

Acute syndrome of pan-epidermolysis and thrombotic storm arising in a patient with systemic lupus erythematosus



Elise Burger, BA, Darlene Gou, MD, Travis Vandergriff, MD, Arturo Dominguez, MD, and
Melissa Mauskar, MD
Dallas, Texas

Key words: acute syndrome of pan-epidermolysis; systemic lupus erythematosus; thrombotic storm; toxic epidermal necrolysis.

INTRODUCTION

The vast variety of clinical presentations in systemic lupus erythematosus (SLE) contributes to its reputation as one of the great masqueraders. Here we report a case of a 39-year-old woman with a history of SLE in whom a fatal combination of acute syndrome of apoptotic pan-epidermolysis (ASAP) and thrombotic storm developed. Differentiating between drug-induced toxic epidermal necrolysis (TEN) in an SLE patient and TEN-like SLE is challenging; SLE patients are often on chronic medications that increase their risk of drug-induced TEN, and TEN is known to occur more commonly in patients with connective tissue disease.¹ Additionally, both can have near-identical histologic findings, with full-thickness epithelial necrosis along with a sparse superficial lymphocytic infiltrate. The unifying concept of ASAP was first introduced in 2004 to describe the clinical constellation that encompasses the many life-threatening clinical situations presenting with massive epidermal cleavage owing to hyperacute apoptotic injury.² Thrombotic storm is a clinical presentation characterized by the rapid onset of multiple thromboembolic occlusions affecting multiple vascular beds including the arterial, venous, and microvascular circulation.³ Typically, there is an inciting trigger such as infection, trauma, or pregnancy, and around half of patients are positive for antiphospholipid antibodies.⁴ These patients have a progressive unexplained recurrence of thrombi that are refractory to acute therapy; therefore, management in the acute setting is extremely difficult.

Abbreviations used:

ASAP:	acute syndrome of apoptotic pan-epidermolysis
IV:	intravenous
IVIg:	intravenous immunoglobulin
SLE:	systemic lupus erythematosus
TEN:	toxic epidermal necrolysis

CASE REPORT

A 39-year-old woman with a medical history of SLE (anti-nuclear antibody, 1:1280; anti-Smith positive, dsDNA⁺, hypocomplementemia, history of proteinuria) and immune thrombocytopenic purpura presented to a local facility with fatigue and abdominal pain, was found to be severely thrombocytopenic with $5 \times 10^9/L$ platelets, and was treated with multiple platelet transfusions, intravenous (IV) methylprednisolone, and intravenous immunoglobulin (IVIg). She had a splenectomy for refractory thrombocytopenia, which was complicated by an intra-abdominal hematoma. An ischemic left foot prompted a below-the-knee amputation. An SLE exacerbation developed with enterocolitis and sepsis, and she was transferred to the intensive care unit. Her condition continued to deteriorate, and sloughing and profound hypotension developed. She was transferred to our hospital at day 36.

On arrival, her temperature was 31.5°C; heart rate, 87; blood pressure, 90 to 100/40 to 50 mm Hg; and blood oxygen saturation was 99% (at fraction of inspired oxygen 40%); she was admitted to the burn

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Correspondence to: Melissa Mauskar, MD, Department of Dermatology, UT Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390. E-mail: Melissa.mauskar@utsouthwestern.edu.

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Fig 1. Clinical photograph. Confluent denudation on chest, abdomen, leg. Nikolsky-positive plaques on breast and arms. Steri-strips over splenectomy incision.



Fig 2. Clinical photograph. Torso with areas of confluent denudation.

intensive care unit. Physical examination found confluent dusky Nikolsky-positive plaques on face, neck, breasts, and arms. Her upper chest, abdomen, mons pubis, and upper left leg showed nearly confluent areas of denudation (Figs 1 and 2). Her right leg showed dusky patches in a reticulate pattern (Fig 3). She had crusted erosions on her lips and crust on her conjunctiva. Overall, greater than 90% total body surface area was denuded or Nikolsky positive.

Initial laboratory analysis found severe lactic acidosis, anemia (hemoglobin, 5.3g/dL) and thrombocytopenia (platelets, $42 \times 10^9/L$). She was coagulopathic with international normalized ratio of 1.3, prothrombin time of 15.1, and partial thromboplastin time of 60.5. Protein S level was decreased (27%, ref 63%-126%).

Imaging found a right femoral vein deep venous thrombosis and multifocal renal cortical infarctions on computed tomography scan. She was started on IV methylprednisolone and continuous renal replacement therapy. A transthoracic echocardiogram showed mitral valve thickening, which was thought to be noninfectious, so ciprofloxacin, gentamycin, and vancomycin were started for potential infectious endocarditis. She was started on prophylactic heparin.



Fig 3. Clinical photograph. Right leg with dusky patches in a reticulate pattern.

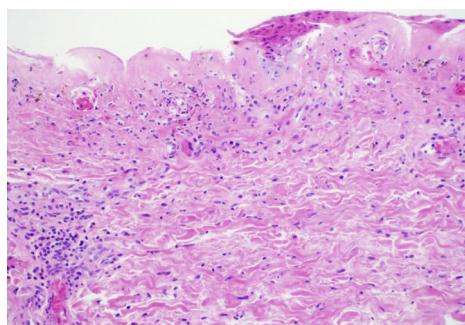


Fig 4. Histologic picture. Biopsy shows epidermal necrosis and detachment, with thrombi occluding papillary dermal vessels. (Hematoxylin-eosin stain; original magnification: $\times 200$.)

Biopsy of the right shin found full-thickness epidermal necrosis with microvascular thrombi (Fig 4), and additional samples showed resolving interface dermatitis. A thrombotic vasculopathy in the setting of an acute SLE flare was favored based on the pathologic findings.

Because of concern for catastrophic anti-phospholipid antibody syndrome or an acute lupus flare, she was started on plasma exchange and IVIg and mycophenolate mofetil. Anticardiolipin, anti- $\beta 2$ glycoprotein I, and antiphosphatidylserine antibodies were negative. A fever and ventilator-associated pneumonia developed with increasing ventilator requirements. Ultimately, vancomycin-resistant *Enterococcus* bacteremia developed, and the family elected to withdraw life-sustaining therapies.

Autopsy determined cause of death as refractory hypotension secondary to third spacing from massive fluid losses from toxic epidermal necrolysis involving more than 90% total body surface area. She was also found to have acute hemorrhagic pancreatitis with extensive necrosis and fat necrosis along her bowel mesentery and omentum.

DISCUSSION

This patient with a history of SLE presented with a widespread vesiculobullous dermatitis and elements of both coagulopathy and hypercoagulability. She initially presented with an anti-nuclear antibody-like syndrome at the outside hospital, and received treatment with multiple antimicrobial drugs including amphotericin B, piperacillin/tazobactam, and cefazolin, a known potential inducer of TEN.^{5,6} She subsequently had Nikolsky-positive lesions and denudation encompassing more than 90% total body surface area. Her lower extremity livedo reticularis was consistent with an SLE exacerbation and potential antiphospholipid antibody syndrome.⁷ Her development of multiple thrombotic events including renal infarctions, ischemic leg requiring amputation, deep venous thrombosis, and microvascular thrombi on biopsy were consistent with a thrombotic storm.⁸ In the reported cases of TEN-like SLE, corticosteroids, IVIg and wound care are described as the cornerstones of treatment.² Most of these reported patients survive and enter remission. In this patient, the severity at initial presentation and critical status at time of transfer to our facility likely caused her lack of response to treatment and ultimate outcome.

The complex presentation, pathologic findings, and disease course in this patient favor the combination of ASAP with a thrombotic storm.^{2,9} ASAP encompasses both drug-induced TEN and TEN-like SLE, which have near-identical presentations and

histologic changes characterized by full-thickness epidermal necrosis. We report this case to bring awareness to the complex presentation and rapid progression of ASAP in the presence of concurrent severe hypercoagulability.

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