Case Report

Sarcoma-associated lichen planus–like paraneoplastic autoimmune multiorgan syndrome with colonic perforation

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Introduction
Paraneoplastic pemphigus (PNP) is a rare autoimmune mucocutaneous disorder of interkeratinocyte adhesion, associated with malignancies. Its polymorphic eruptions are thought to be mediated by anti-plakin and anti-desmoglein autoantibodies that interrupt epidermal cell adhesion, resulting in acantholysis.

Although the initial description of PNP focused on the polymorphic mucocutaneous pathology, the term paraneoplastic autoimmune multiorgan syndrome (PAMS) was established to highlight the systemic involvement of this disease. Respiratory compromise is the most well-described extracutaneous manifestation, and epithelia of the eyes, skeletal muscle, and myocardium can be affected. Gastrointestinal (GI) manifestations have rarely been reported in association with PNP/PAMS. Here we describe a case of sarcoma-associated PAMS with colonic perforation, which, to the best of our knowledge, has not been reported previously.

Case Report
A 68-year-old woman with history of asthma and newly diagnosed poorly differentiated sarcoma with immunohistochemical features suggestive of follicular dendritic cell sarcoma, was admitted with cough, dyspnea, and a diffuse eruption with oral mucosal involvement.

On examination, she appeared alert and oriented. The conjunctivae were injected, and eyelid edema was observed. Lung examination was notable for diffusely diminished breath sounds. Skin inspection revealed hemorrhagic crusting of her lips, erosions in the oral mucosa, numerous lichenoid papules and plaques spread diffusely across the extremities and torso, scalp scaling, and various erosions and bullae on her back, neck, thighs. There was blister extension with pressure over pre-existing bullae and bulla formation with lateral pressure of perilesional skin (ie, positive Asboe-Hansen and Nikolsky signs). Ophthalmic consultation and evaluation identified a corneal epithelial defect.

She underwent skin biopsy, and serologic testing. Histology demonstrated suprabasilar acantholysis (Fig 4), keratinocyte necrosis, and lichenoid infiltrate. A PNP panel was anti-desmoglein 3 IgG+. Indirect immunofluorescence on rat bladder substrate was positive at 1:320, and indirect immunofluorescence on mouse bladder substrate was positive at 1:80, whereas anti–desmoglein 1 IgG antibody was undetectable. Indirect immunofluorescence showed IgG+ cell surface reactivity with monkey esophagus substrates, but negative IgG antibody reactivity on rodent (both rat and mouse) colon tissues.

In view of the clinical, histopathologic, and serologic studies, she was diagnosed with PAMS. Her hospital course was complicated by respiratory failure requiring mechanical ventilation. Chest...
computed tomography findings showed background mosaic attenuation of the parenchyma consistent with small airway disease. After extubation, she continued to struggle with episodes of respiratory distress, ultimately becoming dependent on noninvasive positive pressure ventilation.

Bulbar weakness was present, with dysphagia and poor diaphragmatic excursion. Muscle biopsy indicated a necrotizing myopathy. A comprehensive myositis panel was negative.

A month into her admission, she developed abdominal pain with radiographic findings of pneumoperitoneum. An exploratory laparotomy showed sigmoid perforation with dense inflammatory adhesions between the sigmoid and vaginal cuff/pelvic wall. A sigmoidectomy was performed.

Gross pathology of the excised colon showed a tan-pink mucosal surface with a normal folding pattern consistent with intact diverticula measuring

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**Fig 1.** A and B, The eruption of the hands with papulosquamous phenotype with a lichenoid hue and scale.

**Fig 2.** Labial mucosa involvement with hemorrhagic crusting. The patient was intubated due to respiratory failure.

**Fig 3.** Erythematous rash on the legs, highlighting the polymorphous appearance of the skin eruption. These areas subsequently underwent sloughing.
0.7 cm in greatest depth; no perforated diverticula were seen.

She was treated with 1 g of intravenous methylprednisolone daily for 3 days, intravenous immunoglobulin at the dose of 1 g per day for 2 consecutive days, and 1 g of intravenous rituximab once. She did not respond to the treatment, and due to her grave prognosis, the family subsequently chose to pursue comfort care. The patient unfortunately expired.

**DISCUSSION**

PAMS is a rare autoimmune disease characterized by mucocutaneous abnormalities and lichenoid eruptions.\(^1,6\) Our patient had extensive scaly, flat, lichenoid plaques, and would be classified under the lichen planus-like category of PNP, according to the classification by Nguyen et al.\(^7\)

Beyond the classic mucocutaneous involvement of PNP, our patient demonstrated signs and symptoms of PAMS complications with involvement of the lungs, eyes, muscle, and GI system.\(^3,8\)

GI in PNP has been described in the literature, and the pathophysiology is consistent with epithelium deposition of autoantibodies and complement.\(^1,5,7,9,10\) It is unknown whether cellular immunity contributes to the development of these lesions. Miida et al.\(^5\) reported a case of PNP with colonic erosions, histologically characterized by isolated complement deposition. In our case, we were unable to test for complements, since we did not have tissue stored in the medium required for this testing. The sensitivity and specificity of immunofluorescence reactive to GI mucosa should be further evaluated, with development of more standardized testing.

A similar entity to PAMS, the thymoma-associated autoimmune multiorgan syndrome, characterized by a graft versus host disease-type skin reaction, has been associated with a range of GI manifestations involving mostly colonic pathology or enteropathy.\(^11\)

Our patient is uncommon for multiple reasons. Cases of PNP/PAMS associated with solid tumors and sarcomas are rare in the literature. PNP/PAMS is primarily related to hematologic malignancies.\(^9\) In addition, this is a rare case of colonic perforation related to PAMS. The cases associated with paraneoplastic enteropathy that we identified in the literature involved patients with thymoma-associated autoimmune multiorgan syndrome, and specifically with graft versus host disease-like skin phenotype.

In summary, PAMS is a rare paraneoplastic systemic autoimmune disease defined by mucocutaneous involvement, blisters, erosions, and lichenoid eruptions, with specific histopathologic and immunohistochemical findings.\(^12\) The full scope of its involvement in different organ systems is still being studied. Currently, there is no standardized testing available against rodent colon for PNP patients. Current treatment options rely on immunosuppression and use of immunotherapy. However, despite aggressive therapy, many of these patients are refractory to treatment and succumb to sepsis, multiorgan failure, and respiratory failure, as did our patient.\(^10\)

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**Conflicts of interest**

None disclosed.

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