Biomarkers of alopecia areata in blood reveal systemic immune and cardiovascular abnormalities
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Alopecia areata (AA) is a common nonscarring hair loss disorder with a lifetime risk of 2%. Although AA is characterized by Th1/IFN-skiw, with additional Th2 and IL-23 activation in sculp tis, little is known about its systemic profile in blood. To evaluate the blood profile in AA with a full panel of determine serum biomarkers associated with increased disease severity, we assessed ~150 inflammatory and cardiovascular proteins using OLINK high-throughput proteomics in 35 moderate-to-severe AA patients (>30% scalp involvement, mean age=41.17 years; mean SALT=74.96), in comparison with age-matched healthy individuals, and as a point of reference also to moderate-to-severe psoriasis (n=19, mean PASI=20.41), and atopic dermatitis/AD patients (n=36, mean SCORAD=61.35). 74 proteins were significantly differentially expressed between AA and controls (FDR<0.1, FCX=0.75) including IL-17, IL-22, IFN-γ, IL-6, IL-8, Th1 (CXCL10/CXCL11/L1 L11NG), Th2 (CCL17/CCL27), Th17 markers (CCL20/PL1/S100A12). 86 biomarkers were correlated with clinical severity in AA patients (P<0.05) including Th1 (CCL3), Th2 (CCL11/CCL13), innate (IL1B) and Th17 markers (S100A12). Many cardiovascular/atherosclerosis-related proteins were significantly higher in AA compared to controls, and also correlated with severity, including SELL, SRC, AXIN1, MPO, IL18, and OSM (P<0.05). Pathway analysis showed significant associations between cardiovascular/atherosclerosis and various emerging pathways compared to controls (FDR=4.0, FDR=0.001), which also correlated with clinical severity (P<0.05). This study defined the abnormalities of moderate-to-severe AA and associated circulatory biomarkers. It shows that AA is a systemic disease with immune, cardiovascular and atherosclerosis dysregulation, highlighting the need for systematic treatment approaches.

Natural history and management of basal cell nevus syndrome: Updates from the gorlin syndrome registry
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Background: Patients with basal cell nevus syndrome (BCNS) are at increased risk of developing basal cell carcinomas (BCCs). Long-term data on tumor burden, co-morbidities, and management of BCNS is limited. Method: A prospective, cross-sectional study of self-reported questionnaires and records collected from BCNS patients from Feb 2012 to Oct 2018 by the national Gorlin Syndrome Registry. BCC burden was characterized based on frequency and anatomic distribution. Logistic regression analysis was performed to determine the association of BCSS development with risk factors such as sex, family history, age of diagnosis, symptoms, and sun exposure. Treatment of BCCs and other co-morbid tumors are additionally characterized. Results: 87 BCNS patients (current age: 39.8±20.0 years; age at diagnosis: 16.5±12.4 years; median follow-up duration of a follow-up visit: 1715 BCCs) developing over their lifetime. The number of lifetime BCCs significantly associated with family history of BCNS (p = 0.02) and age (Lifetime BCCs = 5.4*Age, p < 0.0001). A median of 100 BCCs presented on the head, 56 BCCs on the trunk and extremities, and 10 BCCs on the breast and groin. The 27/27 (100%) participating patients with locally advanced or metastatic BCCs, roughly half (13/27) had a hedgehog inhibitor such as vismodegib, sonidegib, or itraconazole. Participants with BCNs are found to have an increased prevalence of tumors of the skin (KCTR, actinic keratoses, SCC, melanoma), brain (meningioma, medulloblastoma), and osteos (fibroma, cyst). Conclusion: The results of this study demonstrate the high burden of BCCs among patients with BCNS. BCSS predominantly developed on sun-exposed area and strongly correlated with increased age. Additional interventions to prevent and treat BCCs are needed. This study establishes a clinical baseline for emerging therapies such as hedgehog inhibitors in the BCNS population.

Atopic dermatitis and risk of major neuropsychiatric disorders: A systematic review and meta-analysis
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Background: There are many papers on the association between antihypertensive drugs and skin cancers, with conflicting results. Three recent meta-analyses on this topic have included different articles and produced different outcomes. Additionally, several new papers were not included in prior meta-analyses, which could impact the conclusions. We conducted a systematic search of full-text articles and evaluated the most contemporary evidence on antihypertensives and basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanoma. We identified 5793 articles. After title/abstract screening, we assessed 88 full text articles for eligibility. The final analysis included 21 articles (including more than 10 million patients) that could be meta-analyzed. We found statistically significant results for ACE inhibitors (melanoma summary relative risk [sRR] 1.08, 95% CI 1.05–1.11), ARBs (melanoma sRR 1.07, 95% CI 1.01–1.14), and beta-blockers (melanoma sRR 1.08, 95% CI 1.01–1.14); BCC sRR 1.17, 95% CI 1.11–1.22), and non-thiazide diuretics (SCC sRR 1.27, 95% CI 1.10–1.47; BCC sRR 1.06, 95% CI 1.03–1.10). In a qualitative evaluation, only three of eight articles reported a statistically significant result for each association. There is evidence from our meta-analysis, that ACE, SCC, loop diuretics (BCC), and ‘photosensitizing antihypertensives’ (SCC). Taken together, the results of our meta-analyses and the evaluation of dose-response reflect a need for more research to understand whether observed associations differ between antihypertensives and skin cancers are causal.