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Can esophageal dilation be avoided in the treatment of severe esophageal stricture caused by eosinophilic esophagitis?

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Summary

Eosinophilic esophagitis (EoE) is an inflammatory immune-mediated disease with predominant eosinophilic inflammation characterized by the presence of esophageal dysfunction symptoms. Treatment delay can be associated with disease complications, like esophageal strictures, that can justify the use of invasive procedures which are not deprived of side effects. We present a case report of a 14 year old child with severe esophageal stricture secondary to EoE, that was treated with topical and systemic corticosteroid before any invasive procedure was considered. After 26 weeks of medical treatment, significant improvement of esophageal dysfunction occurred with histological remission and stricture resolution. In patients with severe esophageal strictures secondary to EoE, the need for esophageal dilation procedures should be considered only after anti-inflammatory treatment.

Introduction

In the last decade, eosinophilic esophagitis (EoE) has been increasingly recognized in clinical practice (1,2). This is an inflammatory immune-mediated condition, with an eosinophilic-predominant inflammatory infiltration, characterized by esophageal dysfunction symptoms (2,3). EoE is also considered an antigen driven disease (4). Food allergens play an important role in pathogenesis of the disease, but aeroallergens have also been implicated as co-factors contributing to the development of EoE (5). Since 2007, two consensuses have been performed concerning its diagnosis and treatment (2,6), and recently an evidenced based approach was used to assess the strength of these recommendations (3). This chronic disease, presenting with persistent and relapsing symptoms (2), differs in clinical presentation accordingly to age. Diagnosis is challenging particularly in children, which can lead to a diagnostic delay that reached up to 6 years in some cohorts (7). In a recently published large retrospective, cohort of patients with eosinophilic esophagitis, the likelihood of a fibrostenotic disease, defined by the presence of esophageal rings, narrowing or strictures, doubled for every 10 years in age increase (8). This is probably dependent on the persistent inflammatory nature of the disease followed by the appearance of fibrosis, if no anti-inflammatory measures are initiated (7). The main treatment of EoE are corticosteroid, as well as dietary intervention indicated in some pa-

tients, namely an elemental diet, an allergy testing-directed elimination diet or an empirical six-food elimination diet (3,9,10). Furthermore, acid suppression by proton pump inhibitors is a concomitant approach, not only useful for diagnostic purposes but also to reduce symptoms (3,11). Esophageal dilation can also be used to provide immediate relief of dysphagia caused by strictures (3,11,12). However, it is an emergency treatment not deprived of side effects, namely esophageal mucosal tears, hemorrhage, perforation and hospitalization due to chest pain after the procedure (2,11,13). We present a case report addressing the medical management as first line treatment of a severe esophageal stricture in an adolescent with eosinophilic esophagitis.

Case Report

The patient, a 14 year old male, with personal history of mild persistent allergic rhinitis previously diagnosed by an allergist, had a history of sensitization to house dust mites, grass and plantago pollen, dog epithelium and *Alternaria* spp. Rhinitis symptoms were treated with oral anti-histamines as rescue medication. The patient started dysphagia complaints in the last two years, especially for solid food, reporting one episode of esophageal food impaction with need of medical care in 2011. These complaints were not exacerbated during pollen season and did not correlate with rhinitis symptoms exacerbations. On March 2013 the patient reached medical care because of an increase of frequency (2 to 3 times/week) and severity of the dysphagia in the previous month, sometimes followed by vomits. Neither weight nor appetite loss was reported. During anamnesis the patient didn't report relation of symptoms with a specific food. The patient had a family history of food allergy (his sister had severe persistent milk allergy).

Upper gastrointestinal endoscopy revealed in the proximal esophagus a circular ring appearance with few linear furrowing and scattered white plaques. A proximal stricture was present at 25 cm from the upper incisor teeth, and passage with an ultra-slim videogastroscope (5.9 mm) was impossible due to lumen narrowing and esophageal mucosa retraction (**figure 1.a**). Biopsies were performed at the esophagus proximal third and four fragments were obtained that showed a dense eosinophilic infiltrate (≥ 50 eosinophils (eos)/high power field (HPF)) and multiple microabscesses. Barium contrast radiography identified a well defined and regular narrowing of all esophagus with a significant decrease of the caliber in the upper third **(figure 2)**. The allergy diagnostic work-up revealed an elevated peripheral blood eosinophilia (1210/mm^3), elevated serum total IgE (957.0 UI/ml). Sensitization to aeroallergens was evaluated by skin prick tests, which were positive to house dust mites, grass and plantago pollen, dog epithelium and *Alternaria* spp. (aeroallergen skin prick test panel included *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae, Lepidoglyphus destructor, Blomia tropicalis,* grass pollen mixture*, Chenopodium, Olea europaea,* dog and cat epithelium*, Salsola, Parietaria judaica, Plantago, Artemisia vulgaris,* cypress*, platanus and Alternaria* spp.; Bial-Aristegui (Bilbao, Spain)). Food sensitization was studied through skin prick tests (allergen extracts provided by Bial-Aristegui (Bilbao, Spain); ≥ 3mm wheal size was regarded as positive) and serum specific IgE (sIgE) including milk, egg, soy, cereals, fish, seafood, nuts and seeds (UniCAP®, Thermo Fisher Scientific, Uppsala, Sweden). The patient showed sensitization to sesame and sunflower seed through skin testing and specific IgE (sesame 2.07 kU/L; sunflower 1.10 kU/L). Specific IgE were positive to milk (1.35 kU/L) and milk proteins (α-lactalbumin 1.23 kU/L; β-lactoglobulin 1.23 kU/L; casein 0.55 kU/L), cereals (wheat 2.36 kU/L; corn 0.50kU/L; rye 1.86kU/L; barley 2.49 kU/L and oatmeal 2.03 kU/L), nuts (almond 0.57 kU/L; walnut 0.53 kU/L) peanut 1.85 kU/L and mollusks (squid 1.54 kU/L; snail 1.11 kU/L). The patient started treatment with a course of oral corticosteroids (prednisolone) during 1 month, associated with topical fluticasone (1000 µg/day), montelukast (10 mg/day). Esomeprazol (40 mg/day) previously started after the first endoscopy was kept. An allergy testing-directed elimination diet to sesame and sunflower seeds was also recommended. Six weeks after treatment, reassessment showed clinical improvement. Endoscopy, performed after a 2-month course of proton pump inhibitors treatment, still maintained circular ring pattern with few longitudinal furrowing and white exudates plaques but the stricture was now traversed by the ultra-slim videogastroscope (**figure 1.b**). Biopsies were performed on the upper, medial and distal esophagus, stomach and duodenum (2 fragments obtained from each location). Histopathology showed, in all the esophageal segments, infiltration by eosinophils (> 25 eos/HPF) and microabscesses. Treatment with topical corticosteroid, montelukast and proton pump inhibitor was kept for more 20 weeks. Eviction diet continued to be recommended, but was not strictly followed by the patient. After 26 weeks of treatment, food impaction or dysphagia symptoms ceased and in the upper digestive endoscopy no esophageal narrowing or stricture was observed, esophageal mucosa was normal and an 8.8 mm diameter videogastroscope progressed easily (**figure 1.c**). Histopathology analysis of the esophagus found rare eosinophils in the mucosa, both in the proximal and distal thirds. Topical corticosteroid was maintained and clinical and histological remission was kept after one year of clinical and endoscopic follow-up.

Figure 1 *- Endoscopic evaluation of esophageal stricture evolution.* **a.** *First endoscopy: proximal esophagus, presenting scattered white plaques, a stricture unsurpassable by an ultra-slim videogastroscope (5.9 mm);* **b.** *Six weeks treatment follow-up endoscopy: proximal esophagus, circular ring aspect with fewer white exudates plaques, stricture was now overpassed by ultra-slim videogastroscope (5.9 mm);* **c**. *Follow-up endoscopy after 26 weeks of treatment: proximal esophagus with normal mucosa, without esophageal narrowing, performed with a videogastroscope (8.8 mm).*

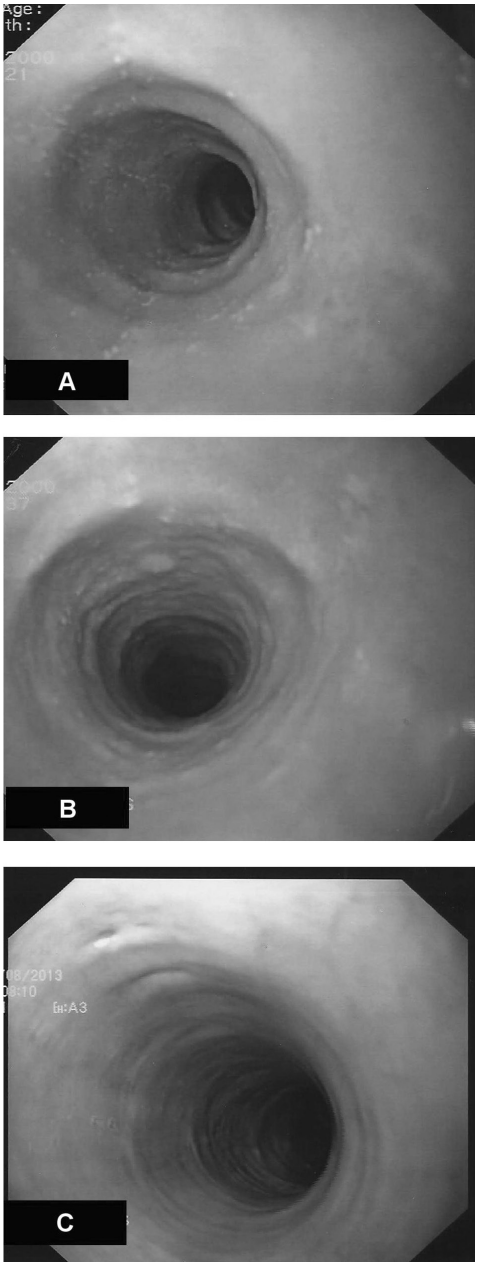
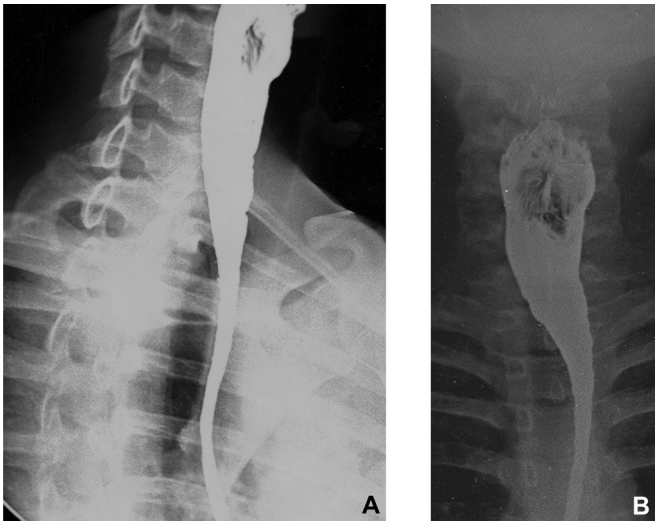


Figure 2 *- Barium esophagogram showing limited esophageal distensability with smooth tapering and concentric regular and well defined narrowing in the upper third of the esophagus.* **a.** *Upright left posterior oblique view;* **b.** *Anteroposterior view.*



Discussion

In this case report a severe esophageal stricture due to eosinophilic esophagitis was completely resolved in 26 weeks with only medical treatment, avoiding mechanical dilation procedures and their inherent risks.

The prominent esophageal eosinophilia that characterizes EoE leads to tissue remodeling, namely subepithelial fibrosis and fibrovascular changes, which predisposes to the formation of esophageal rings and strictures and increases tissue frailty (13). Esophageal dilation allows a mechanical immediate relief of symptoms but has no effect on the underlying esophageal eosinophilic inflammation, therefore stricture recurrence can occur (2,10,12). Moreover this procedure is not deprived of risks (13-15). When accessing the rate of complications of a series of 293 dilation sessions, 9% had deep mucosal tears and 1% risk of perforation (16). Furthermore, in a cohort study, 74% of the questioned patients reported retrosternal pain after the procedure (12). A proximal location in the esophagus and dilation of small-diameter strictures were reported to be associated with higher risk of complications (16). Additionally, when esophageal dilation was used in an initial therapeutic approach in a cost analysis model it was found to be more costly than topical corticosteroids (17). The use of steroid therapy as first-line treatment before esophageal dilation can be an option, though no consensus exists regarding how long medical therapy should be performed before resorting to esophageal dilation and there is lack of evidence ascertaining which esophageal strictures will reverse with only pharmacological and/or dietary therapy

(2,3,13). In a fourteen year follow-up study of thirteen adults with steroid-naïve eosinophilic esophagitis treated only with endoscopic dilation and proton pump inhibitor therapy, at least 3.2 dilations were performed during the first year and dilations maintained at every two years (18). By other side, in the Swiss EoE cohort study with 5 year follow-up period, the use of swallowed topical steroids was associated with lower risk for long-term bolus impactions (OR 0.411, 95%-CI 0.203-0.835, p = 0.014) (19). We present an observational evidence of the isolated use of pharmacological treatment in the improvement of esophageal dysfunction, histological remission and severe esophageal stricture resolution. The clinical favorable evolution without the need of an invasive procedure raises the question if, in this predominantly inflammatory driven disease, the need for esophageal dilation procedures could be avoided or delayed. Anti-inflammatory measures, like systemic and topic corticosteroids use, isolated or combined, and proton pump inhibitors can significantly influence the prognosis of the disease, even in its more severe forms (3). Dietary interventions, in a recent systematic review (9), have been shown to be effective in inducing histologic remission, specially with elemental and six-food elimination diets. These results were not consistent for allergy testing-based food elimination (9). Patient adherence to dietary restrictions can be difficult, particularly in older children's and adults (20), as occurred in this case report. Therefore, the use of more specific elimination diets, like four-food elimination diet, that includes the most common food triggers, and allergy testing-based food elimination could be useful for long term adherence and disease control (9,21). Allergy testing, using skin prick test and specific IgE, still have a limited role in detecting a particular antigen precipitating EoE (22). New tools namely complement resolved diagnosis (CRD) could be useful to assess aeroallergen and food sensitization. Recently, two studies (23,24) assessed, in EoE patients cohorts, sensitization to cross-reactive allergens using CRD. They observed two main different cross-reactive patterns of sensitization, one to PR-10 (24) and the other to profilin (23). Indeed, both suggested that pollen and food sensitizations may contribute to esophageal inflammation in EoE patients. Therefore, CRD could provide more insight into sensitization patterns, identify additional food allergen sensitizations and help in targeting allergy-testing directed elimination diet. However, the clinical utility and efficacy of CRD in guiding specific elimination diet is still not settled (24).

This case report enlightens that, in patients with eosinophilic esophagitis complicated with severe strictures, more evidence is needed to fully understand the role of topical corticosteroid treatment and dietary therapy in comparison with esophageal dilation procedures in the clinical and histological remission of the disease.

Conclusion

In patients with esophageal strictures secondary to eosinophilic esophagitis the need for esophageal dilation procedures could be avoided, even in severe strictures, if systemic and topical anti-inflammatory treatment is first implemented. Prospective studies are needed to compare these interventions, considering patient-reported outcomes, complications and long-term follow up to monitor disease relapses.

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