Pemphigus vulgaris is an inflammatory mucocutaneous disorder involving autoimmune antibodies directed against adhesion molecules of the epidermis, causing keratinocytes to separate from one another resulting in blister formation. Patients with this debilitating disease often experience painful blistering of the skin as well as the oral mucosa. Multiple studies have shown that patients with pemphigus vulgaris develop deep vein thrombosis, pulmonary embolism, as well as cardiac thrombosis. The pathophysiology of these thromboembolic events has not been fully elucidated. This patient presented with history of pemphigus vulgaris and Hashimoto’s thyroiditis. She developed lower extremity deep vein thrombosis, pulmonary embolism and ischemic strokes despite anticoagulation treatment and inferior vena cava (IVC) filter placement. This case report illustrates several mechanisms for the development of these symptoms, future research opportunities for management and prevention of thromboembolic events and ischemic strokes in these patients with pemphigus vulgaris.

Case Presentation

A 65-year-old female presented with acute swelling and erythema of the left lower extremity, as well as progressive decline in mental status of one month duration. Her past medical history was significant for pemphigus vulgaris and Hashimoto’s thyroiditis. Venous doppler confirmed deep vein thrombosis of the left lower extremity. Patient developed left-sided hemiparesis shortly after admission, which prompted evaluation with MRI brain with contrast, MRA and MRV, which showed acute ischemia in bilateral corona lusum and right cingulate gyr. Radiology suggested vasculitis as a likely cause and ruled-out infection as a cause. Patient developed respiratory failure one day after IVC filter placement, requiring intubation and mechanical ventilation.

CT chest confirmed a large saddle pulmonary embolus while being anti-coagulated. ANA, RF, C-ANCA, P-ANCA, protein C, protein S, lupus anticoagulants, anticardiolipin antibody, anti-fII glycoprotein 1 antibodies, as well as factor V Leiden were found to be negative. There was noted decline in her mental status. Follow-up CT brain and CT angiography studies showed extensive progression of previous ischemic areas, with new areas of ischemia in the left precentral gyr convery. Patient eventually passed away from pulmonary complications.

Discussion

A literature review of multiple studies shows an immunopathological link between pemphigus vulgaris and anti-phospholipid syndrome. There is suggestion that these anti-phospholipid antibodies may be controlled after 3 months of treatment. Therefore, it is possible that the patient in our case had coexisting pemphigus vulgaris and anti-phospholipid syndrome, but anti-phospholipid antibodies were not detected during the time of testing due to a history of prolonged immunosuppression. Cell mediated inflammation and cytokine imbalance may also play an important role in the pathogenesis of pemphigus vulgaris. In this patient, vasculitis has been identified as a likely cause of ischemic strokes. Complement activation may be responsible for the association of pemphigus vulgaris with autoimmune vasculitis. We proposed various mechanisms and possible solutions for the association of pemphigus vulgaris with thromboembolic events and ischemic strokes. Further research is warranted on the exact mechanism.

References