Oral, periorbital, and inguinal purpura in a patient with paraproteinemia

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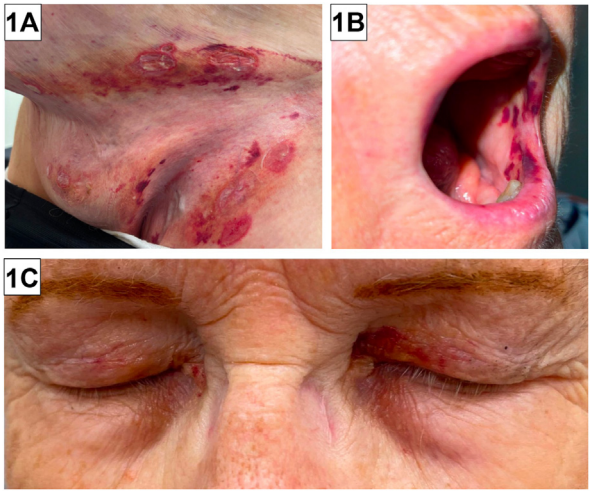

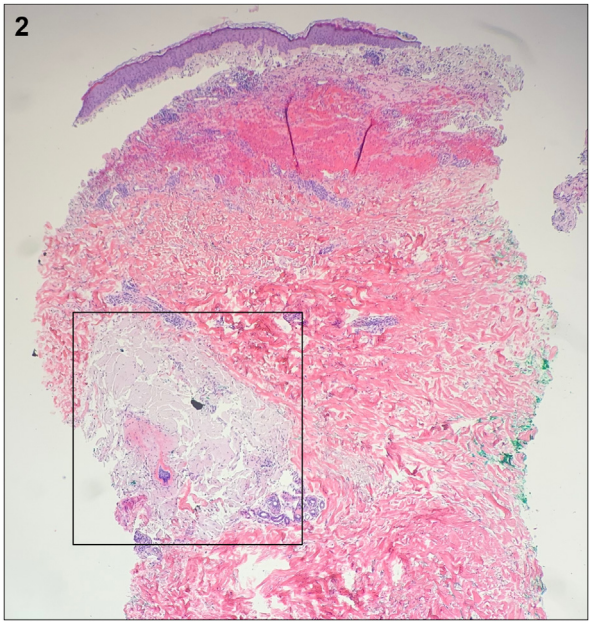

CASE DESCRIPTION

An 82-year-old female presented to dermatology clinic with "blood blisters" for 7 months. She reported associated painful abdominal and inguinal bruising and erosions (Fig 1, *A*). Pertinent past medical history included a recent diagnosis of monoclonal gammopathy of undetermined significance (MGUS). Physical examination revealed ecchymotic macules and patches involving the buccal mucosa, eyelids, inframammary, and infra-abdominal skin (Fig 1, *B* and *C*). Serology for desmoglein 1 and 3, and direct immunofluorescent testing was negative. A punch biopsy of the left inframammary fold was obtained (Fig 2). One month later, she was hospitalized with decompensated diastolic heart failure and elevated NT-proBNP and troponin.

Question 1: What is the most likely diagnosis?

A. Erosive lichen planus

B. Behçet's syndrome

C. Pemphigus vulgaris

D. Systemic AL amyloidosis

E. MGUS with atypical features

Answer:

A. Erosive Lichen Planus — Incorrect. Lichen planus can present as atrophic lesions and ulcers of the skin and oral mucosa that worsen in trauma-prone mucosal areas. However, punch biopsy in this patient did not show the characteristic findings of lichen planus (eg, a lichenoid interface dermatitis).[1]

B. Behçet's syndrome — Incorrect. Behçet's syndrome is an autoimmune, multisystemic disease that presents with oral and genital ulcers and ocular inflammation. However, the diagnosis is dependent on the presence of at least 2 of the 3 described main features along with arthritic symptoms.[2] In this patient's case, there was no genital or ocular involvement and no arthritic symptoms.

C. Pemphigus vulgaris — Incorrect. Pemphigus vulgaris (PV) may also affect the oral mucosa and skin, manifesting as vesicles and bullae evolving into painful erosions. However, this patient's ELISA testing was negative for desmoglein 1 and 3. The histology failed to show suprabasilar acantholysis and direct immunofluorescent testing was negative, making this diagnosis less likely.[2]

D. Systemic AL amyloidosis — Correct. This patient with a history of paraproteinemia (MGUS) and nonhealing inframammary lesions now presenting with oral ulcers, periorbital purpura, and punch biopsy showing dermal amyloid deposition is diagnostic of systemic immunoglobulin light chain (AL) amyloidosis.[3] Diastolic heart failure with elevated BT-proBNP and troponin is associated with shortened life expectancy and poor prognosis.[4] Dermatologists can play a key role in screening for AL amyloidosis as cutaneous manifestations precede other findings in roughly 6% of cases.[5]

E. MGUS with atypical features — Incorrect. MGUS should not be associated with significant systemic or skin findings.

Question 2: Which histologic findings are seen with this diagnosis?

A. Band-like lymphocytic infiltration of the superficial lamina propria with basal cell layer degeneration

B. Suprabasilar acantholysis

C. Pale-pink, hyaline-like material in the papillary and reticular dermis

D. Deep ulceration with perivascular and diffuse inflammation consisting of plasma cells and neutrophils

E. Deep-seated ulceration with a mixed inflammatory infiltrate and proliferating blood vessels

Answer:

A. Band-like lymphocytic infiltration of the superficial lamina propria with basal cell layer degeneration — Incorrect. These features describe oral lichen planus, a T-cell-mediated immune condition

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which can affect the skin and oral, vaginal, and ocular mucosae. Lesions often manifest in friction-prone areas such as the buccal mucosa and lateral tongue and may progress to ulcers.[1]

B. Suprabasilar acantholysis — Incorrect. Acantholysis is a key feature of PV. Indirect immunofluorescence and ELISA can distinguish PV from other immune-modulated vesiculobullous diseases.[1]

C. Pale-pink, hyaline-like material in the papillary and reticular dermis — Correct. Both AL and amyloid transthyretin amyloidosis manifest histologically as pale eosinophilic, amorphous deposition in peripheral tissues with positive Congo Red or Thioflavin T staining.

D. Deep ulceration with perivascular and diffuse inflammation consisting of plasma cells and neutrophils — Incorrect. These nonspecific histologic findings are more consistent with a *Treponema pallidum* chancre. However, diagnosis should be confirmed with *T. pallidum* IgM and IgG antibody tests.[1]

E. Deep-seated ulceration with a mixed inflammatory infiltrate and proliferating blood vessels — Incorrect. Traumatic ulcerative granuloma with stromal eosinophilia most commonly presents in middle-aged adults, affecting the tongue or buccal mucosa. Traumatic ulcerative granuloma with stromal eosinophilia is not associated with systemic amyloidosis.[1]

Question 3: For a patient with light chain paraproteinemia and skin findings suggestive of AL amyloidosis, which diagnostic screening method is most helpful to detect systemic involvement?

A. Abdominal fat pad aspiration

B. Bone marrow biopsy

C. Endomyocardial biopsy

D. Renal biopsy

E. Mass spectroscopy

Answer:

A. Abdominal fat pad aspiration — Correct. For patients with a light chain paraproteinemia and other compatible findings, abdominal fat pad aspiration is 78% to 100% sensitive in detecting systemic AL amyloidosis.[4] The decision to biopsy a visceral organ early is often impractical due to nonspecific presenting symptoms but may be made clinically with a high clinical suspicion of involvement.[4] A biopsy may not be as essential for the diagnosis of amyloid transthyretin amyloidosis, and patients lacking an immunoglobulin paraproteinemia do not require 1.[4]

B. Bone marrow biopsy — Incorrect. Bone marrow biopsy is typically performed after detection of an immunoglobulin light chain abnormality but is more invasive than abdominal fat pad aspiration and has a lower sensitivity (57%). Bone marrow biopsy may be combined with abdominal fat pad aspiration in order to achieve higher sensitivities than abdominal fat pad aspiration alone.[4]

C. Endomyocardial biopsy — Incorrect. Cardiac muscle biopsy is very invasive and can cause significant morbidity. Direct organ biopsy does not demonstrate significantly better sensitivity than abdominal fat pad aspiration and should only be considered if clinical suspicion is very high and fat pad aspiration is thought to be falsely negative.[4]

D. Renal biopsy — Incorrect. Although systemic amyloidosis may affect the kidney causing unexplained proteinuria, direct kidney biopsy is not preferred over abdominal fat pad aspiration.[3]

E. Mass spectroscopy — Incorrect. Mass spectroscopy is not used as an initial diagnostic test for systemic amyloidosis. However, it is utilized after tissue biopsy to guide treatment by identifying the protein subunit responsible for amyloid deposition.

Abbreviations used:

MGUC: monoclonal gammopathy of undetermined significance
PV: pemphigus vulgaris

Conflicts of interest

None disclosed.

REFERENCES

1. Fitzpatrick SG, Cohen DM, Clark AN. Ulcerated lesions of the oral mucosa: clinical and histologic review. *Head Neck Pathol*. 2019;13(1):91-102.
2. Saccucci M, Di Carlo G, Bossù M, Giovarruscio F, Salucci A, Polimeni A. Autoimmune diseases and their manifestations on oral cavity: diagnosis and clinical management. *J Immunol Res*. 2018;2018:6061825.
3. Kelsey A, Smith DH, Meng J, Murphy M, Rothe MJ. Amyloidosis: a story of how inframammary erosions eclipsed inconspicuous periorbital ecchymoses. *Int J Womens Dermatol*. 2016;2(1):18-22.
4. Gertz MA, Dispenzieri A. Systemic amyloidosis recognition, prognosis, and therapy: a systematic review. *JAMA*. 2020;324(1):79-89.
5. Ravindran A, Lackore KA, Glasgow AE, et al. Monoclonal gammopathy of undetermined significance: indications for prediagnostic testing, subsequent diagnoses, and follow-up practice at Mayo Clinic. *Mayo Clin Proc*. 2020;95(5):944-954.