Eosinophilic oesophagitis as a cause of dysphagia and recurrent food impaction in a young male - long way to diagnosis. A case report

Martin Kliment[1], Petr Fojtík[1], Ondřej Urban[1], Aleš Albín[1], David Janík[1], Přemysl Falt[1], Libor Kudělka[2]

[1]Digestive Disease Center, Department of Gastroenterology, Hospital Vítkovice a.s., Ostrava-Vítkovice, Czech Republic
[2]Department of Pathology, PR-LAB s.r.o., Nový Jičín, Czech Rrepublic

Summary

We describe the case of a 32-year-old male with recurrent dysphagia and food impaction caused by eosinophilic oesophagitis. Prior to establishing diagnosis, the patient underwent three oesophagogastroduodenoscopies (EGD) with repeated mucosal biopsies and several diagnoses, e.g. Mallory-Weiss syndrome, gastro-oesophageal reflux disease, were suspected. Despite several mucosal features highly suspicious of being eosinophilic oesophagitis, shown on second EGD, histopathology did not confirm the diagnosis. Histopathologic evaluation of biopsy specimens taken during the third EGD showed eosinophilic infiltration of oesophageal mucosa and confirmed the diagnosis of eosinophilic oesophagitis. The authors conclude that eosinophilic oesophagitis might be a common cause of dysphagia and food impaction in young adults, especially men with associated immunoallergic disorders. This clinical entity is probably underdiagnosed because of the lack of awareness of both endoscopists and pathologists. This might have been the cause of delay of diagnosis in our case, too.

***Key words:** Eosinophilic oesophagitis, dysphagia, food impaction, eosinophil, oesophagogastroduodenoscopy*

Súhrn

Eozinofilná ezofagitída ako príčina dysfágie a opakovaného uviaznutia potravy v pažeráku u mladého muža - dlhá cesta k diagnóze. Kazuistika

Kazuistika popisuje prípad 32-ročného muža s rekurentnou dysfágiou a epizódami uviaznutia potravy v pažeráku, spôsobených eozinofilnou ezofagitídou. Do stanovenia diagnózy pacient podstúpil celkovo tri ezofagogastroduodenoskopie (EGD) s opakovanými biopsiami a bolo vyslovené podozrenie na niekoľko iných ochorení, ako napr. syndróm Mallory-Weiss, gastroezofageálnu refluxnú chorobu. Pri druhej EGD boli prítomné viaceré zmeny sliznice pažeráka podozrivé z eozinofilnej ezofagitídy, diagnóza však nebola histologicky potvrdená. Až histologické vyšetrenie biopsií sliznice pažeráka odobratých počas tretej EGD potvrdilo eozinofilnú ezofagitídu. Autori predpokladajú, že eozinofilná ezofagitída môže byť častou príčinou dysfágie a uviaznutia potravy v pažeráku, hlavne u mladých pacientov s pridruženými alergickými ochoreniami. Toto ochorenie je pravdepodobne poddiagnostikované pre nedostatočnú informovanosť endoskopistov aj patológov. Tento fakt mohol byť príčinou oneskorenej diagnózy aj v popisovanom prípade.

***Kľúčová slova:** eozinofilná ezofagitída, dysfágia, uviaznutie potravy, eozinofil, ezofagogastroduodenoskopia*

Eosinophilic oesophagitis is a chronic inflammatory disorder, characterised by extensive eosinophilic infiltration of oesophageal epithelium without infiltration of other organs in gastrointestinal tract [3,16]. It is a distinct clinico-pathological entity with increasing incidence [1,18,21,22]. Straumann has described increase in the prevalence from 1 to 27 cases per 100 000 inhabitants in one region of Switzerland during the last 16 years [28].

A predisposition of young men with associated immunoallergic disorders has been observed [24]. Pathogenesis of the disease is not clearly understood. It is anticipated that eosinophilic infiltration of oesophageal mucosa might be caused by allergic response to both food and aeroallergens [13,26]. Interleukin-5 and eotaxin, chemotaxin for eosinophils, might play a role in the pathogenesis of the disease [5].

We describe the case of a young man with recurrent dysphagia and food impaction caused by eosinophilic oesophagitis.

CASE REPORT

The patient is a 32-year-old male with two-year history of allergic rhinocon-

junctivitis and positive allergic testing for several aeroallergens. Prior to each pollen season during the years 2001–2003, the patient underwent hyposensitising vaccination with Pollinex Rye vaccine with good effect on the symptoms of allergic rhinoconjunctivitis. Since July 2004, recurrent dysphagia for solids and food impactions have occurred, which lead the patient to undergo the first oesophagogastroduodenoscopy in October 2004. Endoscopy revealed mucosal tear in the gastro-oesophageal junction, which was evaluated by the endoscopist as Mallory-Weiss syndrome. Oesophageal, gastric and duodenal mucosa were normal on endoscopy, as was histopathological evaluation of duodenal mucosa. Since gastro-oesophageal reflux disease was suspected to be the cause of dysphagia, the patient started treatment with omeprazole and cisaprid. The treatment was stopped because of development of toxoallergic exantema after 14 days. Neither dysphagia, nor food impaction had recurred until August 2006, when persisting food impaction developed and the patient underwent the second upper GI endoscopy. The endoscopy revealed impacted bolus of meat in mid-oesophagus. Using a polypectomy snare, the bolus was divided and pushed into the stomach. Thereafter, deep mucosal disruption in mid-oesophagus, 6 cm in length developed (Fig 1). No stricture was observed in the oesophagus. Moreover, the endoscopy showed longitudinal furrows in oesophageal mucosa and concentric mucosal rings throughout the oesophagus (Figs 2 and 3). Gastric and duodenal mucosa were normal on both endoscopy and histopathology. A total of 4 biopsy specimens were taken from both proximal and distal oesophageal mucosa. Histopathology showed dense acute mucosal inflammation with high density of granulocytes and low density of eosinophils,

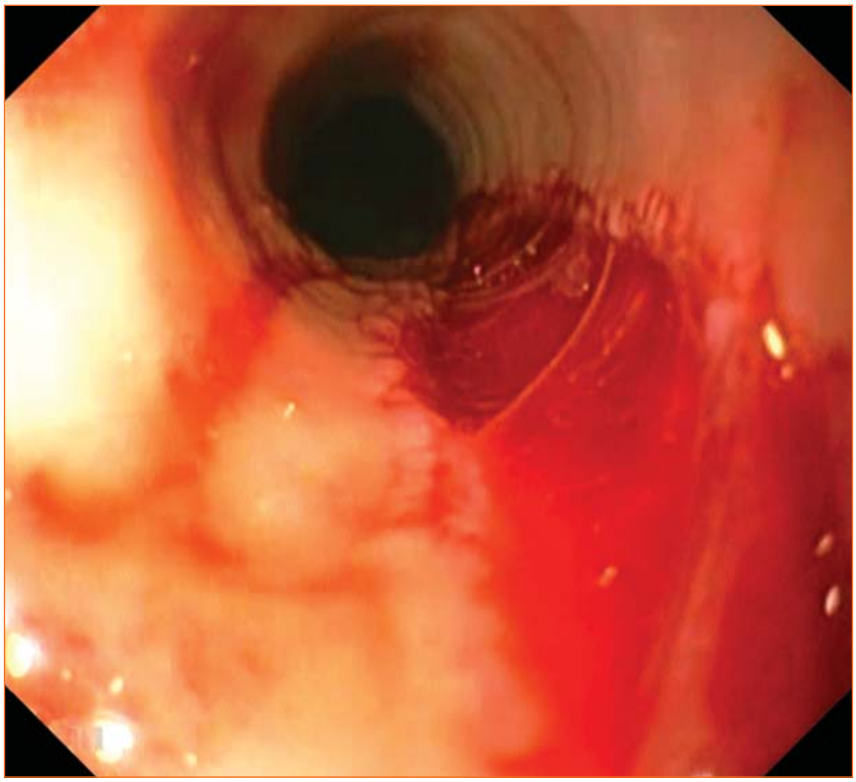

Figure 1
Mucosal disruption in mid-oesophagus that developed after impacted food-bolus had been pushed into the stomach.

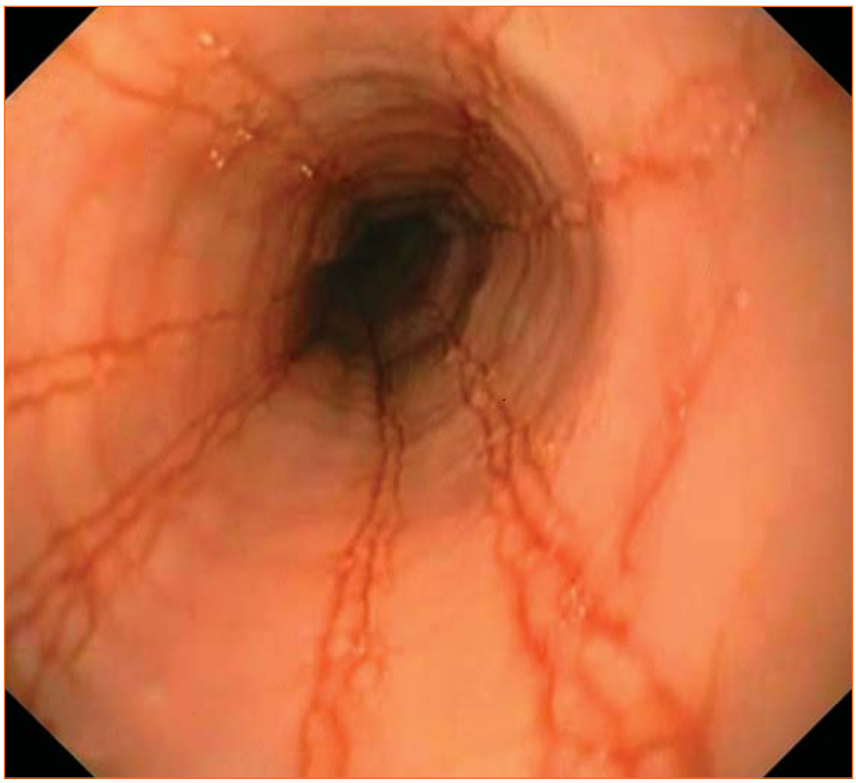

Figure 2
Longitudinal furrows in oesophageal mucosa.

without the features of dysplasia. For the next 14 days, the patient was treated with omeprazole, in order to accelerate the healing of mucosal disruption. Relief of chest pain without recurrence of dysphagia followed. To check the healing of mucosal disruption, the patient underwent the third

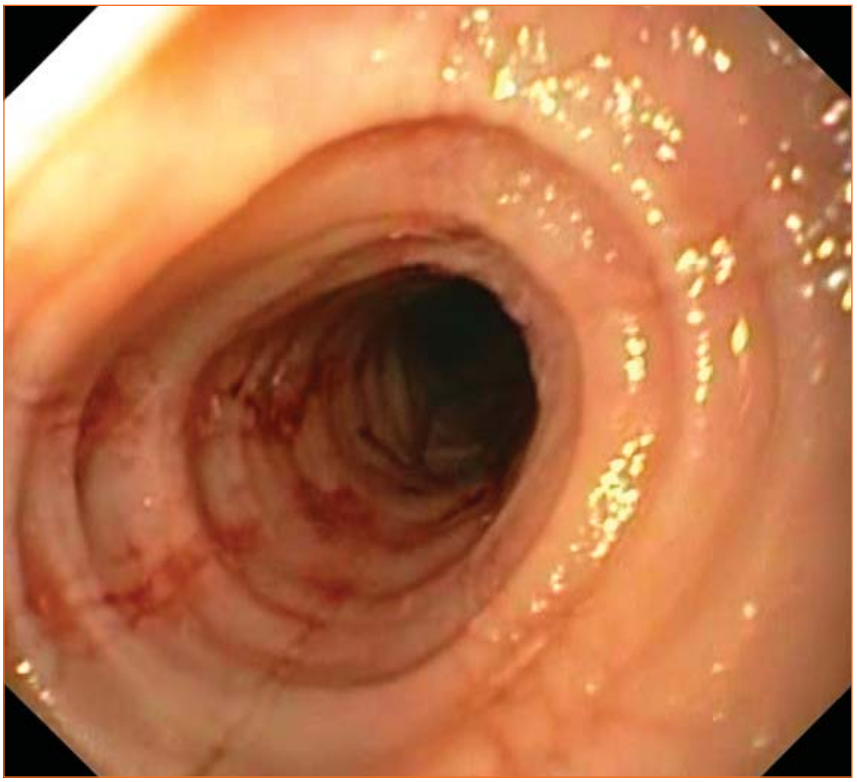

Figure 3
Concentric mucosal rings throughout the oesophagus.

oesophagogastroduodenoscopy in November 2006. The endoscopy showed longitudinal furrows and mucosal rings without mucosal disruption (Figs 4 and 5), which had healed up. No oesophageal stricture was observed. A total of 9 mucosal biopsies from both proximal and distal oesophagus were taken during endoscopy. Histopathologic evaluation showed high density of eosinophils with ≥ 15 eosinophils per high power field in the epithelium and confirmed the diagnosis of eosinophilic oesophagitis (Fig 6). The patient is being intermittently treated with histamine receptor blockers and hyposensitising vaccination therapy, ordered by the allergologist. He shows no recurrence of either dysphagia or food impaction until now.

DISCUSSION

We describe the case of 32-year-old man with two-year history of recurrent dysphagia for solids and food impactions caused by eosinophilic oesophagitis. Establishing the diagnosis took 26 months and necessitated the patient undergoing three oesophagogastroduodenoscopies. The delay of diagnosis might have been caused by the lack of awareness of both, endoscopists and pathologists, about this condition.

The first endoscopy showed mucosal tear in the gastro-oesophageal junction and was evaluated as Mallory-Weiss syndrome by the endoscopist, although there was no history of vomiting. Endoscopic mucosal changes might have been misinterpreted. The development of mucosal tear might have also been caused by recurrent, spontaneously resolved food impactions in the oesophagus that could have been affected by eosinophilic inflammation. Other endoscopic features of eosinophilic oesophagitis might have been overlooked by the endoscopist, because of the lack of awareness of eosinophilic oesophagitis. Oesophageal mucosal disruptions have been described in patients with eosinophilic oesophagitis after oesophageal dilation or after removal of impacted food from the oesophagus [27,30]. Considering the increased fragility, oesophageal mucosa in eosinophilic oesophagitisis is also called crepe-paper mucosa [27]. No biopsy specimen of oesophageal mucosa was taken during the first endoscopy since the endoscopist did not consider eosinophilic oesophagitis.

Second upper GI endoscopy showed linear furrows in oesophageal mucosa and concentric mucosal rings throughout the length of the oesophagus - the most common features, described in 75–90 % of patients with eosinophilic oesophagitis [7,15,22, 23]. Other endoscopic features of eosinophilic oesophagitis include oesophageal strictures, white plaques and small calibre oesophagus occurring in 31 %, 15 % and 10 % of patients respectively [15].

Histopathologic evaluation of biopsy specimens taken during the second endoscopy showed dense mucosal infiltration of leukocytes with the presence of eosinophils. However, the exact number of eosinophils per high power field was not counted.

Eosinophilic oesophagitis is characterised by eosinophilic infiltration of oesophageal epithelium, a tissue in which eosinophils are not normally encountered. The eosinophil density within oesophageal mucosa required for the diagnosis of eosinophilic oesophagitis is defined by ≥ 15 eosinophils per high power field [1,10,15], whereas density of < 5 eosinophils per high power field might be present in patients with gastro-oesophageal reflux disease [24,31]. Other histopathologic features of eosinophilic oesophagitis include superficial layering of eosinophils, eosinophil microabscesses - the cluster of ≥ 4 eosinophils, epithelial hyperplasia, eosinophil degranulation, the presence of other inflammatory cells and subepithelial fibrosis [29]. Endoscopic ultrasonography studies have shown that eosinophilic infiltration may also

affect deeper layers of the oesophageal wall [25].

Histopathologic evaluation of biopsies taken from gastric and duodenal mucosa precluded the diagnosis of eosinophilic gastroenteritis, which is necessary to consider in patients with eosinophilic infiltration of oesophageal mucosa. Eosinophilic gastroenteritis is characterised by peripheral eosinophilia, eosinophilic invasion of the gastrointestinal tract, and clinical symptoms related to the site and tissue layer involved. The stomach and proximal small bowel are the most commonly affected sites [6,8].

The most common presenting symptoms of eosinophilic oesophagitis include dysphagia, food impaction, heartburn refractory to therapy and chest pain [4,15,24]. Dysphagia and food impaction may occur even without the presence of organic oesophageal stricture. Eosinophilic oesophagitis may induce thickening of oesophageal wall with tissue fibrosis, which may lead to impairment of function of the oesophagus with subsequent dysphagia [11,29]. Despite food impaction, no oesophageal stricture was observed in our patient.

Eosinophilic infiltration may not be evenly distributed throughout the oesophageal mucosa. Thereby, it is strongly recommended that biopsies are taken from both the proximal and distal oesophageal mucosa. By using the criterion of ≥ 15 eosinophils /high power field for diagnosis of eosinophilic oesophagitis, Gonsalves et al [15] found that taking one biopsy had a sensitivity of 55 %, whereas taking 5 biopsies increased the sensitivity to 100 %. A low number of biopsies taken during the second upper GI endoscopy might have been the cause for the histopathologist not confirming the diagnosis despite typical endoscopic features of oesophageal mucosa.

Studies have shown, that oesophageal eosinophilic infiltration may be related to an allergic response to both food and aeroallergens. Mishra et al [20] have induced eosinophilic oesophagitis by exposure of experimental mice to the aeroalergen, Aspergillus fumigates. It is believed that environmental allergens play a role in the pathogenesis of eosinophilic oesophagitis. Fogg et al [9] found worsening of symptoms and increase in oesophageal eosinophilia during the pollen season in a patient with allergic rhinoconjunctivitis, bronchial asthma and eosinophilic oesophagitis. Biopsies taken out of the pollen season were normal, which support the theory about possible induction of a localized allergy type of inflammation in the oesophagus by aeroallergens. An aeroallergen might have triggered the eosinophilic oesophagitis in our case, too, since dysphagia and food impactions occurred only during the pollen sea-

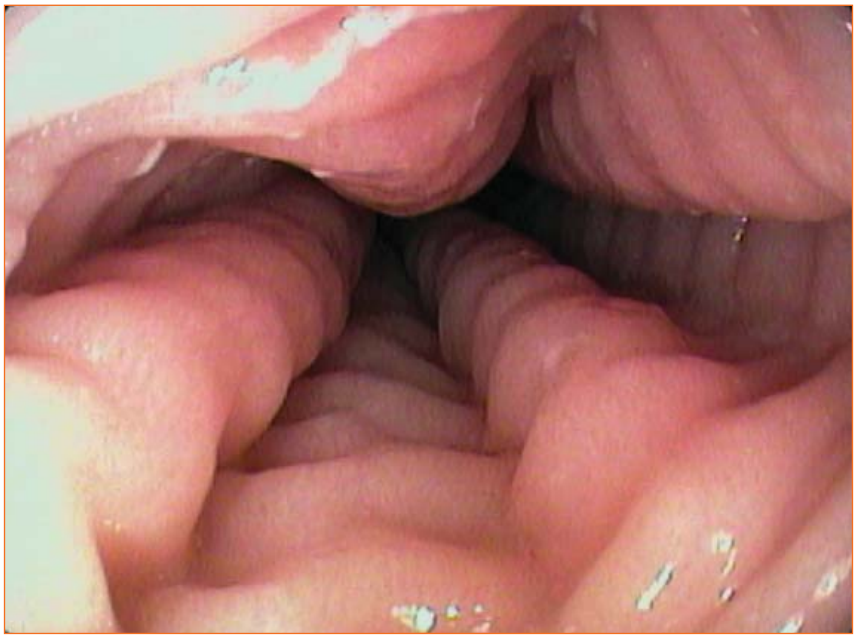

Figure 4
"Corrugated oesophagus" with concentric mucosal rings.

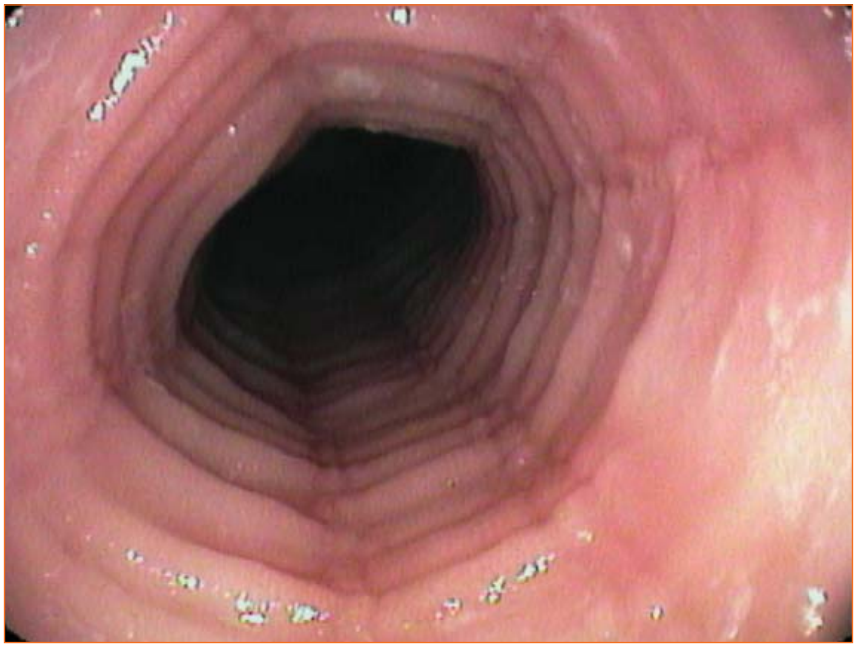

Figure 5
Longitudinal furrows and mucosal rings in the oesophagus.

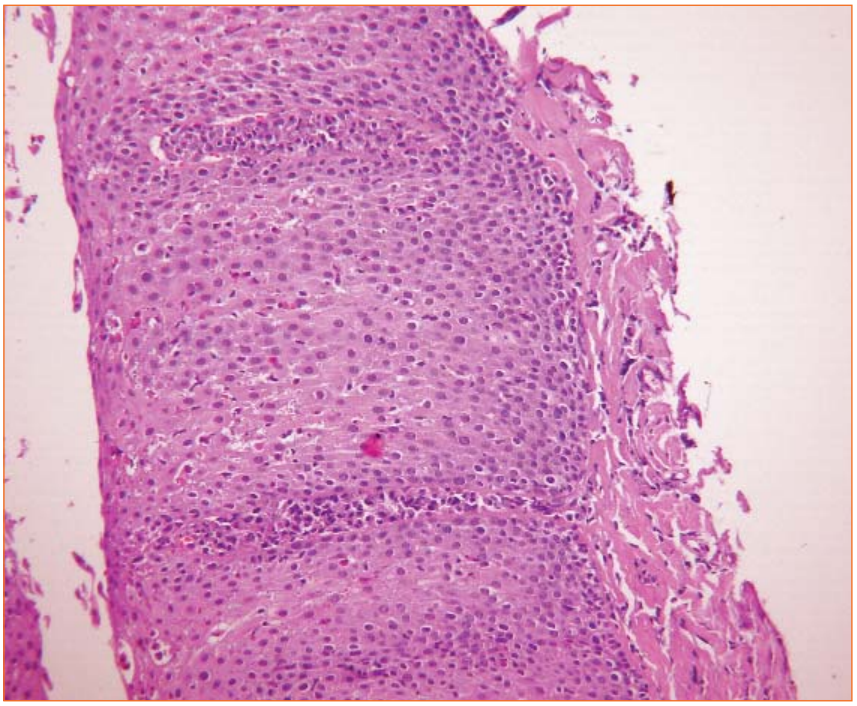

Figure 6
Eosinophilic infiltration of oesophageal epithelium, ≥ 15 eosinophils per high power field. Haematoxilin-eosin, magnification 200x.

son. The patient was asymptomatic during the period out of the pollen season and during the hyposensitisiting vaccination treatment ordered by the allergologist.

Therapeutic approach varies between children and adults. In children, the most common approach is elimination or elemental diet with amino-acid formulas [19]. There are no published data about the effect of diet in adults. Systemic corticosteroids have been shown to be effective in improving both the clinical symptoms and histopathological changes in oesophageal mucosa in patients with eosinophilic oesophagitis [17]. Topical corticosteroid have demonstrated the same efficacy as systemic have and, moreover, because of their maximum topical effect in the oesophagus and high first pass effect in the liver, they lack the systemic side effects [23]. Clinical studies with montelukast, leukotriene receptor antagonist, have demonstrated ineffectiveness in the treatment of eosinophilic oesophagitis, since most of the patients relapsed after discontinuation of therapy [2]. Clinical studies with mepolizumab, anti-interleukin-5 monoclonal antibody, in the treatment of eosinophilic oesophagitis are currently underway [12]. Another therapeutic approach is oesophageal dilation using both rigid and pneumatic dilators. Considering the short-term effect of dilation and the risk of oesophageal disruption, pharmacotherapy is the preferred therapeutic approach at the moment [29].

After confirming the diagnosis, the patient has remained asymptomatic without the need for any treatment. This might have been caused by several factors. Firstly, pushing the impacted food into the stomach might have had the same effect as oesophageal dilation, which could be confirmed by the development of extensive mucosal disruption, frequently developed after oesophageal dilation in patients with eosinophilic oesophagitis [27,30]. Secondly, clinical remission might have been caused by the end of the pollen season. Thirdly, the patient went on treatment with histamine receptor blockers, which might have suppressed eosinophil infiltration of oesophageal mucosa.

A lot of papers have reported the same problems with diagnosing eosinophilic oesophagitis as in this case, mainly because of the lack of the awareness of endoscopists and pathologists [7,14]. In a study by Gonsalves et al [15], the average time from development of first symptoms to confirmation of the diagnosis was 82 months.

Eosinophilic oesophagitis is probably more common than is really diagnosed and may cause recurrent dysphagia and food impaction in young adults. Upper GI endoscopy may show typical features, mainly mucosal furrows and rings, but may also be insignificant. Thereby, it is strongly recommended that repeated biopsies are taken from oesophageal mucosa in young patients with unexplained dysphagia, food impaction, refractory heartburn or chest pain even if normal mucosa is shown on oesophagoscopy.

References

1. Arora A, Yamazaki K. Eosinophilic esophagitis: asthma of the esophagus? Clin Gastroenterol Hepatol 2004; 2: 523-530.
2. Attwood S, Lewis C, Bronder C, Morris C, Armstrong G, Whittam J. Eosinophilic esophagitis: a novel treatment using Montelukast. Gut 2003; 52: 181-185.
3. Attwood S, Smyrk T, Demeester T, Jones J. Esophageal eosinophilia with dysphagia. A distinct clinicopathologic syndrome. Dig Dis Sci 1993; 38: 109-116.
4. Baxi S, Gupta SK, Swigonski N, Fitzgerald J. Clinical presentation of patients with eosinophilic inflammation of the esophagus. Gastrointest Endosc 2006; 64: 473 - 478.
5. Blanchard C, Wang N, Stringer K, Mishra A, Fulkerson P, Abonia J, Jameson S, Kirby C, Konikoff M, Collins M, Cohen M, Akers R, Hogan S, Assa'ad A, Putnam P, Aronow B, Rothenberg M. Eotaxin-3 and a uni-

quely conserved gene-expression profile in eosinophilic esophagitis. J Clin Invest 2006; 116: 536-547.
6. Cello JP. Eosinophilic gastroenteritis - a complex disease entity. Am J Med 1979; 67: 1097-104.
7. Croese J, Fairley SK, Masson JW, Chong A, Whitaker DA, Kanowski PA, Walker N. Clinical and endoscopic features of eosinophilic esophagitis in adults. Gastrointest Endosc 2003; 58: 516-522.
8. Dobbins JW, Sheahan DG, Behar J. Eosinophilic gastroenteritis with esophageal involvement. Gastroenterology 1977; 72: 1312-6.
9. Fogg M, Ruchelli E, Spergel J. Pollen and eosinophilic esophagitis. J Allergy Clin Immunol 2003; 112: 706-797.
10. Fox V, Nurko S, Furuta G. Eosinophilic esophagitis: it´s not just kid's stuff. Gastrointest Endosc 2002; 56: 260-270.
11. Fox V, Nurko S, Teitelbaum JE, Badizadegan K, Furuta G. High-resolution EUS in children with eosinophilic "allergic" esophagitis. Gastrointest Endosc 2003; 57: 30-6.
12. Garrett JK, Jameson S, Thomson B, Collins MH, Wagoner LE, Freese DK, Beck LA, Boyce JA, Filipovich AH, Villanueva LM, Sutton SA, Assa'ad AH, Rothenberg ME. Anti-interleukin-5 (mepolizumab) therapy for hypereosinophilic sundromes. J Allergy Clin Immunol 2004; 113: 115-119.
13. Gleich GJ. Mechanisms of eosinophil associated inflammation. J Allergy Clin Immunol 2000; 105: 651-653.
14. Gonsalves N, Kahrilas P, Hirano I. Eosinophilic esophagitis in adults: emerging entity or misdiagnosed malady [abstract]. Gastroenterology 2005; 128: S1162.
15. Gonsalves N, Policarpio-Nicolas M, Zhang Q, Sambasiva Rao M, Hirano I. Histopahologic variability and endoscopic correlates in adults with eosinophilic esophagitis. Gastrointest Endsc 2006; 64: 313 - 19.
16. Khan S, Orenstein S, Di Lorenzo C, Kocoshis S, Putnam P, Sigurdsson L, Shalaby T. Eosinophilic esophagitis: strictures, impactions, dysphagia. Dig Dis Sci 2003; 48: 22-29.
17. Liacouras CA, Wenner WJ, Brown K, Ruchelli E. Primary eosinophilic esophagitis in children: successful treatment with oral corticosteroids. J Pediatr Gastroenterol Nutr 1998; 26: 380-385.
18. Lucendo A, Carrion G, Navarro M, Pascual J, Gonzalez P, Castillo P, Erdozain J. Eosinophilic esophagitis in adults: an emerging disease. Dig Dis Sci 2004; 49: 1884-1888.
19. Markowitz J, Spergel J, Ruchelli E, Liacouras C. Elemental diet is an effective treatment for eosinophilic esophagitis in children and adolescents. Am J Gastroenterol 2003; 98: 777-782.
20. Mishra A, Hogan S, Brandt E. An etiological role for aeroallergens and eosinophils in experimental esophagitis. J Clin Invest 2001; 107: 83-90.
21. Noel RJ, Putnam PE, Rothenberg ME. Eosinophilic esophagitis. N Engl J Med 2004; 351: 940-1.
22. Potter JW, Saeian K, Staff D, Massey B, Komorowski R, Shaker R, Hogan W. Eosinophilic esophagitis in adults: an emerging problem with unique esophageal features. Gastrointest Endosc 2004; 59: 355-361.
23. Remedios M, Campbell C, Jones D, App D, Kerlin P. Eosinophilic esophagitis in adults: clinical, endoscopic, histologic findings, and response to treatment with fluticasone propionate. Gastrointest Endosc 2006; 63: 3-12.
24. Sgouros S, Bergele C, Mantides A. Eosinophilic esophagitis in adults: a systematic review. Eur J Gastroenterol Hepatol 2006; 18: 211-217.
25. Stevoff C, Rao S, Parsons W, Kahrilas PJ, Hirano I. EUS and histopathologic correlates in eosinophilic esophagitis. Gastroenitest Endosc 2001; 57: 30-36.
26. Straumann A, Bauer M, Fischer B, Blaser K, Simon H. Idiopathic eosinophilic esophagitis is associated with a T(H)2-type allergic inflammatory response. J Allergy Clin Immunol 2001; 108: 954-61.
27. Straumann A, Rossi S, Simon H, Simon H, Heer P, Spichtin H, Beglinger C. Fragility of the esophageal mucosa: A pathognomic endoscopic sign of primary eosinophilic esophagitis? Gastrointest Endosc 2003; 57: 407-412.
28. Straumann A, Simon H. Eosinophilic esophagitis: escalating epidemiology? J Allergy Clin Immunol 2004; 115: 418-419.
29. Straumann A, Spichtin H, Grize L, Bucher K, Beglinger C, Simon H. Natural history of primary eosinophilic esophagitis: A follow-up of 30 adult patients for up to 11,5 years. Gastroenterology 2003; 125: 1660-1669.
30. Vasilopoulos S, Murphy P, Auerbach A, Massey B, Shaker R, Stewart E, Komorowski R, Hogan W. The small-caliber esophagus: an unappreciated cause of dysphagia for solids in patients with eosinophilic esophagitis. Gastrointest Endosc 2002; 55: 99-106.
31. Winter HS, Madara JL, Stafford RJ, Grand RJ, Quinlan JE, Goldman H. Inraepithelial eosinophils: a new diagnostic criterion for reflux esophagitis. Gastroenterology 1982; 83: 818-23.

Correspondence to:
Adresa pre korešpondenciu:
Martin Kliment, MD,
Department of Gastroenterology,
Hospital Vítkovice, a.s.
Zalužanského 1192/15, 70384,
Ostrava-Vítkovice, Czech Republic
e-mail: martin.kliment@nemvitkovice.cz