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Resistance to BRAF and MEK inhibitors in BRAF-mutant melanoma

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The 5-year survival rate for patients diagnosed with metastatic melanoma is only 23%. Nearly half of patients diagnosed with melanoma have BRAF-mutant melanoma in which there is a driver mutation in the MAPK pathway, leading to over activation. Single-agent BRAF inhibitors had some success, but their long term efficacy is limited due to the development of resistance. Current standard of care includes a BRAF-inhibitor in combination with a MEK inhibitor in order to co-target the downstream MEK protein in the hopes of preventing reactivation of the pathway. It has been shown that this combination therapy has also met some difficulty due to the development of resistance. We generated BRAF inhibitor (dabrafenib) and MEK inhibitor (trametinib) resistant cell lines (TDR) by adding increasing concentration of the drugs to the parental cells (drug sensitive cells) for WM115 and WM983 (BRAF mutant melanoma cell lines) until they were rendered resistant. The TDR cells remained viable over increasing concentration of the inhibitor as assessed by the MTT assay. There was maintenance of p-ERK in the TDR cells, which was not observed for the parental cells under similar conditions. qPCR analysis demonstrated that TDR cells had elevated levels of the signaling molecules such as AXL, EGFR, HER3, and IGF1R. These molecules might be potential mediators of resistance to targeted therapy for BRAF-mutant melanoma. Examining potential mechanisms of resistance to BRAF and MEK inhibitors helps expand possible treatment options to aid in long-term success for BRAF-mutant melanoma patients.

Commercial disclosure: None identified.

15607

Dapsone to treat moderate to severe hidradenitis suppurativa: A retrospective case-series

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Background: Management of hidradenitis suppurativa (HS) is challenging since no single treatment provides consistently effective results, leaving patients with frequent relapses. Dapsone, a sulfonamide drug, combines antimicrobial and antiinflammatory properties that address aspects of HS pathogenesis. Few studies have evaluated the efficacy of oral dapsone on HS, especially in severe disease.

Objective: This study aimed to evaluate the clinical outcomes of patients with moderate to severe HS treated with dapsone.

Methods: This retrospective chart review evaluated HS patients treated with oral dapsone over the past 10 years at one center. Treatment outcomes were classified based on Hurley staging, physician exam, and symptom progression, as reported in the medical record. Adverse effects and concomitant treatment with dapsone were reviewed.

Results: Nineteen patients with moderate to severe (Hurley stage II-III) HS treated with oral dapsone were identified. Within 1-3 months on dosages of dapsone varying from 25-100 mg/day, 3 patients (15.8%) had a clinically significant improvement in symptoms, 10 patients (52.6%) had a slight improvement, and 6 patients (31.6%) had no change in disease state; no patients deteriorated. The majority of the patients who improved were also on other medications (immunomodulators or antibiotics), most commonly adalimumab. Two of 3 patients with clinically significant improvement, 8 of 10 patients with slight improvement, and 2 of 6 patients with no change received combination therapy. On average, time to response was 2 months. 4 patients experienced adverse effects, with nausea being most common; otherwise, dapsone was well tolerated.

Conclusions: Dapsone may have some efficacy for moderate to severe HS and seems well tolerated.

Commercial disclosure: None identified.

15613

Patch testing in patients with suspected shoe contact dermatitis

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Background: Shoe dermatitis is a common contact dermatitis resulting from footwear. The allergens that cause shoe dermatitis vary depending on the footwear constituents, climate, and living habits.

Objective: To determine the characteristics and common allergens responsible for shoe dermatitis in Taiwan.

Methods: A retrospective study was undertaken of patients with suspected shoe dermatitis from the Taipei City Hospital patch test database. Cases were excluded when foot dermatitis medicamentosa was suspected before patch testing. All patients were patch tested with the European Standard series (Chemotechnique Diagnostics AB, Vellinge, Sweden).

Results: Forty- two patients in the database met the criteria and were enrolled in the study. Pruritus was the chief complaint of 25 (59.52%) patients. Soles (76.19%) and heels (28.57%) were the most common sites involved. The most common causative allergens were potassium dichromate (58.50%) and nickel sulfate (58.50%), following by methyldibromo glutaronitrile (56.2%) and cobalt chloride (53.7%). The leading causative allergens in our study are commonly used as a leather tanning agent, shoe accessories and in glue, respectively.

Limitations: Patch test reactivity to samples from the culprit shoes and shoe series were not followed.

Conclusions: The present findings indicate that the common culprit allergens of shoe dermatitis were potassium dichromate and nickel sulfate. Close and prolonged contact with shoe bottom based on a hot and humid climate may be the reason different from other studies.

Commercial disclosure: None identified.

15615

Infantile hemangiomas with minimal and arrested growth: Clinical features and treatment outcomes with 0.5% topical timolol maleate

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Background: A minority of infantile hemangiomas (IHs) showing minimal or arrested growth (MAG) are becoming recognized in the literature. Still, the clinical features and treatment outcomes of IH-MAGs have not been well investigated.

Objective: This study aimed to better understand the clinical characteristics of IH-MAGs and treatment response with topical timolol.

Methods: We retrospectively reviewed medical records and clinical photos of the 31 patients diagnosed with IH-MAGs. Treatment response with topical timolol was assesed in both IH-MAGs and classic IHs groups.

Results: Of the 1038 patients with IHs, only 31 patients (3.0%) were diagnosed with IH-MAGs. The lesions with non-proliferative components were more distributed on the lower half of the body (61.5%) than the one with proliferative components (18.2%). In 14 patients treated with topical timolol, the global assessment scores (GAS) showed 2.21 and 3.14 at 3 and 6 months, respectively, which were considerably higher and rapid in rate than that of classic IHs.

Limitations: This study was retrospectively designed with small sample size.

Conclusions: Though the prevalence of the IH-MAGs could be relatively low, understanding of its clinical features will help differentiate with other disease. Furthermore, this type of lesion might be more responsive to topical timolol than classic IHs.

Commercial disclosure: None identified.