386 Biomarkers of alopoea 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-γ-skewing, with additional TH2 and IL-23 activation in scalp tissues, little is known about its systemic profile in blood. To evaluate the blood proteome in AA, we measured 650 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, FDR<0.05) including innate immunity (IL-6, IL-8), Th1 (CXCL9/CXCL10/CXCL11/IFNG), Th2 (CCL13/CCL21/CCL24), innate (IL8) and Th7 markers (S100A12). Many cardiovascular/atherosclerosis-related proteins were significantly higher in AA compared to controls, and also correlated with severity, including SELP, SRC, AXL1, MPO, IL10, and OSMD (P<0.05). Pathway analysis showed significant inflammatory/cytotoxic pathways, 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 athero-sclerosis dysregulation, highlighting the need for systemic treatment approaches.

388 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 questions and charts collected from BCNS patients from Feb 2012 to Oct 2018 through 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 BCC 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 participants (current age: 39.8 ± 20.0 years; age at diagnosis: 16.5 ± 12.4 years) reported a median of 1 BCCs developed 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. Of the 27/87 (31%) participants with locally advanced or metastatic BCCs, roughly half (13/27) had tried a hedgehog inhibitor such as vismodegib, sonidegib, or itraconazole. Participants with BCNS are found to have an increased prevalence of tumors of the skin (KCTT), actinic keratosis, 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. BCNs 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.

389 Atopic dermatitis and risk of major neuropsychiatric disorders: A population-based cohort study

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Atopic dermatitis (AD) is a chronic skin disease now recognized to have systemic inflammation and immune factors that may include neuro-immunological abnormalities that are increasingly implicated in neuropsychiatric disorders. Although AD has been previously associated with anxiety, depression, and attention-deficit/hyperactivity disorder (ADHD), longitudinal studies of both children and adults are scarce. We conducted a cohort study using a U.S. population-based electronic health records database to examine the association between AD and several major psychiatric and neurodevelopmental disorders in both children and adults. A total of 446,802 adults and 434,659 children with AD were identified using a previously validated algorithm and validated for internal practice, and index date with 2,877,147 adult and 1,983,589 pediatric controls. Using Cox regression, we found that adults with AD were at greater risk for incident depression (HR 1.05, 95% CI 1.01-1.09), autism (1.02, 95% CI 0.98-1.06), and non-thiazide diuretics (SCC sRR 1.27, 95% CI 1.10-1.47; BCC sRR 1.17, 95% CI 1.11-1.22), thiazides (SCC sRR 1.50, 95% CI 1.43-1.58; BCC sRR 1.38, 95% CI 1.31-1.46), and atopic dermatitis/AD patients (n=20,432, including more than 10 million patients) that could be meta-analyzed. We found that AD was significantly associated with anxiety (HR 1.18, 95% CI 1.16-1.20), depression (1.20, 95% CI 1.18-1.22), and depression (1.21, 95% CI 1.19-1.23), and serious mental illness (HR 1.17, 95% CI 1.15-1.20), and non-thiazide diuretics (SCC sRR 1.27, 95% CI 1.10-1.47; BCC sRR 1.17, 95% CI 1.11-1.22), thiazides (SCC sRR 1.50, 95% CI 1.43-1.58), and non-thiazide diuretics (SCC sRR 1.27, 95% CI 1.10-1.47; BCC sRR 1.16, 95% CI 1.10-1.20). In a qualitative evaluation, only three of eight articles reported a significant association between AD and serious mental illness. Our study data were limited to a single Veterans Affairs center, which may not be generalizable to other settings. Field-directed AK therapies were prescribed only in a minority of patients living with HIV. Optimization of field-directed AK need not impede the potential to prevent keratoacanthoma carcinoma development in patients living with HIV.

390 Antihypertensives and risk of melanoma and keratinocyte carcinoma: A systematic review and meta-analysis

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We reviewed 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 review and meta-analysis to evaluate the most contemporary evidence on antihypertensives and basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanoma. We identified 5794 articles. After title/abstract screening, we assessed 88 full text articles. We included a total of 3,480 patients in HAVACS with at least 2 infectious disease clinic visits with follow-up for a mean (SD) of 8.6 (5.6) years. Among this cohort, 98 (2.8%) patients had at least 1 diagnosis of AK. For AK treatment, 61 patients (64%) underwent lesion-directed cryotherapy, 22 patients (22%) received 5-fluorouracil, 14 patients (14%) received imiquimod, 7 patients (7%) received diclofenac, 1 patient (1%) received ingenol mebutate, and 1 patient (1%) underwent photodynamic therapy. Our small data were limited to a single Veterans Affairs center, which may not be generalizable to other settings. Field-directed AK therapies were prescribed only in a minority of patients living with HIV. Optimization of field-directed AK need not impede the potential to prevent keratoacanthoma carcinoma development in patients living with HIV.