Background and Aims
We identified several cases in which a histopathologic diagnosis of Candida esophagitis was made in a patient with no known risk factors and an esophagus specifically described as endoscopically normal. A diagnosis of Candida esophagitis in such patients tended to generate questions from the submitting clinicians. Therefore, after an unenlightening literature search, we designed and carried out a study to:
1. Determine the prevalence of fungal esophagitis in the background of an endoscopically normal esophagus, and
2. Compare the demographic and clinical characteristics of such patients to those of patients with endoscopic esophageal abnormalities.

Methods
We used the Miraca Life Sciences database to analyze demographic, clinical, endoscopic and histopathologic data from all patients with esophageal biopsies submitted to a national pathology laboratory from 1/2008 through 6/2012. We extracted all patients who had a histopathologic diagnosis of fungal esophagitis and assigned them to two groups; those whose endoscopic report stated that the esophagus was normal and those who had any endoscopic abnormality in the esophagus. Patients whose endoscopic report did not mention the esophagial findings were excluded. Histologic slides of all “normal esophagus” cases were reviewed for confirmation of fungal infection. The demographic and clinical characteristics of the two groups were then compared using the t-test and odds ratios.

Results
There were 399,878 patients with esophageal biopsies (median age 58 years; 54% female); 7,637 patients had a histopathologic diagnosis of Candida esophagitis (median age 62 years; 57% female). The esophagus was not mentioned in the endoscopic report of 225 patients, who were excluded.

The endoscopy report mentioned one or more abnormality in the esophagus of 7,286 patients (median age 62 years; range: 1 to 98; 58% female); a normal esophagus was reported in 126 patients (median age 52 years; 73% female). The findings are summarized in Table 1. Patients with an endoscopically normal esophagus were 10 years younger (p<0.0001) and more likely to be female. Compared to those with esophageal abnormalities, patients with a normal esophagus were significantly less likely to present with dysphagia or odynophagia, but significantly more likely to have dyspepsia and abdominal pain, and slightly more likely to have GERD.

Review of the slides revealed that approximately half of the cases showed invasive fungal hyphae with associated neutrophilic inflammation, while the remaining cases showed invasive hyphae with rare eosinophils, neutrophils, or no inflammation.

Study Highlights
1. 1.7% percent of patients with histologically documented fungal esophagitis were reported to have a normal esophagoscope.
2. These patients, none of whom was known to be immunocompromised, were younger, more often women, and more likely to present with dyspepsia and abdominal pain than dysphagia.
3. Because of their demographic and clinical characteristics, the index of suspicion for fungal esophagitis in these patients was extremely low.

References

Table 1 – Demographic data and presenting symptoms in patients with histologic fungal esophagitis with and without endoscopic abnormalities in the esophagus

<table>
<thead>
<tr>
<th></th>
<th>Histologic Candidiasis with endoscopic abnormality</th>
<th>Histologic Candidiasis without endoscopic abnormality</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent Female</td>
<td>58%</td>
<td>73%</td>
<td>1.05 (1.31–2.90)</td>
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<tr>
<td>Age (median)</td>
<td>62 years</td>
<td>52 years</td>
<td>P=0.0001</td>
</tr>
<tr>
<td>Dysphagia/ Odynophagia</td>
<td>33%</td>
<td>21%</td>
<td>0.65 (0.36–0.80)</td>
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<tr>
<td>Dyspepsia</td>
<td>10%</td>
<td>15%</td>
<td>1.57 (0.62–2.48)</td>
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<tr>
<td>Abdominal pain</td>
<td>26%</td>
<td>37%</td>
<td>1.67 (1.16–2.40)</td>
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<tr>
<td>GERD</td>
<td>28%</td>
<td>33%</td>
<td>ns</td>
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