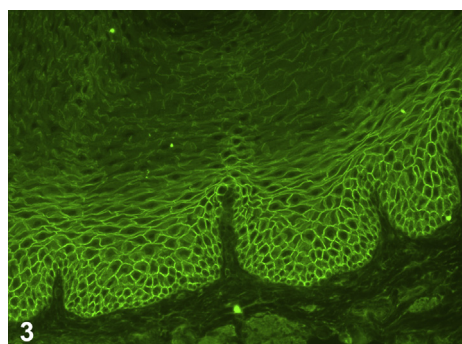
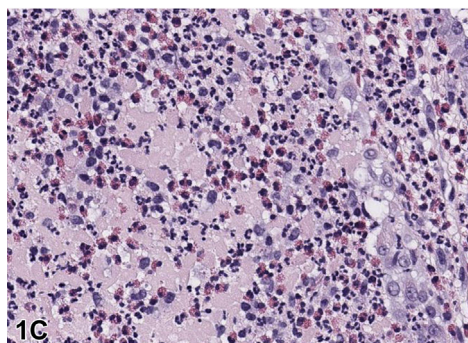
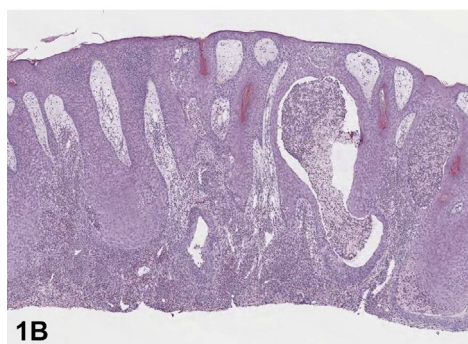


Conjunctivitis, mucosal erosions, and moist cutaneous plaques



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A 25-year-old man with juvenile myoclonic epilepsy presented to the emergency department with a fever and 2-month history of recurrent painful mouth sores. A review of systems obtained from his mother was notable for weight loss, eye irritation, and an uncharacteristically wide-based gait. The physical examination found conjunctival injection, erosions on the labial and buccal mucosa, and moist malodorous exophytic periumbilical (Fig 1, A) and inguinal (Fig 2) plaques. Comprehensive metabolic panel and complete blood count were unremarkable; HIV screen was negative. The results of histopathologic examination of the periumbilical plaque are shown in Fig 1, B and C.

Question 1: What is the most likely diagnosis?

- A. Secondary syphilis
- B. Pyoderma gangrenosum
- C. Pyodermatitis-pyostomatitis vegetans
- D. Pemphigus vegetans
- E. Herpes simplex virus infection

Answers:

A. Secondary syphilis — Incorrect. Secondary syphilis is caused by the spirochete *Treponema pallidum*. It typically presents 1 to 3 months after the appearance of the primary chancre and is characterized by a generalized papulosquamous rash. Condyloma lata, moist exophytic plaques containing spirochetes, may develop in the oral and anogenital regions.

B. Pyoderma gangrenosum — Incorrect. Pyoderma gangrenosum is a neutrophilic dermatosis associated with a variety of systemic disorders including inflammatory bowel disease, arthritis, and blood dyscrasias. The classic lesion starts as a painful papule, pustule, or nodule that ulcerates with a violaceous undermined border. A rare superficial vegetative form of pyoderma gangrenosum has been described.

C. Pyodermatitis-pyostomatitis vegetans — Incorrect. Pyodermatitis-pyostomatitis vegetans, associated with inflammatory bowel disease, is characterized by sterile pustules on edematous mucosa that rupture to form “snail track” erosions. Pustules and brown annular vegetating plaques may develop on the skin, particularly overlying intertriginous areas.

D. Pemphigus vegetans — Correct. Pemphigus vegetans is the rarest variant of pemphigus vulgaris, an autoimmune bullous disease of the mucous membranes and skin characterized by IgG autoantibodies against the keratinocyte adhesion protein desmoglein (DSG) 3.¹ It is clinically divided into the Neumann type, with extensive often intertriginous vegetations overlying blisters and erosions as

observed in this case, and the relatively benign Hallopeau type, with grouped or annular pustules progressing to verrucous cobblestoned plaques.²

E. Herpes simplex virus infection — Incorrect. Herpes simplex virus infection may be primary or recurrent. The classic presentation is umbilicated vesicles in the orolabial or anogenital regions that rupture to form painful ulcerations. The exophytic lesions of herpes simplex vegetans, a variant associated with immunodeficient states, can mimic verrucous carcinoma.

Question 2: Which of the following is an appropriate test to confirm the diagnosis?

- A. Direct fluorescence antigen testing
- B. Rapid plasma reagin
- C. Direct immunofluorescence (DIF)
- D. Endoscopy
- E. Fluorescent treponemal antibody absorption test

Answers:

A. Direct fluorescence antigen testing — Incorrect. Direct fluorescence antigen testing is a diagnostic test for herpes simplex virus and varicella zoster virus. Immunofluorescence analysis is performed on cells obtained by vigorously scraping the base of a vesicle.

B. Rapid plasma reagin — Incorrect. Rapid plasma reagin is a nontreponemal test used to screen for syphilis and monitor response to treatment.

C. DIF — Correct. DIF of a perilesional biopsy specimen can be performed to distinguish pemphigus vegetans from its histologic mimic pyodermatitis-pyostomatitis vegetans. Characteristic features on light microscopy include acantholysis, intraepidermal eosinophilic microabscesses, epithelial hyperplasia, papillomatosis, spongiosis, acanthosis, and eosinophilic infiltrates in the dermis.¹ DIF commonly shows IgG and complement protein 3 on the cell surface of keratinocytes. Variations reported in the literature include a linear immunofluorescence pattern and IgA deposits.

Alternatively, the diagnosis may be confirmed with detection of circulating DSG3 autoantibodies via indirect immunofluorescence or enzyme-linked immunosorbent assay performed on serum. Autoantibodies against DSG1, desmocollins, and periplakin have been reported.^{1,3} Both indirect immunofluorescence on monkey esophagus (Fig 3) and enzyme-linked immunosorbent assay to DSG3 and DSG1 were positive in this case.

D. Endoscopy – Incorrect. Endoscopy combined with histopathologic examination of the gastrointestinal tract is useful in the diagnosis of inflammatory bowel disease. Its utility as a screening tool may especially benefit patients with pyoderma gangrenosum and pyodermatitis-pyostomatitis vegetans.

E. Fluorescent treponemal antibody absorption test – Incorrect. Fluorescent treponemal antibody absorption test is used to diagnose syphilis. It is a treponemal-specific test that remains positive after curative therapy.

Question 3: What is the most appropriate initial therapy?

- A. Benzathine penicillin G
- B. Systemic corticosteroids
- C. Angiotensin-converting enzyme inhibitors
- D. Acyclovir
- E. Carbon dioxide laser

Answers:

A. Benzathine penicillin G – Incorrect. Benzathine penicillin G is an antibiotic recommended by the Centers for Disease Control and Prevention as the treatment of choice for non-penicillin-allergic adults with syphilis.

B. Systemic corticosteroids – Correct. Systemic corticosteroids are the mainstay of treatment for pemphigus vegetans, although topical or intralésional corticosteroids may be sufficient in mild cases. Other agents reported in the literature include immunosuppressants such as azathioprine, cyclophosphamide, cyclosporine, methotrexate, and mycophenolate mofetil; immunomodulators such as extracorporeal photopheresis, intravenous immune globulin, rituximab, and tumor necrosis

factor- α inhibitors; anti-inflammatories such as dapsone and tetracycline antibiotics; and retinoids such as acitretin and etretinate.^{1,4} Attention to nutrition and wound care is important. Given the potential for morbid and even fatal infectious complications, antibiotic therapy is often indicated.¹ This patient experienced resolution of his lesions with a combination of prednisone and rituximab.

C. Angiotensin-converting enzyme inhibitors – Incorrect. Angiotensin-converting enzyme inhibitors have not shown efficacy in the treatment of pemphigus vegetans. In fact, captopril was the first medication reported to induce this disorder. The mechanism is unclear; however, like penicillamine, it contains a sulfhydryl group capable of reacting with components of the keratinocyte membrane. Drug binding is hypothesized to produce acantholytic lesions through direct toxic or antibody-mediated effects.⁵ Pemphigus vegetans has also been reported in association with illicit drug use.²

D. Acyclovir – Incorrect. Acyclovir is a systemic antiviral agent used in the treatment of herpes simplex virus infections. It is also used for daily suppressive therapy.

E. Carbon dioxide laser – Incorrect. Carbon dioxide laser would not be the most appropriate initial therapy for pemphigus vegetans; however, it has been reported as a successful treatment for recalcitrant lesions.⁴

Abbreviations used:

DIF: direct immunofluorescence
DSG: desmoglein

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