EDITORIAL

Liver cirrhosis as a predisposing risk factor for esophageal candidiasis: Bystander or culprit?

Candida esophagitis is the most common infectious disease of the esophagus and the most common gastrointestinal opportunistic disorder among individuals infected with human immunodeficiency virus (HIV). Ou et al [1] conducted a study using a retrospective chart review of non-HIV-infected patients with esophageal candidiasis and particularly aimed to elucidate the role of liver cirrhosis in esophageal candidiasis. I have long thought that retrospective chart reviews are usually poorly done and are subject to all sorts of biases and confounding issues. The editorial allowed me to review the article presented by Ou et al [1] and feel that it shared many of these problems. Actually, most of the clinical relevant data of esophageal candidiasis were gathered from HIV-infected patients. Fungal infections have not been adequately studied in patients with liver cirrhosis [2]. The main interest had been focused on acute liver failure and liver transplantation [3,4]. The current study is a unique one to focus on esophageal candidiasis in patients with liver cirrhosis thus far and did identify discussion-worthy issues regarding specific risks in cirrhotic patients.

In the current study [1], the diagnosis of esophageal candidiasis was primarily based on endoscopic findings. Overall, 3017 of 43,217 non-HIV-infected patients had liver cirrhosis. The incidence of esophageal candidiasis in cirrhotic patients was higher than that in noncirrhotic patients (0.8% vs. 0.36%). Liver cirrhosis was identified as an independent risk factor for esophageal candidiasis (odds ratio, 1.74; 95% confidence interval, 1.06–2.87). Moreover, cirrhotic patients tended to be asymptomatic compared with noncirrhotic patients (45.8% vs. 9%). Antifungal treatment did not decrease the mortality of patients with esophageal candidiasis during hospitalization.

Esophageal candidiasis is a common opportunistic infection in patients when their immunity was compromised. These included patients with acquired immunodeficiency such as HIV infection, iatrogenic immunodeficiency such as organ recipients receiving immunomodulation therapy, cancer patients receiving chemotherapy, and other patients who required long-term steroid therapy. It also occurs in patients receiving long-term antibiotic and proton pump inhibitor therapy, and in patients with major comorbidities such as diabetes mellitus and renal failure. Esophagogastroduodenoscopy (EGD) is a reliable method used to diagnose esophageal candidiasis by revealing the typical endoscopic appearance of multiple raised small and thick white plaques on the esophageal mucosa and histopathology of yeast cells and pseudohyphae from biopsy specimens. The prevalence of esophageal candidiasis in non-HIV-infected patients is approximately 0.3% [5]. Although it is not a major issue, for the first time, Ou et al [1] reported that the incidence rate of esophageal candidiasis in cirrhotic patients was 0.8%, which was likely overestimated because not all patients with liver cirrhosis were systemically evaluated by endoscopic examination and not all of the diagnoses were confirmed by histopathology.

Patients with liver cirrhosis have compromised immunity and are predisposed to bacterial infections and selected fungal infections because of reduced opsonization in blood and ascites, reduced antibody production, increased immunosuppressive cytokines, disturbances in complement, and reduced leukocyte function, all of which contribute to the susceptibility of cirrhotic patients to infections [2,6]. Therefore, it is not surprising to find that liver cirrhosis was identified as an independent risk factor for esophageal candidiasis, and the incidence of esophageal candidiasis was higher in cirrhotic patients with Child–Pugh class C.

The common presenting symptoms of esophageal candidiasis are nonspecific such as odynophagia, dysphagia, and retrosternal pain. As observed in the current study, none of the cases in both groups underwent EGD because of suspected esophageal candidiasis. Moreover, it is often difficult to recognize the symptoms for esophageal candidiasis because it usually occurs in concomitance with other diseases. In the current study, almost half of the patients with liver cirrhosis were asymptomatic. The results should be interpreted carefully. It is unclear why a large proportion of patients had no symptom(s) but underwent EGD. I believed that screening endoscopy had been and should be performed in many patients with newly diagnosed liver cirrhosis, which had been highly recommended by international guidelines.

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and consensus [7]. It is likely that screening endoscopy has led to a higher proportion of asymptomatic patients with liver cirrhosis in the current study.

Fungal colonization of superficial mucosal sites usually precedes invasive infection. Systemic antifungal treatment of esophageal candidiasis was recommended in a recent clinical practice guidelines proposed by the Infectious Diseases Society of America [8]. Patients with cirrhosis or acute fulminant liver failure are at increased risk of acquiring bacterial and selected fungal infections [2–4]. A recent prospective cohort defined the predisposing factors to infection-related mortality in hospitalized patients with cirrhosis [9]. Potentially preventable second bacterial and fungal infections independently increase mortality in hospitalized patients with cirrhosis. Early prevention of these second infections is suggested. However, whether esophageal candidiasis affected the outcomes of patients with liver cirrhosis was not reported by Ou et al [1]. Instead, they found no difference in the mortality during hospitalization between patients with and without antifungal treatment, and also found that antifungal treatment did not decrease the mortality in cirrhotic patients with esophageal candidiasis. The impact of fungal infection on the clinical outcomes appeared different between prior studies and the current one. It is likely that the type of fungal infection (chest and urinary tract vs. esophagus), and disease entity of hosts (acute vs. chronic, compensation vs. decompensation, and therapeutic endoscopy vs. screening endoscopy, hospitalized vs. outpatient) was unsimilar between these studies. Therefore, does it matter if esophageal candidiasis occurs in patients with liver cirrhosis? The issue needs to be clarified by further study as suggested by the authors.

Conflicts of interest

The author declares that he has no potential, perceived, or real conflicts of interest.

References


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