021. The Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines were followed. The study was prospectively registered in Prospero (ID: 273840). The pooled effect size is presented as odds ratio (OR) with 95% confidence interval (CI). A total of 87 articles were identified; 9 articles were included. Using the Newcastle Ottawa scale (NOS), the quality of studies ranged from 5 to 7, suggestive of moderate quality. 1248 patients in the published literature had FFA (mean age: 58.9, 95.7% female) and were compared with 1459 control subjects (mean age: 56.9, 89.8% female). Six (66.67%) studies assessed the use of sunscreen and moisturizers 5 years before the onset of FFA. Nine studies evaluated the association between sunscreen and FFA (n = 9); the pooled OR was 1.45 95%CI [1.11-1.90], $P = .0068$. For the 8 studies exploring the relationship between facial moisturizers and FFA, the pooled OR was 1.26 (95% CI 1.10-1.43), $P = .006$. The results of this study suggest that both sunscreen and moisturizers likely increase the risk of FFA by 45% and 26% respectively. Due to lack of randomized controlled trials and small number of studies, the causality of this association could not be ascertained. As such, high-quality studies are needed.

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**Extraocular sebaceous carcinoma in a patient on long-term methotrexate therapy**

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Introduction: Sebaceous carcinoma (SC) is a rare and aggressive malignant tumor that arises from the adnexal epithelium of the sebaceous glands. It can either occur sporadically or in association with Muir-Torre syndrome (MTS), wherein these tumors are associated with internal malignancies. Chronic immunosuppression is a known risk factor for the development of SC with reports of its occurrence in patients on long term azathioprine and cyclosporine therapy. It has been suggested that immunosuppressive drugs could directly interact with DNA mismatch repair mechanism or might unmask a previously silent MTS phenotype predisposing to their development. This case describes the occurrence of SC in a patient on long term methotrexate therapy which has never been reported before.

Case Report: A 54-year-old male, on low dose methotrexate therapy for the management of limited scleroderma for past 12 years presented with a yellowish-pink ulcerated exophytic mass on the right parietal area of scalp for past one year. Histopathology revealed a dermal tumor composed of lobules and nests of cells having variable sebaceous differentiation with focal necrosis, scattered mitoses and atypical forms. A diagnosis of SC was made and the patient was sent to the surgical oncologist. No evidence of metastasis was found and wide local excision of the tumor was done with margins. Histopathologic evaluation of the specimen confirmed SC of grade 1 with TNM path stage of pT3 (size >4 cm, depth of invasion of 2 mm). The patient did well postoperatively and was counselled for close follow-up with the oncologist.

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