Potential Association Between Pemphigus Vulgaris and Eosinophilic Esophagitis: A Report of Two Cases

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Key Clinical Message

Dysphagia in pemphigus vulgaris (PV) patients should not be attributed solely to PV. Eosinophilic esophagitis (EoE) can coexist and requires endoscopic evaluation and biopsy for accurate diagnosis. Both conditions may share underlying immune mechanisms, emphasizing the importance of precise diagnosis and targeted treatment.

Introduction

Pemphigus vulgaris (PV) and eosinophilic esophagitis (EoE) are autoimmune and immune-mediated disorders, respectively, that impact distinct organ systems[1,2]. PV is characterized by the presence of autoantibodies targeting desmogleins, leading to skin and mucosal blistering[1]. EoE, on the other hand, involves eosinophilic infiltration of the esophageal epithelium, typically associated with allergic conditions[2]. The concurrent presentation of PV and EoE is rare and poses significant diagnostic challenges[3]. This report examines two cases where patients experienced both conditions, highlighting the need for careful differentiation between esophageal involvement by PV and EoE. These cases illustrate the importance of thorough diagnostic workup, including endoscopy and biopsy, to ensure accurate diagnosis and effective treatment.

Case 1:

Case History and Examination: A 47-year-old male patient presented to the emergency department with difficulty swallowing after eating a piece of steak. He reported several episodes of food getting "stuck" in his esophagus. This dysphagia was not associated with any other alarming signs, including weight loss or fever. Four months prior, he was diagnosed with PV after presenting with painful blisters and erosions all over his body following painful oral erosions. At that time, physical examination revealed flaccid bullae and erosions all over his body (Figure 1a), with no genital or ocular lesions, no lymphadenopathy, and no associated systemic signs. PV was confirmed by a skin biopsy revealing suprabasal epidermal acantholysis and direct immunofluorescence showing intercellular deposits of C3 and IgG in the epidermis. He had been treated with oral prednisone at a dosage of 1 mg/kg/day, which was tapered over 4 weeks, leading to full remission with no relapse on follow-up three months later.

Methods: Differential Diagnosis, Investigations, and Treatment The initial differential diagnosis for the patient's current presentation included esophageal involvement by PV and EoE. An urgent upper endoscopy revealed a meat bolus lodged in the mid-esophagus along with esophageal rings and furrows (Figure 1b). Multiple biopsies were taken to rule out esophageal involvement by PV and EoE. Histology showed 20 eosinophils per high-power field with no signs of PV, confirming a diagnosis of EoE.

Results: outcome and follow-up

The patient was restarted on prednisone at a dosage of 0.5 mg/kg per day and maintained on oral proton pump inhibitors (PPI). Three weeks after resuming prednisone, the patient's esophageal symptoms subsided. At a six-month follow-up, there were no signs of relapse of either EoE or PV.

Case 2:

Case History and Examination A 55-year-old male with no significant past medical history presented with a two-month history of difficulty swallowing solid food without any systemic alarming signs. Endoscopy revealed a stenotic gastroesophageal junction, with furrows and a web-like structure observed above it (Figure 2b). Biopsies taken from these areas demonstrated numerous eosinophils, consistent with a diagnosis of eosinophilic esophagitis (EoE). The patient was started on oral steroids at a dosage of 1 mg/kg per day for four weeks, followed by a tapering regimen, which led to significant improvement in his dysphagia. He remained asymptomatic for six months. After this period, the patient sought a dermatology consultation for an acute rash. He presented with flaccid bullae on his chest, back, buttocks, lower legs, and anterior oral mucosa (Figure 2a).

Methods: Differential Diagnosis, Investigations, and Treatment The differential diagnosis for the acute rash included PV and other autoimmune blistering diseases. A skin biopsy and direct immunofluorescence (DIF) confirmed the diagnosis of PV, showing suprabasal epidermal acantholysis and intercellular deposits of C3 and IgG in the epidermis. The patient was initially treated with oral prednisone at a dosage of 1 mg/kg per day for four weeks, followed by a tapering regimen. He was then switched to azathioprine at a dosage of 2 mg/kg per day due to relapse after stopping the systemic steroid.

Results: outcome and follow-up

Ten months later, he experienced a relapse in both EoE and PV upon stopping azathioprine. A decision was made to start him on dupilumab, beginning with a 600 mg loading dose, followed by 300 mg every two weeks. This treatment resulted in full remission of both diseases, and the patient was kept on it as a chronic therapy.

Discussion

The coexistence of PV and EoE in these two cases presents a unique clinical scenario, with only one case report in the medical literature presenting a similar association[3]. highlighting the complexity and interplay of autoimmune diseases. PV is an autoimmune blistering disorder primarily affecting the skin and mucous membranes, while EoE is a chronic immune-mediated esophageal condition characterized by eosinophilic infiltration and esophageal dysfunction, predominantly associated with allergic conditions[1,2]. Both cases underscore the necessity of a thorough and multidisciplinary diagnostic approach when dealing with patients presenting with new or unusual symptoms, particularly in those with known autoimmune conditions. In Case 1, the patient developed dysphagia and esophageal impaction, which necessitated a biopsy to distinguish between esophageal involvement by PV and EoE. In Case 2, the patient initially presented with symptoms of EoE, which were managed successfully, only to later develop PV. The diagnosis of EoE in both cases was confirmed by endoscopic findings and biopsies demonstrating significant eosinophilic infiltration. The presence of both conditions in the same patients suggests a possible shared immunopathogenic mechanism, although the exact pathophysiology remains unclear[3]. The simultaneous occurrence of both conditions is exceptional in the medical literature, and dysphagia in PV patients is often empirically attributed to mucosal involvement of the esophagus by PV[4,5]. The shared pathogenesis of PV and EoE might be linked to the involvement of desmoglein (DSG) proteins, mainly DSG-1[6]. Our findings are consistent with a previously reported case by Gue et al. in 2017 documenting a 13-year-old boy with PV and EoE, emphasizing the possible dysregulation of DSG 1 as a common etiologic factor in both conditions[3]. Eosinophils play a central role in EoE and have also been implicated in the pathogenesis of PV, suggesting a shared pathogenic mechanism[1,2]. The significant improvement in both EoE and PV symptoms in our patient treated with dupilumab, a monoclonal antibody targeting the IL-4 receptor alpha that is FDA-approved for the treatment of EoE and used off-label for recalcitrant PV cases[7–9], suggests that Th2-mediated pathways might be a common underlying mechanism in both diseases[10–12].

Conclusion :

The coexistence of PV and eosinophilic esophagitis EoE in these cases highlights the complex interplay between autoimmune diseases and underscores the necessity of a thorough and multidisciplinary diagnostic approach. Our findings demonstrate that EoE should be considered in PV patients presenting with dysphagia, as it is essential not to attribute such symptoms solely to esophageal involvement by PV. The significant improvement observed in both conditions with the use of dupilumab suggests a shared Th2-mediated pathway, opening new avenues for therapeutic intervention. Further research is needed to elucidate the underlying mechanisms linking PV and EoE.

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Figure legends

Figure 1a: Flaccid bullae and erosions on lower legs and buttocks

Figure 1b: **esophagogastroduodenoscopy revealing impacted food bolus, esophageal rings and furrows.**

Figure 2a: bullae and erosions on the back of the patient

Figure 2b: esophagogastroduodenoscopy revealing a web like structure in the distal esophagus.