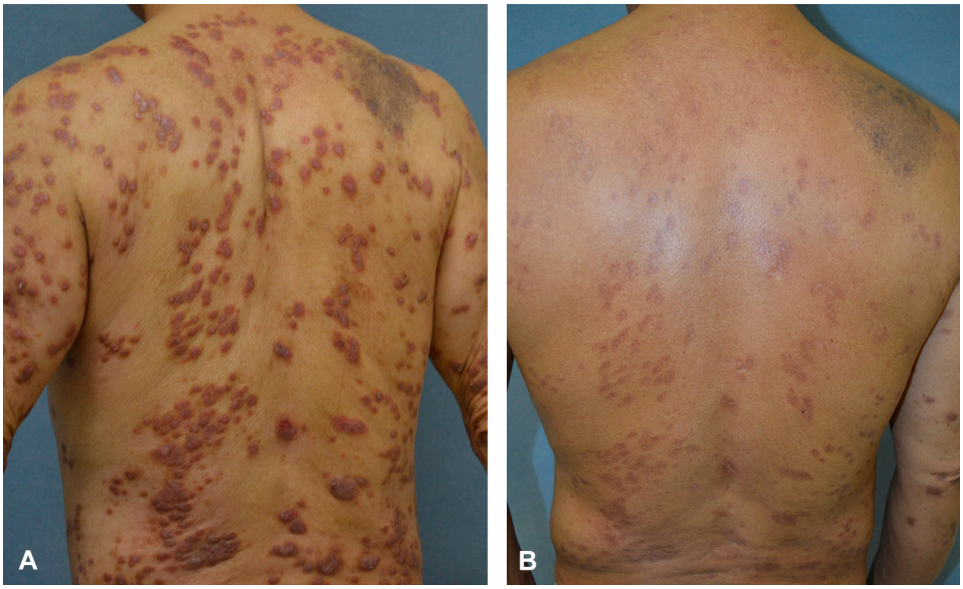

Fig 1. Generalized prurigo nodularis. Patient 1 before (**A**) and after (**B**) a course of modified Goeckerman therapy.

Pfizer, and Merck. Dr Berger is a consultant for Hyperion Therapeutics and Prescription Solutions. Mr Sorenson and Dr Levin have no conflicts of interest to declare.

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REFERENCES

1. Akiyama T, Carstens MI, Carstens E. Enhanced scratching evoked by PAR-2 agonist and 5-HT but not histamine in a mouse model of chronic dry skin itch. Pain 2010;151(2):378-83.
2. Rukwied RR, Main M, Weinkauf B, et al. NGF sensitizes nociceptors for cowhage- but not histamine-induced itch in human skin. J Invest Dermatol 2013;133(1):268-70.
3. Steinhoff M, Neisius U, Ikoma A, et al. Proteinase-activated receptor-2 mediates itch: a novel pathway for pruritus in human skin. J Neurosci 2003;23(15):6176-80.
4. Sonkoly E, Muller A, Lauerma AI, et al. IL-31: a new link between T cells and pruritus in atopic skin inflammation. J Allergy Clin Immunol 2006;117(2):411-7.
5. Johansson O, Liang Y, Emtestam L. Increased nerve growth factor- and tyrosine kinase A-like immunoreactivities in prurigo nodularis skin — an exploration of the cause of neurohyperplasia. Arch Dermatol Res 2002;293(12):614-9.
6. Liang Y, Jacobi HH, Reimert CM, et al. CGRP-immunoreactive nerves in prurigo nodularis—an exploration of neurogenic inflammation. J Cutan Pathol 2000;27(7):359-66.
7. Wallengren J, Sundler F. Phototherapy reduces the number of epidermal and CGRP-positive dermal nerve fibres. Acta Derm Venereol 2004;84(2):111-5.
8. Tartar D, Bhutani T, Huynh M, et al. Update on the immunological mechanism of action behind phototherapy. J Drugs Dermatol 2014;13(5):564-8.

http://dx.doi.org/10.1016/j.jaad.2014.09.050

PsAPASH: A new syndrome associated with hidradenitis suppurativa with response to tumor necrosis factor inhibition

To the Editor: A 50-year-old man with refractory and multitherapy-resistant hidradenitis suppurativa was referred for evaluation after having been unsuccessfully treated with dapsone, oral isotretinoin, and several cycles of antibiotics (clindamycin-rifampin, tetracycline, cephalosporin) (Fig 1, *A*). He had hidradenitis suppurativa since the age of 43 years, was overweight and a heavy tobacco smoker, and had a medical history of acne, diabetes mellitus type 2, arterial hypertension, hypertriglyceridemia, hiatal hernia, depression, and psoriatic arthritis (PsA). Active acne pustules and comedonal lesions were observed on the face and neck; painful sterile abscesses and hypertrophic scars were present at the axillae and were classified as hidradenitis suppurativa Hurley II stage of severity. The patient had also erythematous scaly lesions on the scalp associated with severe joint and diffuse inflammation leading to the clinical diagnosis of PsA (Psoriasis Area Severity Index score 1.2; DAS28-CRP4 5.78; pain visual analog scale score 70). Two ulcerative lesions on his right leg had a dusky erythematous undermined edge (Fig 1, *B*), and were clinically and histologically diagnosed as pyoderma gangrenosum after the exclusion of diagnoses including neutrophilic disorders, vasculopathies, and infections. His quality of life was severely hampered by disability and social discomfort.

Adalimumab is a highly specific tumor necrosis factor (TNF)-alfa inhibitor, binding to both soluble

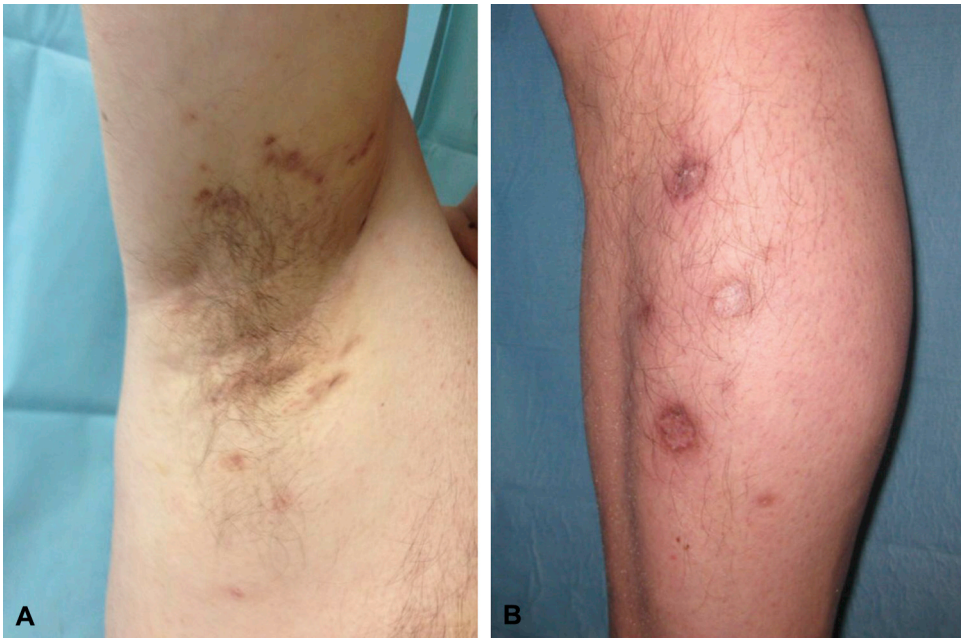

Fig 1. Clinical details of PsAPASH syndrome. Hidradenitis suppurativa: scarring and multiple interconnected painful lesions localized at the axillae (Hurley stage II) (**A**). Ulcerative lesions localized at the lower extremities clinically and histologically diagnosed as pyoderma gangrenosum (**B**).

and membrane-bound TNF-alfa. TNF-alfa is a proinflammatory cytokine with a pathogenetic role in several immune-mediated diseases such as psoriasis, hidradenitis suppurativa, and pyoderma gangrenosum. The efficacy and safety of adalimumab in treating PsA is largely demonstrated, whereas limited evidence of its off-label use in treating hidradenitis suppurativa, pyoderma gangrenosum, or concomitant skin disorders has been reported.[1-3] Randomized, double-blind, placebo-controlled studies have assessed the efficacy and safety of adalimumab therapy in patients affected by hidradenitis suppurativa.[1,2]

Adalimumab therapy was initiated at a dose of 40 mg every other week. A marked and rapid improvement in PsA and psoriatic skin lesions (Psoriasis Area Severity Index score 0; DAS28-CRP4 1.21; pain visual analog scale score 0) with concomitant clinical remission of hidradenitis suppurativa and pyoderma gangrenosum was observed after 4 weeks of treatment. The effect was durable over the 36 weeks of treatment, and adalimumab was well tolerated.

Hidradenitis suppurativa is notoriously difficult to treat. Currently available therapeutic options including antibiotics (clindamycin-rifampin-tetracycline), isotretinoin, and dapsone. If antibiotics are ineffective, excisional surgery remains a valid therapeutic approach. In our case, hidradenitis suppurativa associated with PsA, acne, and pyoderma gangrenosum was successfully treated with adalimumab. Adalimumab was administered at the recommended dose for PsA therapy, leading to the resolution of the clinical symptoms of psoriasis and complete remission of hidradenitis suppurativa and pyoderma gangrenosum. Similar to the spectrum of recently described autoinflammatory syndromes, namely PASH (pyoderma gangrenosum, acne, and hidradenitis suppurativa), PAPA (pyogenic arthritis, acne, and pyoderma gangrenosum), and PAPASH (pyogenic arthritis, pyoderma gangrenosum, acne, and hidradenitis suppurativa), the concomitant diagnosis of PsA, pyoderma gangrenosum, acne, and hidradenitis suppurativa may represent a new syndrome; the acronym could be PsAPASH.[4,5] As shown in this case, TNF-alfa inhibition may represent a promising therapeutic strategy for treating multiple concomitant skin disorders, such as that with common pathogenic mechanisms. However, further clinical observations will be helpful to establish the prevalence of this clinical entity and its treatment.

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Funding sources: None.

Disclosure: Dr Chimenti has been a consultant for Abbvie (adalimumab manufacturer) and for Merck (infliximab manufacturer). Dr Saraceno has been a consultant for Abbvie. Drs Babino, Chiricozzi, and Zangrilli have no conflicts of interest to declare.

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REFERENCES

1. Miller I, Lynggaard CD, Lophaven S, Zachariae C, Dufour DN, Jemec GB. A double-blind placebo-controlled randomized trial of adalimumab in the treatment of hidradenitis suppurativa. Br J Dermatol 2011;165:391-8.
2. Kimball AB, Kerdel F, Adams D, et al. Adalimumab for the treatment of moderate to severe hidradenitis suppurativa: a parallel randomized trial. Ann Intern Med 2012;157:846-55.
3. Reddick CL, Singh MN, Chalmers RJ. Successful treatment of superficial pyoderma gangrenosum associated with hidradenitis suppurativa with adalimumab. Dermatol Online J 2010;16:15.
4. Hsiao JL, Antaya RJ, Berger T, Maurer T, Shinkai K, Leslie KS. Hidradenitis suppurativa and concomitant pyoderma gangrenosum: a case series and literature review. Arch Dermatol 2010;146:1265-70.
5. Marzano AV, Trevisan V, Gattorno M, Ceccherini I, De Simone C, Crosti C. Pyogenic arthritis, pyoderma gangrenosum, acne, and hidradenitis suppurativa (PAPASH): a new autoinflammatory syndrome associated with a novel mutation of the PSTPIP1 gene. JAMA Dermatol 2013;149:762-4.

http://dx.doi.org/10.1016/j.jaad.2014.10.002

Synchronous Paget disease of the breast and axilla

To the Editor: Mammary Paget disease (MPD) and extramammary Paget disease (EMPD) are rare acquired skin disorders having clinical features that are similar to those of inflammatory or infectious skin disorders. MPD is mostly associated with high-grade ductal carcinoma in situ, whereas EMPD arises in areas rich in apocrine glands. EMPD is classified into primary and secondary EMPD; the latter is associated with underlying malignancy and may arise as a result of epidermal invasion of malignant adenocarcinoma cells.

We report a rare case of synchronous Paget disease. A 63-year-old woman presented concomitantly with crusting and erosion of the right nipple, with brown plaques on the left axilla. Breast lesion biopsy specimen indicated underlying foci of ductal carcinoma in situ, which required total mastectomy and sentinel lymph node biopsy. Axilla biopsy specimen indicated EMPD, which required simple resection of the left axilla lesion. Both tumors were located in the epithelium (Figs 1 and 2), and axillary sentinel lymph node biopsy specimen yielded negative results. Because the operative margins were negative and both tumors were staged as TisN0M0, the treatment was deemed adequate. Gross cystic disease fluid protein-15 and estrogen receptor were expressed in the breast, but not in the axilla tumor cells. Immunohistochemical and pathological analyses indicated that neither of these were secondary metastatic lesions, but suggested that they arose from independent tumorigenic events.

Cases of synchronous MPD and EMPD are extremely rare; to our knowledge, only 2 other cases have been reported. This report is the first to our knowledge that describes the simultaneous diagnosis of synchronous Paget disease of the breast and axilla.

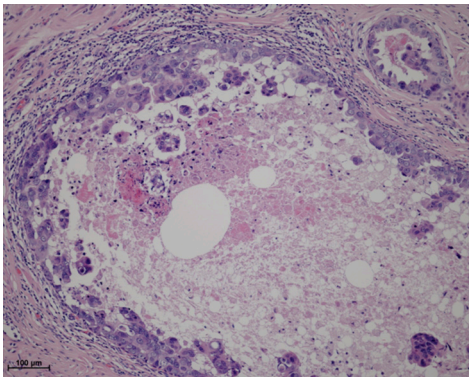

Fig 1. Total mastectomy of the right breast revealed Paget disease with underlying foci of ductal carcinoma in situ (shown above). (Hematoxylin-eosin stain; original magnification: ×100.)

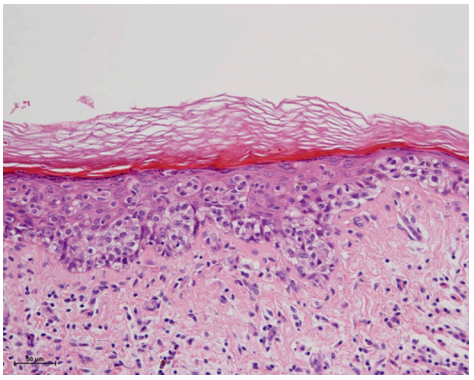

Fig 2. In the axilla, atypical large cells with prominent nuclei and pale cytoplasm are present diffusely within the epidermis. (Hematoxylin-eosin stain; original magnification: ×200.)