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Immunofluorescence Negative Bullous Pemphigoid in a Hemodialysis Patient with Recurrent Ischemic Stroke

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DESCRIPTION

A 62-year-old male with diabetic nephropathy on maintenance hemodialysis twice weekly with a history of recurrent ischemic stroke in June 2022 and August 2022 presented with right hemiparesis on November 10, 2022. He was on sustained release nifedipine and carvedilol for his blood pressure and received pregabalin for his chronic pruritis. His parathyroid hormone (PTH) in September 2022 was 324 pg/mL. He was advised thrice weekly dialysis in view of persistent pruritis for which the patient did not oblige. On admission, computerized tomography (CT) and magnetic resonance imaging of the brain revealed an acute infarct in the left centrum semiovale. Workups involving causes of recurrent ischemic stroke including cardioembolism, hyperhomocysteinemia, anatomical and prothrombotic workups were negative. After 5 days of hospital admission, the patient developed tense pruritic bullous lesions on the medial aspect of the left leg with non-healing ulcers (Figure 1) followed by involvement of the right leg and upper limbs sequentially. Laboratory examinations revealed hemoglobin: 8.6 g/dL, white blood cells:

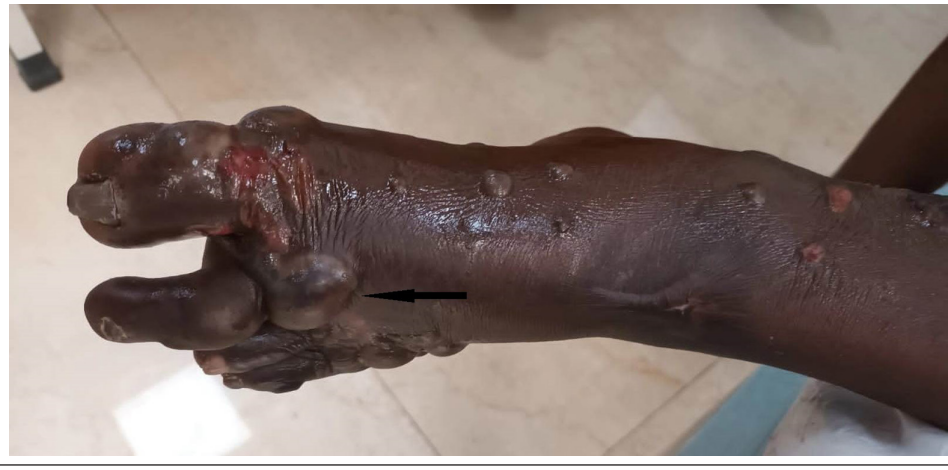

Figure 1. Medial aspect of the left leg showing tense bullous lesions (black arrow) with non-healing ulcers

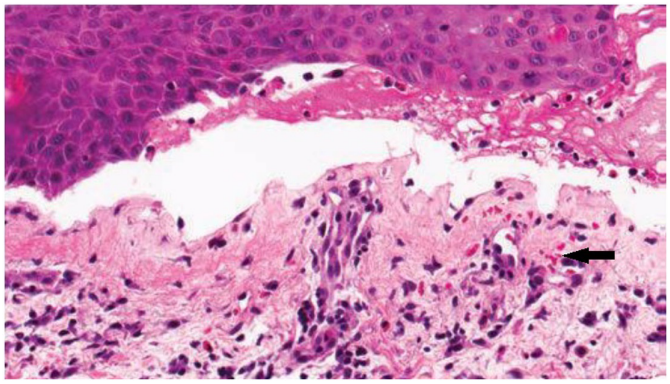

Figure 2. Histopathology of the skin showing subepidermal blisters, associated superficial dermal inflammatory infiltrate with the edge of the blister revealing eosinophils in the papillary dermis (black arrow) with focal extension of inflammatory cells into the spongiotic epidermis.

12 040/mm^3, and platelets: 174 000/mm^3. Peripheral blood smear showed normocytic anemia with neutrophilic leukocytosis without evidence of atypical cells. The dermatologist advised a skin biopsy which revealed subepidermal blisters, associated superficial dermal inflammatory infiltrate with the edge of the blister revealing eosinophils in the papillary dermis (Figure 2), and focal extension of inflammatory cells into the overlying spongiotic epidermis suggestive of bullous pemphigoid. Immunofluorescence did not reveal any significant deposits. Computerized tomography of the thorax and abdomen failed to reveal any obvious solid organ malignancy. After comprehensive discussion, it was decided to start steroids at the dose of 1 mg/kg/day with topical steroids, which resulted in partial clinical resolution of bullae in 3 weeks (Figure 3). The patient was advised to continue low-dose steroids (5 mg prednisolone) beyond 3 weeks with a bimonthly follow-up in the dermatology department.

DISCUSSION

Bullous pemphigoid is an autoimmune blistering dermatosis in hemodialysis patients with an incidence of 2.5-42.8/million in Europe.[1] General risk factors for bullous pemphigoid include cognitive impairments, bipolar disorders, Parkinson's disease, chronic analgesic use, spironolactone use, and a bedridden state.[2] Risk factors in end stage kidney disease for bullous pemphigoid are chronic pruritis, sun exposure, neurological disorders, old age, medications like nifedipine and furosemide, mechanical trauma, and repeated skin injury.[3] Our patient had risk factors like chronic pruritis due to suboptimal dialysis, old age, recurrent cerebrovascular accidents, and nifedipine use for the development of bullous pemphigoid. Recurrent ischemic stroke and bullous pemphigoid may be part of the same autoimmune spectrum probably due to sharing of BPAG-1 antigen expressed by the neurons and Schwann cells of the central nervous system and skin.[4] The progression of atherosclerosis, thrombosis, plaque rupture, and ischemic stroke in bullous pemphigoid may be attributed to endothelial dysfunction and inflammatory markers like interleukin-6, tumor necrosis factor alpha, and soluble E selectin.[5] Bullous pemphigoid may be associated with squamous cell carcinoma of the lung, gastric cancer, and certain hematological conditions like mycosis fungoides[6] highlighting the importance of ruling out internal malignancies in this clinical scenario. Our patient's peripheral blood smear did not reveal any atypical cells, and CT screening of the thorax and abdomen grossly ruled out any solid organ tumors. Our case is unique since the direct immunofluorescence was negative. Possible reasons for negative direct immunofluorescence

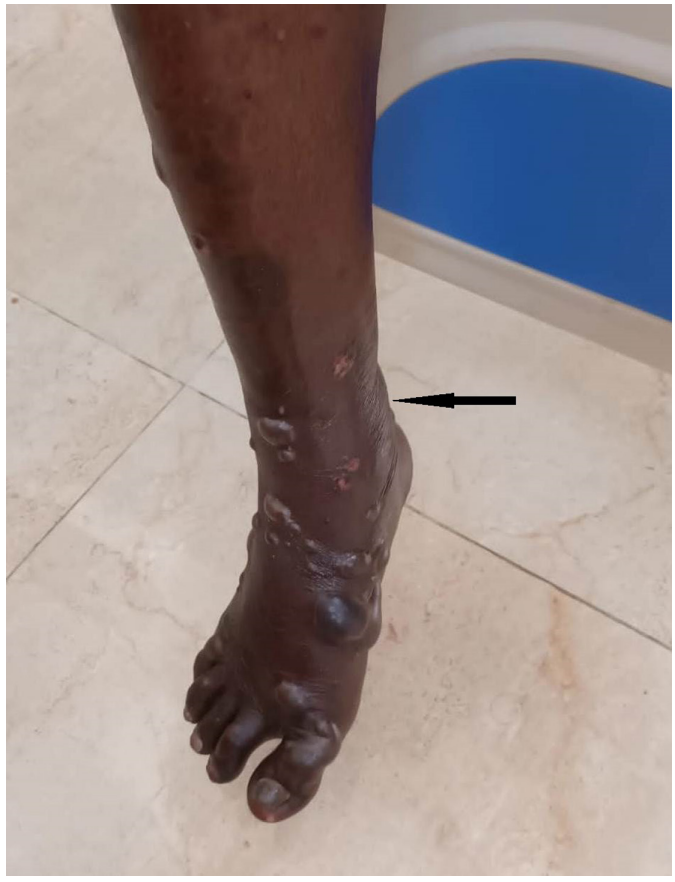

Figure 3. Right leg showing partially healed lesions (black arrow) with few scattered bullous lesions at the end of 3 weeks.

MAIN POINTS

- Bullous pemphigoid is an autoimmune bullous dermatosis in hemodialysis patients possessing risk factors such as old age, neurological disorders, chronic pruritis, and medications like nifedipine.
- Neurological and psychiatric manifestations are commonly associated with bullous pemphigoid.
- Immunofluorescence negative bullous pemphigoid may be due to low immune complex load, sampling error, or use of steroids.
- Prompt histopathological diagnosis and treatment with steroids may result in profound clinical resolution.

include a low antigenic load, sampling error, or use of systemic steroids in treatment.[1] Bullous pemphigoid is a chronic disease process which may require treatment from 4 weeks to 6 months with steroids, azathioprine, methotrexate, or doxycycline.[1,4] Response to treatment is dependent on clinical severity and comorbidities like old age, end-stage renal disease, underlying malignancy, and neurological dysfunction.[1,3,4] Prompt recognition and immediate treatment with topical and systemic steroids will have a profound clinical resolution in bullous pemphigoid.[4]

Ethics Committee Approval: N/A

Informed Consent: Written informed consent was obtained from patient who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – G.G.M.; Design – R.G., G.G.M.; Supervision – S.S., J.V.; Resources – G.G.M.; Materials – R.G.; Data Collection and/or Processing – G.G.M., R.G.; Analysis and/or Interpretation – G.G.M.; Literature Search – G.G.M.; Writing Manuscript – G.G.M., R.G., J.V.; Critical Review – S.S.

Declaration of Interests: The authors have no conflict of interest to declare.

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