CANDIDA COLONIZATION AND CANDIDIASIS OF THE ESOPHAGUS IN ALCOHOLIC LIVER DISEASE PATIENTS

Zoltán Péter, M.D.
Flór Ferenc Hospital of Pest County
1st Department of Internal Medicine and Gastroenterology

Tutor and program director:
Prof. Zsolt Tulassay M.D., Member of HAS

Semmelweis University, School of PhD Studies
Clinical Medicine Doctoral School
Gastroenterology Program

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INTRODUCTION

The incidence of disseminated Candida infection has dramatically increased in the last few years. The colonizing fungal flora of the gastrointestinal tract is considered as the primary source of infection, disruptions of the integrity of gastrointestinal mucosa are portal of entry of the organisms. Parallel to this, thanks to the alternative medicine as well, the interest in Candida infection of the gastrointestinal tract increased.

The most frequent manifestation of Candida infections of the gastrointestinal tract is esophagitis, therefore, my goal was to study the hardly ever examined esophageal fungal colonization. As this was not investigated so far in alcoholic liver disease (ALD) patients, I performed my research in this respective population. I also studied the non-examined questions of fungal esophagitis in alcoholic liver disease, such as the complaints of the patients and the single-dose treatment.

AIMS

We looked for answers to the following questions:
- how frequent is the fungal colonization in ALD patients?
- do our records support the appropriateness of determining the number of colony forming units for identifying colonization?
- how does the severity of liver disease impact the colonization?
- can we determine coherence between the fungal colonization of the pharynx and the fungal colonization of the esophagus?
- what kind of complaints do the ALD patients have who suffer of fungal esophagitis?
- in what ratio do the specific symptoms occur?
- how frequent are the esophageal symptoms?
- what is the rate of symptom-free fungal esophagitis among ALD patients?
- what is the rate of clinical cure as a result of single-dose fluconazole treatment of fungal esophagitis in ALD patients?
- what is the rate of mycological eradication as a result of single-dose fluconazole treatment of fungal esophagitis in ALD patients?

**METHODS**

All three parts of our study were performed in ALD patients. In the first part we studied the Candida colonization of the esophagus, in the second one we studied the symptoms of patients with fungal esophagitis and in the third one we studied the effectiveness of single-dose fluconazole treatment in fungal esophagitis.
Candida colonization of esophagus in alcoholic liver disease patients

One hundred consecutive inpatients with ALD were asked to enroll in the study. Data of 93 patients could be evaluated, 65 of them had alcoholic liver cirrhosis. A group of 22 patients without liver disease, who underwent upper gastrointestinal endoscopy because of dyspeptic symptoms and a group of 20 patients with hepatitis C virus associated liver disease acted as controls. After a culture of oropharyngeal scrapings on Sabouraud's medium the patients underwent an upper gastrointestinal endoscopy and using a cytology brush, surface material was obtained from the esophageal mucosa. Direct smears, and after serial dilutions, cultures on Sabouraud's medium were performed. Fungal esophagitis was defined as a characteristic or suspicious endoscopic picture of fungal esophagitis and the presence of fungi documented by a positive culture and/or smear. Colonization was defined as the lack of esophageal plaques suspicious of mycosis with the presence of a positive smear and/or culture.

Symptoms of fungal esophagitis in alcoholic liver disease

Data of 517 alcoholic liver disease patients were studied retrospectively (group I). Out of the 41 cases with fungal
esophagitis, data of 38 could be evaluated. In the prospective part 93 alcoholic liver disease patients were enrolled. 13 patients had fungal esophagitis, which were later documented by mycological examinations as well. The following symptoms were studied: odynophagia, dysphagia, anorexia, nausea, vomiting abdominal pain, weight loss, bloating, haematemesis, melena, thoracic pain, singultus, acidic regurgitation and occult gastrointestinal bleeding.

**Single-dose fluconazole treatment of fungal esophagitis in alcoholic liver disease**

In a prospective, randomized study 22 alcoholic liver disease patients were included in two groups. Patients of the first group received a single oral dose of 150 mg fluconazole, those of the second group were given a 7-day treatment of daily 50 mg oral fluconazole. There were two drop-outs from the single-dose group. Clinical cure was defined as the disappearance of the previously detected fungal plaques, mycological eradication was considered in cases of clinical cure where the presence of fungi could be demonstrated neither on smears, nor by cultures.
RESULTS

Candida colonization of the esophagus of ALD patients

Based on our definitions, out of the 39 ALD patients (41.9 %) with fungi in their esophagus there were 18 cases (19.3 %) of fungal esophagitis and 21 cases (22.5 %) of fungal colonization (figure 1.).

![Graph showing Candida species, colonization and esophagitis in ALD and control patients.](image)

**Figure 1. Rate of Candida species, colonization and esophagitis in the esophagus of ALD and control patients**

Regarding the total presence of fungi the difference was
significant only compared to the control group with dyspeptic symptoms. We did not find significant difference between the groups in respect of colonization, while fungal esophagitis was significantly more frequent in ALD patients than in the control groups.

Out of 13 patients with the endoscopic diagnosis of fungal esophagitis 5 had less than 100 colonies (in 4 cases less than 50 colonies).

Significantly more fungal colonization and fungal esophagitis was found in those 30 patients (32.2 %) of the ALD group in whom the culture of the oropharyngeal swabs yielded growth of fungi in (table 1.).

<table>
<thead>
<tr>
<th>Oropharyngeal swab</th>
<th>positive n = 30</th>
<th>negative n = 63</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophagitis</td>
<td>11 (36.6 %)</td>
<td>7 (11.1 %)</td>
</tr>
<tr>
<td>Colonization</td>
<td>12 (40.0 %)</td>
<td>9 (14.2 %)</td>
</tr>
</tbody>
</table>

p = 0.00001
Fungi were found in 46 of the 93 patients with ALD (table 2.). Out of them 23 had fungi in both, their oropharyngeal scrapings and esophageal brushings. The same species could be identified from both sites in 18 of them (39 % of the 46 patients). The difference between the rate of patients with fungi in their oropharynx and esophagus respectively, was not significant.

Table 2. Distribution of ALD Patients According to the Presence of Fungi in the Oropharynx and Esophagus

<table>
<thead>
<tr>
<th>Fungi</th>
<th>Number of patients (%)</th>
</tr>
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<tbody>
<tr>
<td>Exclusively in the oropharynx</td>
<td>7 (8 %)</td>
</tr>
<tr>
<td>Exclusively in the esophagus</td>
<td>16 (17 %)</td>
</tr>
<tr>
<td>In the oropharynx and in the esophagus</td>
<td>23 (25 %)</td>
</tr>
<tr>
<td>No fungi</td>
<td>47 (50 %)</td>
</tr>
<tr>
<td>Total</td>
<td>93 (100 %)</td>
</tr>
</tbody>
</table>

\[ p = 0.095 \]

Applying the Child-Pugh classification for the 65 patients with liver cirrhosis, no significant differences were found in the rate of colonization and fungal esophagitis regarding the severity of the liver disease.
Symptoms of fungal esophagitis in alcoholic liver disease

Comparing the symptoms of patients with and without fungal esophagitis of group II, we found significant difference only in the rate of bloating.

The rate of symptoms among the 51 patients (38 patients of group I. and 13 patients of group II.) with fungal esophagitis was: anorexia 23 (45.0 %), abdominal pain 22 (43.1 %), vomiting 17 (33.3 %), nausea 15 (29.4 %), occult gastrointestinal bleeding 12 (23.5 %), weight loss 9 (17.6 %), melena 7 (13.7 %), bloating 6 (11.7 %), acidic regurgitation 3 (5.8 %), haematemesis 2 (3.9 %), thoracic pain 2 (3.9 %), singultus 1 (1.9 %), odynophagia 0 and dysphagia 0. In 7 patients (13.7 %) none of the studied symptoms could be identified.

Single-dose and 7-day treatment of fungal esophagitis in ALD patients

There were no significant differences between the two groups in the treatment outcome, defined as clinical cure and mycological eradication (table 3.) In all three patients who failed to achieve a clinical cure, the pathogen was C. albicans.
Table 3. Comparison of the treatment outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>single-dose treatment (n = 9)</th>
<th>7-day treatment (n = 11)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical cure</td>
<td>8</td>
<td>9</td>
<td>0.6</td>
</tr>
<tr>
<td>Mycological eradication</td>
<td>4</td>
<td>3</td>
<td>0.4</td>
</tr>
</tbody>
</table>

CONCLUSIONS

1. ALD is a predisposing factor for the presence of candida species in the esophagus and fungal esophagitis
2. the presence of Candida species in the oropharynx is a predictive factor for esophageal fungal colonization or fungal esophagitis
3. the colony forming unit number of the sample taken from the esophagus is inappropriate for determining fungal colonization
4. a standard method for the study of Candida colonization of the esophagus is required
5. we found a total lack of esophageal symptoms (odynophagia, dysphagia) among our ALD patients with fungal esophagitis
6. the diagnosis of fungal esophagitis can be established only by endoscopy, not even the suspicion of fungal esophagitis can be raised based on the symptoms of the patients

7. regarding the mycological eradication and the clinical cure, the single-dose fluconazole treatment is as effective as the 7-day treatment in fungal esophagitis of ALD patients
PUBLICATIONS RELATED TO THE THESIS


Abstracts and congress presentations


17. Péter Z, Kóbori L, Szalman K, Gálfi Zs, Telegdy L. Rizikótényező-e a májtranszplantáció előtti pozitív Candida


OTHER PUBLICATIONS
