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Cutaneous spectrum of VEXAS syndrome

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VEXAS (Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic) syndrome is a newly described disease due to somatic mutations in *UBA1*, encoding ubiquitin-activating enzyme 1. Patients with VEXAS syndrome have hematologic features, such as macrocytic anemia and myelodysplastic syndrome, and systemic inflammation, including cutaneous involvement. Our aim was to characterize the spectrum of skin manifestations in a large cohort of patients with VEXAS. 87 males and 1 female with genetically confirmed VEXAS syndrome were included in this retrospective study. Mean age at disease onset was 64 years (range 39-78). Most patients (n=71, 81%) had skin involvement. Initial disease presentation was confined to skin in 16 patients (18.2%) or to skin with systemic features in 19 (21%) patients. Skin lesions were painful/tender (n=15, 21.1%) or pruritic (n=13, 18.3%), characterized by erythema (n=20, 28.2%) or nodules (n=17, 23.9%), and occurred most frequently in an acral distribution (n=25, 35.2%). 110 skin biopsies were performed in 45 patients. Skin biopsies were interpreted as small or medium vessel vasculitis (n=29, 26.4%), Sweet syndrome (n=24, 21.8%), connective tissue disease (n=9, 8.2%), or erythema nodosum (n=7, 6.4%). Histologic review of 11 cases identified a neutrophilic predominance (n=6, 54.5%) in the epidermis (n=2, 18.2%), papillary dermis (n=6, 54.5%) and reticular dermis (n=5, 45.5%). Skin lesions improved with glucocorticoids in 85.5% of patients (n=47/55), but relapse after tapering was common (60%, n=33/55). Severe injection site reactions to anakinra were frequent (64.3%, n=9/14). Skin lesions are a common, early feature of VEXAS syndrome and share similarities in clinical and histologic presentation with other inflammatory skin disease. Appearance of the spectrum of skin findings in VEXAS will facilitate early diagnosis.

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Skin cancer risk in people living with HIV during the antiretroviral therapy era

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Background: Chronic immunosuppression is an important risk factor for non-keratinocyte skin cancers (NKSCs). Prior studies showing elevated risk of NKSCs in people living with HIV (PLWH) have focused on pre-1996 data prior to widespread antiretroviral therapy (ART). Objective: To quantify risk of NKSCs in PLWH during the ART-era. Methods: Using linked data from HIV and cancer registries in 12 U.S. regions (1996-2018), we calculated standardized incidence ratios (SIRs) for 23 NKSCs comparing risk in PLWH with and without AIDS to the general population. Poisson regression was used to assess risk factors for NKSCs. Results: Among PLWH (n=585,706) there were 2,743 NKSCs diagnosed during 4,575,794 person-years (median follow-up 7.5 years, interquartile range [IQR] 3.6-11.5), most commonly Kaposi sarcoma (KS, 82%), melanoma (12%), and lymphomas (2.6%). PLWH had elevated risk for KS (SIR 147; 95% CI 141-153), diffuse large B-cell lymphoma (DLBCL; 5.19, 3.13-8.11) and Merkel cell carcinoma (MCC; 3.15, 1.93-4.87). Adnexal cancer risk (SIR 2.01; 95% CI 1.12-3.31) was elevated for people with AIDS (n=359,823 individuals; median follow-up 7.2 years). KS risk was elevated in non-Hispanic black individuals (IRR 1.30; 95% CI 1.18-1.45), men who have sex with men (2.69; 2.38-3.05), and those with AIDS (3.60; 3.23-4.02). Melanoma risk in PLWH was decreased among non-Hispanic Black (IRR 0.06; 95% CI 0.04-0.09) and Hispanic (0.13; 0.09-0.19) individuals and increased with age (1.94; 1.73-2.18). Combined NKSC risk (all types, excluding KS) was not elevated for PLWH overall or among those with a prior AIDS diagnosis. Conclusion: Oncoviruses contribute importantly to skin carcinogenesis in PLWH, including KS (KS-associated herpesvirus), MCC (Merkel cell polyomavirus) and DLBCL (Epstein-Barr virus). The highly elevated risk for KS suggests that PLWH may benefit from routine skin surveillance. Excluding KS, PLWH with or without AIDS have similar risk for NKSCs compared to the general population during the ART-era.

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Halved incidence of scrub typhus after travel restriction to confine a surge of COVID-19 in Taiwan in 2021

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Scrub typhus is a rickettsial disease that is usually transmitted by mite exposure. Infected patients may present with a fever, fatigue, headache, and muscle pain. A blackish skin lesion, called eschar, is pathognomic. The mortality rate in untreated cases is high. The first case of scrub typhus in Taiwan was reported in 1908 during the Japanese colonization. In this article, using the National Infectious Disease Statistics System (NIDSS) from the Taiwan CDC, we analyzed the dynamic incidence of scrub typhus from 2016 to 2021, both seasonally and geographically. In addition, we asked whether the recent travel restrictions and social distancing policy in Taiwan (19 May to 27 July 2021), implemented due to the COVID-19 outbreak, would change the incidence of scrub typhus. The results showed that scrub typhus was most common in summer, with an incidence almost twofold greater than that in winter or spring. Most cases were identified in rural regions. Interestingly, there was a significant 52% reduction in the summer incidence in 2021, compared to the average summer incidence of the past 5 years. This reduction coincided with the countrywide lockdown measures and travel restrictions. The restricted measures for outdoor activities may have contributed to the reduced incidence of scrub typhus.

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Severity of COVID-19 in patients with dermatomyositis: A single center, retrospective observational cohort study

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Although dermatomyositis (DM) patients have been included in studies evaluating COVID-19 risk and severity in large cohorts of patients with chronic immune-mediated diseases, there is little data specifically evaluating these in DM patient cohorts. We performed a single-center, retrospective cohort study to evaluate the severity of COVID-19 in DM patients compared to patients with other dermatologic-immune-mediated diseases (DIMDs), and to assess for risk factors related to severe COVID-19 disease courses. Our DIMD cohort included 7,758 COVID-19 positive patients, 30 of whom had DM and 7,728 who had an alternative DIMD at time of diagnosis. COVID-19 was severe enough to require hospitalization in 7/30 DM patients (23.3%), one of whom required ICU care (3.1%) and another who died (3.1%). In an unadjusted chi-square analysis, there was a marginally significant increase in hospitalization rate among DM patients compared to other DIMD patients (23% vs. 12%, p=0.09). When controlling for age, sex, corticosteroid use, biologics use, and comorbidities, the weighted hospitalization rate was 23% in the DM cohort vs. 15% in the DIMD cohort (OR=1.73 [95% CI, 0.74-4.06]). Our study suggests that DM patients have an increased risk of developing severe COVID-19 compared to patients with other DIMDs, even after controlling for comorbidities and corticosteroid use. Although a relatively high rate of corticosteroid use (20%) and comorbidities likely contributed to severe COVID-19 in some DM patients, our results suggest other risk factors contribute to COVID-19 risk/severity in DM patients. Awareness of this risk is important for clinicians caring for DM patients in order to optimize their care and protection from a severe COVID-19 disease course.

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Diagnostic overlap of drug-induced acute interstitial nephritis with cutaneous involvement and drug-induced hypersensitivity syndrome

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A common clinical dilemma is distinguishing maculopapular exanthem (MPE) with systemic symptoms from severe cutaneous drug reactions, such as drug-induced hypersensitivity syndrome (DIHS). Drug-induced acute interstitial nephritis (DI-AIN) with MPE can be especially challenging to differentiate from DIHS with renal involvement. It is crucial to distinguish DI-AIN from DIHS as the prognosis and treatment differ. Our goal was to estimate the percentage of published DI-AIN cases meeting RegiSCAR criteria for DIHS and characterize the outcomes. We conducted a systematic literature search in MEDLINE (1946-2020) to find studies of DI-AIN with MPE, including DI-AIN with DIHS. Two data collectors performed independent review and data abstraction, including age, sex, RegiSCAR criteria, mortality, and drug culprit. Thirty-seven studies with 43 cases met the selection criteria. Of 28 published DI-AIN cases, 35.7% met RegiSCAR criteria for possible DIHS and 7.1% for probable/definite DIHS. Among these cases, mortality was 23.1% (possible) and 21.4% (probable/definite), respectively, compared to 6.25% for cases not meeting DIHS criteria. This review highlights that many DI-AIN cases meet RegiSCAR criteria for possible DIHS. A DIHS diagnosis may have been missed in some cases due to the diagnostic overlap between these conditions. Since there was a trend toward higher mortality in DI-AIN cases that met RegiSCAR criteria for possible DIHS, research is needed to clarify whether these cases are DIHS and whether treatment with oral corticosteroids improves outcomes.

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Association of bullous pemphigoid and hypertension: A systematic review and meta-analysis

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Bullous pemphigoid (BP) is a chronic, autoimmune skin disorder characterized by subepidermal blistering in various regions of the body. Blister formation is caused by the production of autoantibodies to hemidesmosomal BP antigen 1 (BP230) and BP antigen 2 (BP180). Observational studies have suggested a possible association between BP and hypertension, with hypertension reported as the most frequent comorbidity in BP patients in several studies. We conducted a systematic review and meta-analysis to better elucidate the relationship between BP and hypertension. Ovid MEDLINE, Embase, Web of Science, and Cochrane databases were searched for clinical studies on bullous pemphigoid patients with hypertension, from inception to February 28, 2021. PRISMA guidelines were followed. 11 case-control studies were included in the meta-analysis, with a total of 71,812,699 study participants. Among them, 22,814 were patients with BP. The mean ages of BP patients and controls were 75.4 and 76.1, respectively. The proportion of females among the BP group was 49.9%. Using random effects modeling, the odds ratio (OR) for hypertension in patients with BP was found to be significant when compared with controls (OR=1.28 [95% confidence interval (CI) 1.04-1.56]). Subgroup analyses showed a significant association between BP and hypertension in studies with greater than 1000 BP cases (OR=1.56 [95% CI 1.19-2.04]). Whereas no association between BP and hypertension was observed among studies conducted in Europe (OR=0.94 [95% CI 0.52-1.68]), significant associations were found among studies conducted in Asian countries (OR=1.31 [95% CI 1.09-1.58]) and the United States (OR=1.96 [95% CI 1.90-2.03]). These findings suggest that BP is significantly associated with hypertension. Patients with BP may need to be closely monitored for comorbid hypertension. Despite our effort to not select papers that bias the data, there could still be bias in the selection process.