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**Letter**

**Dapsone for treatment of erythema nodosum**

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**Letter**

Erythema Nodosum (EN) is the most common form of septal panniculitis, with over 100 reported infectious, malignant, inflammatory, idiopathic, and autoimmune causes [1,2]. The histopathology reveals a mixed inflammatory infiltrate with lymphocytes, histiocytes, neutrophils, and eosinophils in subcutaneous fat septae accompanied by immune complex deposition [3]. Treatment is divided into symptomatic therapy with non-steroidal anti-inflammatory drugs (NSAIDs), systemic corticosteroids, or therapy targeting the underlying cause of EN when identifiable. We hypothesized that dapsone, an antibacterial agent with anti-inflammatory properties that are particularly effective in conditions characterized by abnormal or dysfunctional neutrophil function, might be an effective treatment for EN [4]. Despite being utilized as an anti-inflammatory agent in many cutaneous conditions, to our knowledge, no existing reports highlight the use of dapsone for EN.

IRB approval was obtained to search the Partners Healthcare Research Patient Data Registry, a centralized registry of more than 1.8 million patients, for individuals with a diagnosis of EN and a prescription for dapsone between January 1993 and June 2014. Of 25 patients identified, three were confirmed as having received dapsone specifically for the treatment of EN (Table 1).

All three patients had recalcitrant and recurrent EN. Our findings in these patients demonstrate a temporal relationship between dapstone initiation and resolution of EN, offering an alternative therapy for EN that lacks immunosuppression and is frequently well-tolerated. Although the exact mechanism allowing for dapstone's beneficial effects is unknown, we hypothesize that its anti-inflammatory and anti-microbial effects may play a role both in addressing various underlying causes of EN and primarily inhibiting the pathogenesis of EN. Further studies are warranted to investigate the mechanism of these beneficial results.

Although dapstone has the potential to induce methemoglobinemia, hemolysis, and agranulocytosis, many of these effects are dose-related and hemolysis can be avoided through G6PD deficiency screening [4]. The doses used in the three patients presented here were 75mg daily or less, and no adverse hematologic events were observed. Other adverse effects associated with dapstone include peripheral motor neuropathies and a hypersensitivity syndrome occurring in approximately 1% of patients [4].

Our findings are limited by a small patient sample that may not be representative of all patients with EN. Additional investigation is required to characterize both dapstone's effectiveness for EN and the incidence of adverse effects associated with its use. Furthermore, because dapstone is also used to treat a number of conditions known to cause EN (leprosy, Behcet's disease, systemic lupus erythematosus, pemphigus vulgaris, toxoplasmosis) [1,4], investigations elucidating the biologic mechanism for the efficacy of dapstone in EN may allow clinicians to better predict which patients are most likely to benefit from this therapy.

We report three cases of recurrent EN recalcitrant to standard therapies. Addition of dapstone resulted in improvement in all three patients. Dapstone's anti-inflammatory and anti-neutrophil effects suggest that it may be an effective and well-tolerated agent for patients with contraindications to or lack of response to either NSAIDs or systemic corticosteroids. Further studies are needed to determine the patient population in which dapstone treatment of EN may be most effective.

**Table 1.** Patients with erythema nodosum who experienced improvement after dapstone therapy

Case No.	Patient Sex/Age	Comorbidities	Previous Therapies	Maximum dapstone daily dosing	Time to improvement of or resolution of lesions after dapstone initiation	Total dapstone treatment time with improvement of or resolution of lesions	Concurrent medications with dapstone initiation	Discontinued or decreased medications due to dapstone efficacy	Side-effects experienced
1	F/39	Cystic fibrosis Primary biliary cirrhosis	Indomethacin, prednisone	50mg	4 weeks; complete resolution	3 months	Prednisone 40mg	Prednisone completely tapered off	None
2	M/33	Recurrent pericarditis	Ibuprofen, hydroxychloroquine	50mg	3 weeks; complete resolution	9 months	Hydroxychloroquine 400mg daily	None	None
3	F/29	Crohn's disease Psoriasis	Prednisone, 6-MP, infliximab	75mg	4 weeks; improvement	10 months	6-MP 25mg daily, infliximab 10mg/kg every 4 weeks	Infliximab decreased from 10mg/kg to 7.5mg/kg every 4 weeks	None

Abbreviations: 6-MP, 6-mercaptopurine

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