SHORT COMMUNICATION

Spesolimab Rapidly Resolved Capillary Leak Syndrome Associated with Generalized Pustular Psoriasis

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Generalized pustular psoriasis (GPP) is a rare and potentially life-threatening dermatosis. A subset of patients may develop capillary leak syndrome (CLS), which is characterized by oedema, hypotension, serous effusions and respiratory failure (1). Treatment options for GPP-associated CLS remain extremely limited (2). Spesolimab, an interleukin-36 receptor antibody, was recently approved for the treatment of acute GPP flares and has demonstrated rapid efficacy in both clinical trials and real-world settings (3–5). However, its potential role in the management of CLS has not yet been reported. Here, we describe a patient with GPP complicated by CLS who was successfully treated with spesolimab.

A 40-year-old woman with no prior history of psoriasis presented with rapidly progressive erythema and pustules. Twenty-three days before admission, she developed a sore throat and was prescribed non-steroidal anti-inflammatory drugs (NSAIDs). Five days before hospitalization, she noted painful cervical swelling followed by diffuse erythema. She was treated elsewhere with antibiotics and NSAIDs for presumed lymphadenitis. Three days later, high fever (38.5°C), worsening rashes, lip erosions, pustules and bilateral conjunctival injection developed. With a tentative diagnosis of severe drug eruption, she was referred to our hospital.

CASE REPORT

On admission, she exhibited confluent dark-red erythema with numerous pustules (Fig. 1A). Laboratory tests showed leukocytosis (8,600/μL, 84% neutrophils), hypoalbuminaemia (3.2 g/dL) and elevated C-reactive protein (CRP; 18.4 mg/dL). Suspected medications were discontinued, but her condition did not improve and instead worsened, suggesting GPP rather than drug eruption. Histopathology revealed Kogoj's spongiform pustules (Fig. 1B). Oral etretinate and subcutaneous ixekizumab (160 mg on day 2) were started, but skin lesions improved minimally (Fig. 1C).

On day 6, she developed dyspnoea, hypoxaemia (SpO_2 85% on room air, requiring 3 L/min oxygen), systemic oedema and hypotension. Chest computed tomography revealed bilateral ground-glass opacities and pleural effusions (Fig. 1D). Laboratory data showed leukocytosis (34,000/μL), severe hypoalbuminaemia (1.5 g/dL) and CRP (19.6 mg/dL), consistent with CLS. Intravenous (IV) spesolimab (900 mg) was given with granulocyte/monocyte adsorption apheresis (GMA). Within 24 h, erythema faded, pustules resolved and oxygenation improved (Fig. 1E). Oedema gradually subsided. Chest imaging showed regression of pulmonary infiltrates (Fig. 1F). Albumin replacement

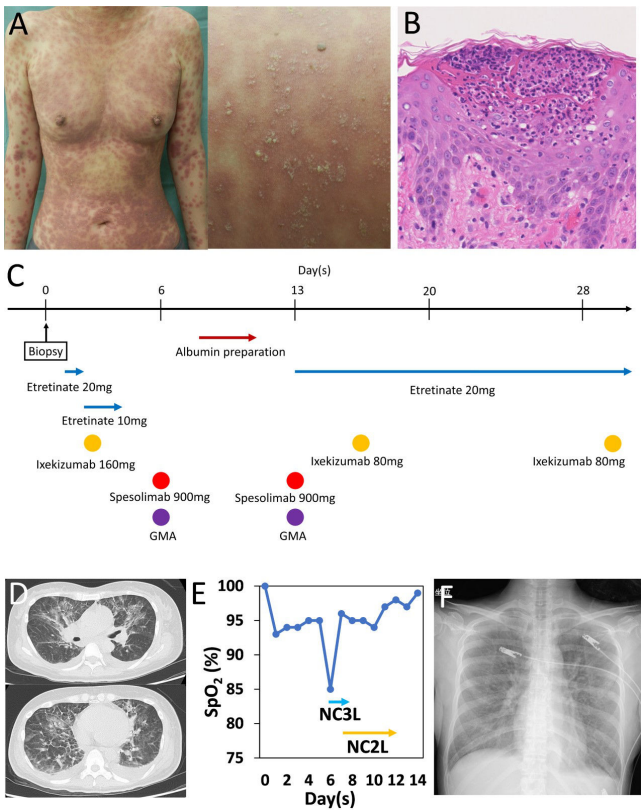

Fig. 1. Clinical, histological and radiological features of generalized pustular psoriasis complicated by capillary leak syndrome treated with spesolimab. (A) Clinical presentation at admission: widespread dark-red erythema with confluent pustules. (B) Histopathology of lesional skin showing Kogoj's spongiform pustules (haematoxylin and eosin staining). (C) Timeline of treatments: etretinate, ixekizumab, spesolimab, GMA and albumin replacement. (D) Chest computed tomography before spesolimab showing bilateral ground-glass opacities and pleural effusions. (E) Oxygenation improved rapidly after spesolimab administration. (F) Chest X-ray after therapy showing marked regression of infiltrates and effusions. GMA, granulocyte/monocyte adsorption apheresis; NC, nasal cannula.

was performed on days 8–10. A second infusion of spesolimab (900 mg IV) with GMA was given on day 11, followed by ixekizumab (80 mg SC) on day 15. She gradually improved and was discharged on day 20. The genetic analysis revealed no mutations in *IL36RN* or *CARD14*.

DISCUSSION

This case emphasizes CLS as a severe systemic complication of GPP. CLS reflects vascular hyperpermeability causing plasma leakage, hypoalbuminaemia and respiratory failure (1). Spesolimab has demonstrated efficacy for cutaneous flares (3–5), and here, it also led to rapid recovery of CLS within 24 h. The improvement in oxygenation and pulmonary oedema indicates benefit beyond skin disease, possibly through suppression of vascular hyperpermeability. Although GMA and ixekizumab were co-administered, the temporal association suggests spesolimab as the decisive therapy. To our knowledge, this is the first report of GPP-associated CLS successfully treated with spesolimab. Further cases are needed to establish its role in this critical complication.

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Ethics committee: The patient in this manuscript has given written informed consent to publication of her case details.

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