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Urticaria and a rare mutation: A case of neutrophilic urticarial dermatosis

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Neutrophilic urticarial dermatosis (NUD) is a rare condition characterized by a transient urticarial eruption which is typically accompanied by systemic symptoms including fevers, arthralgias, night sweats and fatigue. About 50 cases have been described to date. The histology is specific revealing a neutrophilic interstitial and perivascular infiltrate with leukocytoclasia but lacking leukocytoclastic vasculitis. In this case we discuss a 59-year-old Caucasian woman with history of CML treated with dasatinib who presented with a 10-month history of painful urticaria, arthralgias, fevers and fatigue. A biopsy was consistent with NUD and a comprehensive work-up while unremarkable for connective tissue diseases or a monoclonal gammopathy, did reveal a heterozygous mutation in NLRP3. Furthermore, dasatinib was also held as it was thought to potentially unmask this unusual entity. This case highlights the importance of recognizing subtle features of a rare entity in order to avoid diagnostic delays and pursue appropriate treatment.

Commercial disclosure: None identified.

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Histopathology patterns of drug rash with eosinophilia and systemic symptoms syndrome

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Background: Drug reaction with eosinophilia and systemic symptoms (DRESS) or drug-induced hypersensitivity syndrome (DIHS) is a potentially life-threatening cutaneous adverse reaction to a drug and/or its metabolites. Despite being a relatively common severe cutaneous drug eruption, the histopathology of DRESS/DIHS is poorly characterized1. Various histopathologic features of patients diagnosed with DRESS/DIHS have been described. The present study sought to characterize the histopathologic findings of DRESS cases diagnosed at the University of Colorado Hospital from September 2008-September 2018 and determine correlation to culprit drug and clinical characteristics.

Methods: ICD-9 and ICD-10 diagnosis codes were used to identify patients that had a diagnosis of DRESS/DIHS from September 2008 to September 2018. These patient's charts were reviewed, and a RedCAP data sheet was used to record various data points including culprit medication, histopathologic findings and clinical parameters.

Results: A total of 94 cases of DRESS/DIHS were surveyed. Preliminary data shows that among the surveyed cases, antibiotics were identified as culprits in 60 cases of DRESS (63.8%); anticonvulsants were identified as culprits in 21 cases of DRESS (22.3%); anti-tumor agents in 15 cases (16%). In several of cases, two or more culprit medications were noted. Of the 21 cases of DRESS with implicated anticonvulsants, only 6 had histopathology results. Histopathology for these patients was diverse including stratum corneum findings such as normal, basket weave, and orthokeratosis.

Conclusions: Given the lack of clarity between clinical and histopathologic features of DRESS/DIHS this study can potentially identify histopathologic disease patterns with respect to specific medications and guide treatment.

Commercial disclosure: None identified.

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More moderate levels of disease severity at baseline related to achievement of treatment targets with apremilast: Results from a pooled analysis

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Background: Baseline characteristics of patients achieving PASI 50% of patients not reaching PASI targets reported DLQI ≤5 (PASI ≥3, 59.3%; PASI ≥5, 52.2%).

Methods: Patients initially randomized to APR who completed the Week 32 visit were grouped based on Week 32 PASI response status (PASI<3 versus ≥3; PASI<5 versus ≥5). Baseline and longitudinal changes in PASI and proportions of patients achieving DLQI5 were reported for the groups. Mean data are presented.

Results: 771 patients completed the Week 32 visit. 30% (n=230) and 50% (n=384) achieved a PASI<3 or PASI<5 at Week 32, respectively. Patients who achieved PASI<3 had lower mean baseline PASI scores than those who didn't achieve the target (15.5 versus 18.4). A similar relationship was observed for patients achieving PASI<5 versus those not achieving the target (15.8 versus 19.5).

Patients who achieved PASI<3 had faster and greater improvements in PASI (mean decrease) versus patients who did not achieve PASI<3: Week 4 (−7.3 versus −5.9), Week 16 (−12.5 versus −9.3), and Week 32 (−14.0 versus −9.3). The majority of patients achieving PASI<3 or PASI<5 (83.6% and 81.4%, respectively) also achieved DLQI≤5; >50% of patients not reaching PASI targets reported DLQI≤5 (PASI≥3, 59.3%; PASI≥5, 52.2%).

Conclusions: Overall, patients who achieved PASI treatment targets with APR had more moderate skin disease at baseline. More than half of the patients not achieving PASI targets with APR achieved DLQI ≤5.

Commercial disclosure: This study was sponsored by Celgene Corporation.

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Celastrol-enriched plant cell culture extract inhibits specific psoriasis T_H17 pathway in 2D and 3D induced human models of psoriasis

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Background: Psoriasis is an immune-mediated inflammatory disease in which T_H17 pathway is mainly involved. Systemic interventions with biologics that specifically block this pathway are effective to treat severe psoriasis. However, for efficient topical treatment, small molecules are more suitable than antibodies to penetrate and target epidermal keratinocytes, the key players in psoriasis. Celastrol, a well described triterpene, is present in low amount in *Tripterygium wilfordii* roots. By using plant cell culture, we were able to boost celastrol production in bioreactors. Here, we evaluated immune modulator effect of celastrol-enriched extract (CEE) in T_H17/T_H22 psoriasis induced models in vitro and ex vivo in view of its dermatologic usage.

Methods: 2D models: i) human CD4+ T lymphocytes, ii) NHEK, or iii) 3D models (reconstituted human epidermis-RHE) were stimulated by anti-CD3/CD28 (i) or by cytokine cocktail (ii and iii) in the presence of CEE. Psoriasis biomarkers were assessed by either ELISA (hCD4+ and RHE) or RT-qPCR (NHEK).

Results: In 2D stimulated models, CEE dose-dependently inhibited the expression of induced T_H17 cytokines (i and ii). In 3D models (RHE), IL-8 expression was significantly reduced.

Conclusions: These findings showed clearly that CEE inhibited: T_H17/T_H22 cytokines, key inflammatory parameters and psoriasis-associated biomarkers. Therefore, skin homeostasis could be restored by these modulator effects. Moreover, this high added value CEE was obtained by an ecofriendly bioprocess in contrast to traditional roots obtained extracts. This is the first time, a well defined immune-modulator CEE is proposed for adjuvant care in psoriasis prophylaxis.

Commercial disclosure: None identified.