CLINICAL VIGNETTE

Esophageal involvement in a Patient with Epidermolysis Bullosa Acquisita

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Epidermolysis Bullosa Acquisita (EBA) is a rare acquired subepithelial mucocutaneous blistering disease that develops in adulthood. The mechanism of the disease involves the production of antibodies against Type VII collagen, which is a main component of anchoring fibrils in the basement membrane zones of skin and mucosa. The immune-mediated disruption of the anchoring fibrils contributes to cleavage within the basement membrane zone and causes clinical blistering. This disease is separate from the inherited genetic process called Recessive Dystrophic Epidermolysis Bullosa, which occurs in infancy.

Clinically, the process affects the skin resulting in the formation of non-inflammatory tense vesicles and bullae that rupture leaving erosions. They commonly occur in areas that are prone to minor trauma. Mucosal involvement is common in classical EBA and can manifest as erosions or adhesions on the oral, nasal, ocular, pharyngeal, laryngeal, esophageal, or anogenital mucosa.

Case Presentation

The patient is a 66-year-old Caucasian male diagnosed with Epidermolysis Bullosa Acquisita in 2009-2010 based on his clinical presentation and skin biopsies. He was given a course of Azathioprine, which put him in remission for approximately 4 years. He had a flare of his disease eight months before he sought consultation for dysphagia. He was initially treated with steroids, which were of minimal effect, and then Dapsone. During this time period, he experienced dysphagia for solid food and lost a total of 30 lbs. His dysphagia was progressive and he found it difficult to eat enough to sustain his weight. A prior gastrointestinal endoscopy in 2011 revealed a normal appearing esophagus with a possible Schatzki Ring, which was not dilated. A repeat endoscopy by an outside physician in 2014 was aborted due to the presence of multiple mucosal blebs in the oral pharynx. He was seen in consultation at UCLA and was referred to a clinical dietitian who placed him on a program of increased caloric intake and supplements and blended solid foods. An esophagram revealed no obvious obstruction, mucosal defect, or stricture in the esophagus. He was noted to have moderate gastroesophageal reflux while supine. His physical exam aside from his multiple areas of skin blistering and scarring was otherwise unremarkable. A repeat endoscopy revealed mucosal blistering and disruption in the posterior pharynx. There was an esophageal stricture just below the cricopharyngeus associated with marked erythema, mucosal fragility and blistering. The scope could not be passed through the stricture. A balloon dilator was used to gently dilate the area of stricture to 9 mm after which the endoscope could be passed through to the duodenum. Biopsies were not taken at that time. Subsequent to the dilation, the patient reported his ability to eat solid food without difficulty for the first time in eight months. He continues to take a Proton Pump Inhibitor to protect his lower esophagus from acid reflux.

Discussion

Epidermolysis Bullosa Acquisita (EBA) is a non-hereditary form of Epidermolysis Bullosa first described in 1895.[1] Prior to the availability of immunofluorescent biopsy analyses, some of the earlier cases described may have been due to Porphyria Cutanea Tarda, pemphigus, or pemphigoid. Esophageal involvement in Epidermolysis Bullosa Acquisita has been described in the literature. In a 2014 report from Japan, three Japanese patients with EBA presented with a 3-5 year history of repetitive bullous skin lesions, healing with mild scars, and milia formation, as well as oral mucosal lesions.[2] In addition, all three patients complained of dysphagia, odynophagia, and heartburn. Gastrointestinal endoscopy showed extensive esophageal erosions as well as stricture and stenosis. Type VII collagen has been shown to be expressed in esophageal mucosa. Patients with EBA frequently present with oral mucosal lesions, but esophageal involvement has been less common. A study from Brazil describes 4 out of 12 patients with EBA and esophageal involvement. Esophageal involvement may be more prevalent than previously reported.[3]

Of interest is the finding that autoantibodies to Type VII collagen are present in the human colon, and patients with Crohn's disease also have autoantibodies to type VII collagen. Inflammatory bowel disease is associated with multiple cutaneous lesions; pyoderma gangrenosum, erythema nodosum, annular erythemas, and vascular thrombosis. EBA is also recognized as an extraintestinal manifestation of IBD. Crohn's disease is the most frequently associated condition with EBA. There are 25 cases reported in an article by Livden et al[4] in 1978. In the article by Chen et al,[5] it was found that 25% of EBA patients have an associated IBD. In 51 patients with EBA, 12 had Crohn's disease and one had ulcerative colitis. Full length Type VII collagen was detectable in colonic mucosa using western blotting; Type VII collagen was also found in human colonic basement membrane.

Esophageal dilation is rarely mentioned in the literature. In the paper by De Angelis et al,[6] 34 patients underwent balloon dilation for EBA associated esophageal stricture. Ninety-three dilations were performed. Complications included cervical esophageal perforation and transitory dysphagia. Thirty patients were feeding within 24 hours. Most of these procedures were done with fluoroscopically guided balloon dilation without endoscopy. In the paper by Alshammari et al,[7] seven children with Epidermolysis Bullosa and esophageal stricture were dilated with endoscopic balloons. All were successful with no complications.

Summary

We described a patient with established EBA with associated esophageal involvement and stricturing of the proximal esophagus. Esophageal involvement is relatively rare in EBA and should be a recognized complication in patients with EBA who present with dysphagia. Though the literature is limited, strictures in EBA can be treated cautiously with balloon dilation with a good clinical response. EBA is associated with development of autoantibodies to Type VII collagen, which is also seen in Crohn's disease and coexisting Crohn's disease should be considered in patients with typical symptoms and a diagnosis of EBA.

REFERENCES

1. **Elliott GT**. Two cases of epidermolysis bullosa. *J cutan Genitourin Dis*. 1895;13:10
2. **Ishii N, Furumura M, Hamada T, Mori O, Ohzono A, Ueda A, Karashima T, Nakama T, Tsuruta D, Takedatsu H, Fujita H, Hashimoto T**. Oesophageal involvement in epidermolysis bullosa acquisita. *Br J Dermatol*. 2015 Jan;172(1):288-90. doi: 10.1111/bjd.13224. Epub 2014 Nov 19. PubMed PMID: 24975454.
3. **Delgado L, Aoki V, Santi C, Gabbi T, Sotto M, Maruta C**. Clinical and immunopathological evaluation of epidermolysis bullosa acquisita. *Clin Exp Dermatol*. 2011 Jan;36(1):12-8. doi: 10.1111/j.1365-2230.2010.03845.x. PubMed PMID: 20456382.
4. **Livden JK, Nilsen R, Thunold S, Schjønsby H**. Epidermolysis bullosa acquisita and Crohn's disease. *Acta Derm Venereol*. 1978;58(3):241-4. PubMed PMID: 78639.
5. **Chen M, O'Toole EA, Sanghavi J, Mahmud N, Kelleher D, Weir D, Fairley JA, Woodley DT**. The epidermolysis bullosa acquisita antigen (type VII collagen) is present in human colon and patients with crohn's disease have autoantibodies to type VII collagen. *J Invest Dermatol*. 2002 Jun;118(6):1059-64. PubMed PMID:12060403.
6. **De Angelis P, Caldaro T, Torroni F, Romeo E, Foschia F, di Abriola GF, Rea F, El Hachem M, Genovese E, D'Alessandro S, Dall'Oglio L**. Esophageal stenosis in epidermolysis bullosum: a challenge for the endoscopist. *J Pediatr Surg*. 2011 May;46(5):842-7. doi: 10.1016/j.jpedsurg.2011.02.017. PubMed PMID: 21616238.
7. **Alshammari J, Quesnel S, Pierrot S, Couloigner V**. Endoscopic balloon dilatation of esophageal strictures in children. *Int J Pediatr Otorhinolaryngol*. 2011 Nov;75(11):1376-9. doi: 10.1016/j.ijporl.2011.07.031. Epub 2011 Sep 1. PubMed PMID: 21889217.

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