response to this class of agents alone or as a manifestation of systemic differentiation syndrome.

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OBSERVATION

Acute Generalized Pustular Psoriasis Treated With the IL-17A Antibody Secukinumab

We describe a patient with acute generalized pustular psoriasis (GPP) treated with the new anti–interleukin (IL)-17A antibody, secukinumab, who showed a remarkable response with almost complete resolution of pustulation after the first injection. To our knowledge, there are no data in the literature evaluating the efficacy of secukinumab in GPP.

Report of a Case | A man in his 50s with a 7-year history of GPP was admitted with an acute, severe flare of pustulation. On examination, he was febrile, drowsy, and had disseminated, partly confluent lakes of painful pustules primarily over the trunk as well as the upper and lower extremities, with widespread erosions on the lower legs. There was generalized erythema involving 80% of his body surface area (BSA), and his GPP area and severity index was 47.6 (Figure 1A). The GP area and severity index is calculated in the same way as the psoriasis area and severity index except that the scale score is substituted with a pustule score. The dermatology life quality index (DLQI) on admission was 25.

Laboratory findings on admission revealed neutrophil leukocytosis with white blood cell count of 21.2 × 10^9/L (reference range, 4.3-10.1 × 10^9/L), neutrophil count, 18.81 × 10^9/L (reference range, 1.9-7.0 × 10^9/L), and C-reactive protein level, 129.0 mg/L (reference range, <5.0 mg/L). To convert white blood cells and neutrophils to number per microliter, divide by 9.524; C-reactive protein to nanomoles per liter, multiply by 0.001; C-reactive protein to nanomoles per liter, multiply by 0.001.

Treatment with the recently approved drug for psoriasis vulgaris, secukinumab, was started. During hospitalization, we administered a total of 3 subcutaneous 300-mg doses, 1 dose every week (days 0, 7, and 14).

Within 48 hours after the first dose, there was defervescence, improvement in his general state, and resolution of pustules with marked reduction in erythema. Complete absence of pustulation was achieved by day 7 (Figure 1B). White blood cell count, C-reactive protein level (Figure 2A), and erythrocyte sedimentation rate were continuously declining to normal levels. Immunohistological staining of specimens from a lesion on the right upper arm at day 7 showed reduction both in IL-17 expression and neutrophil infiltration in the dermis and epidermis compared with day 1.

Interestingly, we observed minor relapses 3 to 4 days after each secukinumab injection, which were characterized by temporary extension of erythema and development of new pustules. However, the patient’s condition continuously improved over the following weeks (Figure 2B). Seven
weeks after initiating therapy (4 weeks after the last injection), the patient presented in an excellent general state (DLQI, 5), though 5 days earlier he had developed a minor flare with new pustules on the lower legs and minor erythema on the trunk. Therefore, we initiated maintenance therapy with injection of 300 mg of secukinumab every 4 weeks.

Discussion | Recent research suggests that GPP and pustular psoriasis (PP) are distinct clinical entities, rather than versions of the same disease.\(^2\) Histologically, GPP is characterized by neutrophilic infiltration into the dermis and epidermis, forming subcorneal macropustules.\(^3\) Since migration of neutrophils to psoriatic lesions is mediated by IL-17,\(^4\) neutralization of IL-17A seems to be a promising treatment option in GPP.

In an open-label phase 3 study of Ixekizumab, another anti-IL-17A monoclonal antibody that has exhibited promising results in patients with moderate to severe PP, rapid and clinically significant improvement was seen in 5 patients with GPP.\(^5\) In consideration of these findings, we decided to use secukinumab to treat the severe flare of GPP in the present patient.
From the beginning, the therapy showed remarkable efficacy in both clinical symptoms and laboratory findings, with an almost complete disappearance of pustulation 48 hours after the first injection. Though 3 to 4 days after each injection, the patient developed minor flares of new pustules, he continuously improved. These small recurrences decreased over time and may be attributed to on-off phenomena of the antibody.

In conclusion, the patient showed a rapid response to secukinumab with regard to the cutaneous and systemic manifestations of severe GPP, indicating that this new targeted therapy might also be used to treat PP. Prospective randomized clinical trials are required to further evaluate the efficacy and safety of IL-17 inhibitors for the treatment of GPP.

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Well-Differentiated Syringofibrocarcinoma in a Patient With Clouston Syndrome

An elderly man presented with syringofibrocarcinoma of the foot, which prompted examination and workup that confirmed a diagnosis of Clouston syndrome (hidrotic ectodermal dysplasia).

Report of a Case | A man in his early 80s presented after surgical excision of a large tumor on the right dorsal foot. He had a lifelong history of wispy hair on the lateral scalp, short thick fingernails with distal separation, and dystrophic toenails with distal wedge-shaped subungual hyperkeratosis (Figure 1A). His palms and soles had generalized mild hyperkeratosis and discrete large areas of pink papillomatous plaques. His shins had large scales and erythema. He had no eyelid cysts, and the few teeth he retained appeared normal; he had no history of delayed loss of deciduous teeth. His mother, maternal grandmother, sister, and brother reportedly had similar skin, hair, and nail findings. Both the patient and his brother developed tumors on a foot around age 80 years. The present patient’s tumor is shown in Figure 1B. It was treated with surgical excision and fifth-ray resection followed by placement of a split-thickness skin graft and healed well.

Pathologic review of the surgical specimen showed thin cords and anastomosing strands of epithelial cells extending down from the epidermis with adjacent fibrotic changes consistent with syringofibroadenoma (Figure 2A). Deeper were islands of well-differentiated adnexal neoplasm with areas of squamous and poroid features consistent with a well-differentiated invasive tumor in the setting of syringofibroadenoma (Figure 2B).

The differential diagnosis for dominantly inherited hair and nail dysplasia with palmoplantar keratoderma and syringofibroadenomas includes Clouston syndrome, caused...