



# The First Asian Case Report of Eosinophilic Esophagitis in an Asymptomatic Adult: What About a Proton Pump Inhibitor Trial?

## To the Editor:

We read with great interest the report of the first case of eosinophilic esophagitis (EE) in Asia, incidentally found during upper endoscopy screening for gastric cancer in an asymptomatic Chinese adult, which fulfilled endoscopic and histopathologic criteria for EE.<sup>1</sup> Indeed, the Kalixanda study,<sup>2</sup> the first assessment on the prevalence of EE in an adult asymptomatic population, has sketched a potential scenario in which EE in symptomatic adults may only represent the tip of the iceberg, in the same way as celiac disease, whilst asymptomatic or oligosymptomatic patients are commonly missed.

Notwithstanding, several remarks on this issue should be discussed. In the Kalixanda study, possible EE was defined if 5-14 eo/HPF, probable EE if  $\geq 15$  to <20 eo/HPF, and definite EE if  $\geq 20 \text{ eo/HPF}$ . Despite the patients enrolled not having consulted a doctor in the previous year, the rate of patients with erosive esophagitis or troublesome reflux symptoms (possible EE [13/25, 10/25], probable EE [2/7, 3/7], definite EE [0/4, 3/4], respectively) was significantly high, indicating that it was not a fully asymptomatic population sample and that severe gastroesophageal reflux disease (GERD) may occur with minor or absent clinical impact. As such, the recent American Gastroenterology Association review on the management of GERD<sup>3</sup> has focused on the artificial division in the Montreal consensus between GERD and episodic heartburn, since reflux may not be perceived by the patient to be troublesome due to insufficient frequency or severity, but may be equally responsive to proton pump inhibitors (PPI) in clinical and histopathologic terms. Of note, the authors point out that the incidence of GERD is increasingly growing in Asia due to obesity and diet, as has occurred during the last decade in the West. In this regard, our group recently reported 2 young males suffering from recurrent food impaction with histopathologic features of EE.<sup>4</sup> Neither of the patients had classical symptoms of GERD (heartburn, regurgitation, nausea, epigastric or chest pain) but both had endoscopic reflux features and 1 had clinicopathologic remission on PPI therapy.

The recent first consensus statement on the diagnosis of EE<sup>5</sup> has established the need of precluding GERD by means of pH testing or high-dose PPI as a major premise before diagnosing EE. Unfortunately, no histopathologic follow-up after acid suppression was done in the Kalixanda study or in the Chinese patient. EE has been historically diagnosed based on histopathologic criteria due to the common belief that GERD is related to a low-grade intraepithelial eosinophilic infiltration, commonly <7 eo/HPF. In contrast to this belief, recent reports have demonstrated that GERD may induce esophageal high-grade eosinophil recruitment similar to that found in EE.<sup>6</sup>

In conclusion, a PPI trial is mandatory before diagnosing EE in patients fulfilling histopathologic criteria for EE, regardless of clinical and endoscopic features. We strongly encourage the authors of the Asian report to assess the histopathologic outcome of this patient after acid suppression in order to preclude GERD definitely.

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#### Authors' reply to Molina-Infante et al

We appreciate Dr Molina-Infante et al's comments, but, based on the current evidence, we do not agree with their point of view.<sup>1</sup> According to the recent guidelines published by the American Gastroenterology Association, we agree that "symptomatic" eosinophilic esophagitis (EE) should be diagnosed in the absence of pathologic gastroesophageal reflux disease (GERD) as evidenced by a normal pH monitoring study of the distal esophagus or lack of response to high-dose proton pump inhibitor (PPI) medication.<sup>2</sup> However, for "asymptomatic" EE, though not uncommon in the general population of Western countries,<sup>3</sup> the management strategy for asymptomatic patients is still not available.<sup>2</sup> This is due to the uncertain natural history of asymptomatic EE. Furthermore, our current case was incidentally found to have EE with the presence of neither GERD symptoms (esophageal or extraesophageal) nor endoscopic evidence of reflux esophagitis. Thus, there existed no treatment targets for PPI. Though Dr Molina-Infante et al successfully treated the dysphagia in 2 suspected EE patients with PPI,<sup>4</sup> this result might simply be suggestive of the diagnosis of either pure GERD or EE with coexisting GERD in their patients. The success of PPI treatment cannot be justification for the strategy that all asymptomatic "patients" with histologically-proven EE should be given PPI trial. We do not believe that a PPI trial would add any diagnostic or therapeutic benefits to our presented subject. Nevertheless, we suggest that asymptomatic EE patients be closely followed for the development of clinical symptoms and periodic endoscopy performed to look for persistent esophageal eosinophilia and/or the development of esophageal morphologic abnormalities.

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