

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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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)- α inhibitor, binding to both soluble

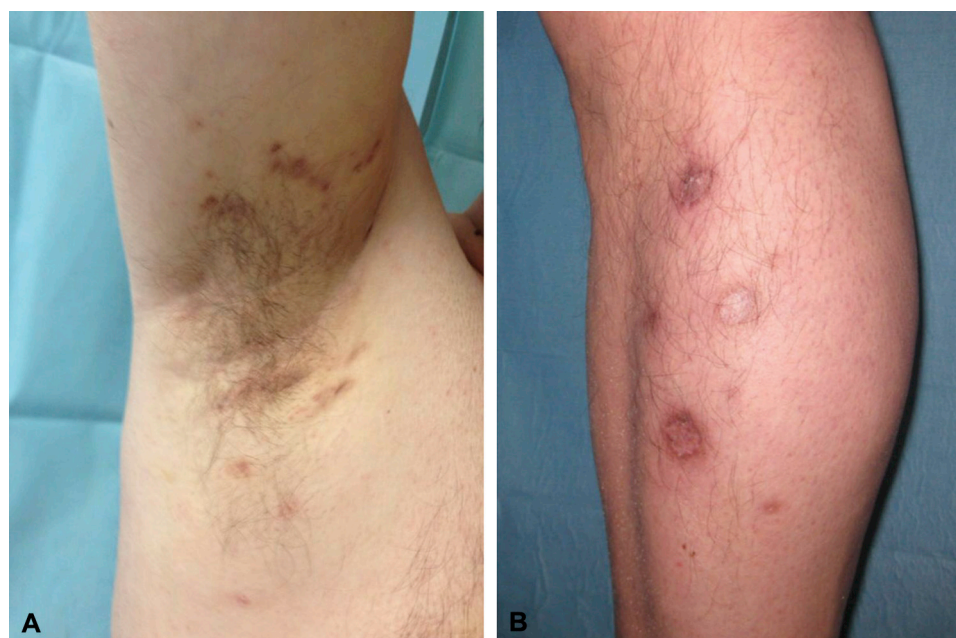


Fig 1. Clinical details of PsAPASH syndrome. Hidradenitis suppurativa: scarring and multiple interconnected painful lesions localized at the axillae (Hurley stage II) (**A**). Ulcerative lesions localized at the lower extremities clinically and histologically diagnosed as pyoderma gangrenosum (**B**).

and membrane-bound TNF- α . TNF- α 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- α 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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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

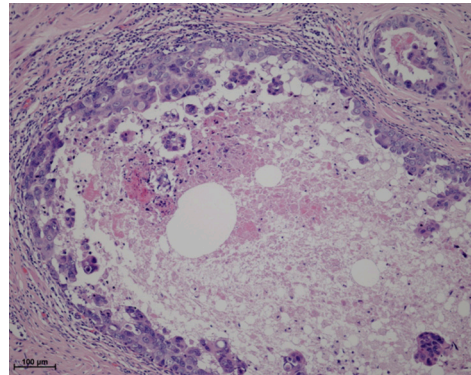


Fig 1. Total mastectomy of the right breast revealed Paget disease with underlying foci of ductal carcinoma in situ (shown above). (Hematoxylin-eosin stain; original magnification: $\times 100$.)

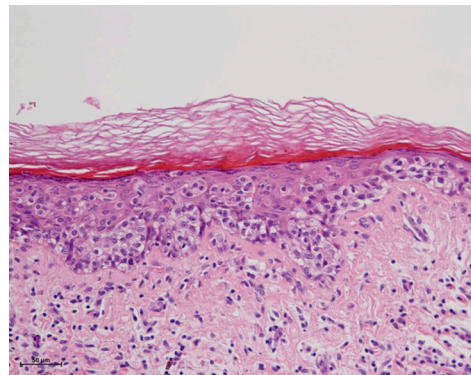


Fig 2. In the axilla, atypical large cells with prominent nuclei and pale cytoplasm are present diffusely within the epidermis. (Hematoxylin-eosin stain; original magnification: $\times 200$.)

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.