https://doi.org/10.5021/ad.2018.30.1.100

# A Case of Acute Generalized Exanthematous Pustulosis after Injection of an Erythropoiesis-Stimulating Agent

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Dear Editor:

Erythropoiesis-stimulating agents (ESAs) are now the most widely used drugs for anemia in chronic kidney disease (CKD) patients. Anemia in CKD patients is mainly because of insufficient erythropoietin production and since the late 1980s, recombinant human erythropoietin has been used to manage anemia in these patients. The reported adverse effects are thrombotic events and rarely, pruritus and acne on the skin[1]. Acute generalized exanthematous pustulosis is characterized by the rapid appearance of sterile, non-follicular pustules and is strongly associated with antibiotic use[2]. Rarely, ESA injections can be a cause of acute generalized exanthematous pustulosis (AGEP); Schmutz et al.[3] reported only one such case. We introduce an interesting case of AGEP that developed after ESA injections.

A 43-year-old woman presented with multiple vesicles and pustules on her neck and trunk with chronic fever (near 39°C) for 2 days. She was diagnosed with stage 5

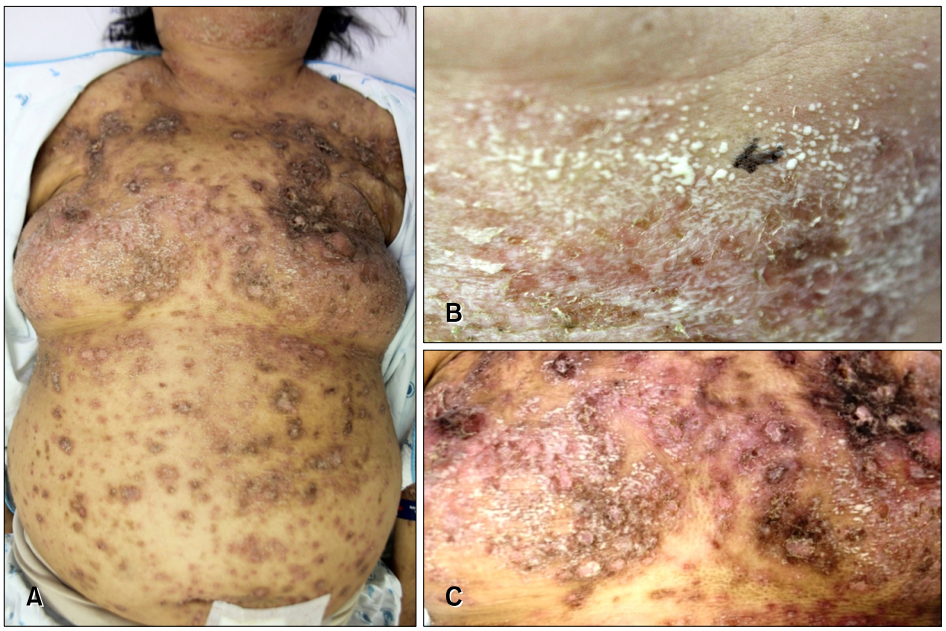


**Fig. 1.** (A) Multiple miliary pustules on the neck and trunk. (B) A close-up view on the neck. (C) A close-up view on the chest.

Received July 28, 2016, Revised December 28, 2016, Accepted for publication January 5, 2017

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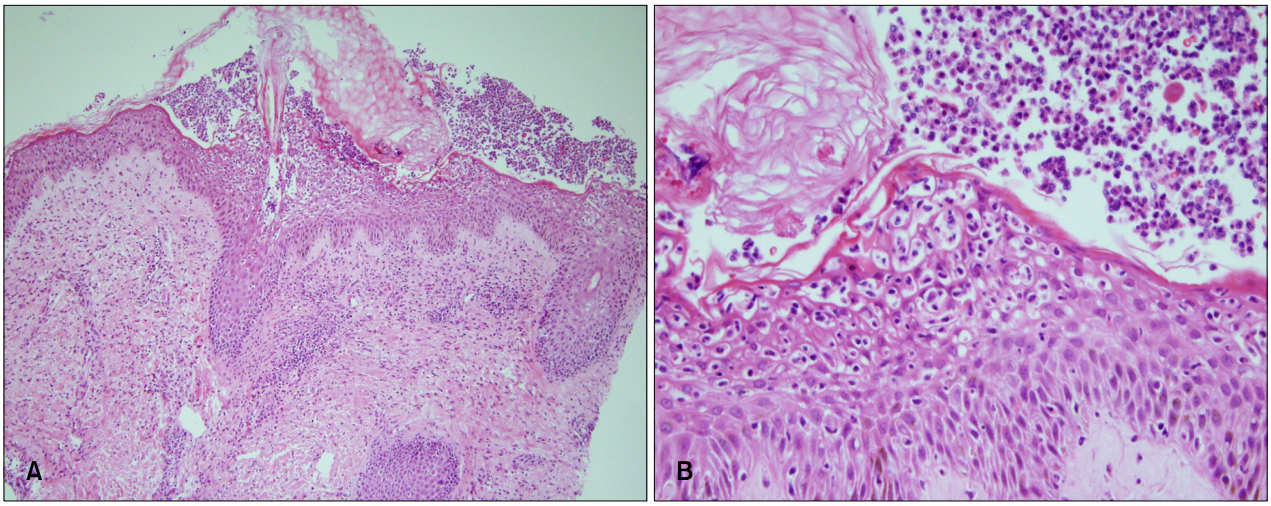


**Fig. 2.** Subcorneal pustule with papillary edema and mixed inflammatory infiltrate of mainly neutrophils and eosinophils (H&E; A: ×100, B: ×200).

chronic renal disease 2 years previously and had been undergoing peritoneal dialysis. She had planned to inject ESA 3 times per week to treat anemia related to CKD. She had severe itching on her whole body 1 day after the first subcutaneous ESA injection and 2 days after the fourth injection; thereafter, the multiple pustules appeared. Physical examination revealed excoriated hyperkeratotic patches on her trunk and multiple pustules and erythematous patches with scales on her neck and trunk (Fig. 1). Her eosinophil level was 2.5% before the injections, but rose to 13% until presentation. A skin biopsy of the neck showed a subcorneal pustule in the epidermis and overall infiltration of inflammatory cells on the upper dermis (Fig. 2). We discontinued the ESA and treated with oral prednisolone (20 mg/d) and oral antihistamine. Topical steroid agents with wet dressings were applied to the skin lesions. After 7 days, skin lesions had almost disappeared except for localized desquamation.

The pathogenesis of AGEP is not well understood; however, genetic susceptibility has been suggested as a possible cause[2]. Cutaneous eruption is related to pharmacogenetic variations in drug-metabolizing enzymes and human leukocyte antigen (HLA) associations. The results of genetic analysis of this patient were HLA-B44, HLA-B51. Some studies have reported that HLA-B51 is associated to AGEP[2], while others have suggested that end-stage renal disease (ESRD) is associated to HLA-B51[4]. We think that our patient may have a genetic susceptibility as a risk for the development of AGEP in ESRD. Another mechanism of AGEP is considered an autoimmune reaction. Because ESAs can stimulate the immune system to develop autoantibodies[5], AGEP could be developed by antigen-antibody complexes. The immune mechanism of AGEP is specific T cells producing large amounts of neutrophil-attracting cytokines. However, some studies about AGEP have reported elevated interleukin-5, which could explain the eosinophilia[2]. In our case, it is possible that AGEP arose from CD4+ T cells with a Th2 cytokine pattern. Our patient displayed features of AGEP with its characteristic morphology, histology, and course. Therefore, ESAs should be added to the list of potential causes of AGEP.

## CONFLICTS OF INTEREST

The authors have nothing to disclose.

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