Original Research Article

A study of esophageal candidiasis in patients with ca esophagus

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Received: 09-09-2024 / Revised: 22-09-2024 / Accepted: 02-10-2024

Abstract

Esophageal candidiasis is a condition mostly seen in immunocompromised patients. It is usually caused by Candida albicans, but other species are occasionally found Esophageal candidiasis has strong assosiation with esophageal cancer. Esophageal candidiasis is also the risk factor for development of esophageal cancer in addition to other risk facors like smoking, alcohol, GERD.

Keywords:esophageal,candidiasis

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Introduction

Esophageal candidiasis is a condition mostly seen in immunocompromised patients. It is usually caused by Candida albicans, but other species are occasionally found[7]. Patients at high risk are those infected with HIV, patients with hematologic malignancies or those receiving chemotherapy for solid tumors, and patients with congenital immunodeficiencies such as idiopathic CD4þ lymphopenia or chronic mucocutaneous candidiasis. Especially in the latter patient groups, infection is often prolonged and refractory to treatment. Chronic mucocutaneous candidiasis (CMC) is a heterogenous group of clinical syndromes characterized by chronic or recurrent infections of the skin, nails and mucous membranes caused by Candida spp. Recently, several reports have suggested an association between CMC with oral squamous cell carcinomas[3,4,11] and esophageal carcinomas[6,8,9,10], especially in patients with autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED). Esophageal carcinoma has also been described in CMC patients with concurrent IgA deficiency[8,9], which is associated with the development of solid and lymphoid tumors[7]. Here, we describe two patients with chronic esophageal candidiasis who developed esophageal carcinoma. One subject was diagnosed with autosomal dominant CMC due to mutations in the DNA sequence encoding the signal transducer and activator of transcription 1 (STAT1). The second patient had isolated refractory esophageal candidiasis for over 10 years, without other manifestations of CMC. Multiple etiologic factors play a role in the development of squamous cell carcinoma of the esophagus, among which alcohol consumption and smoking are the most important. The incidence of esophageal squamous cell carcinoma varies considerably among geographic regions, probably caused by a combination of common environmental risk factors and inherited predisposition. Ingestion of nitrosamines in food and tobacco have long since been implicated as risk factors for the development of esophageal cancer. Candidiasis is often found in patients with esophageal carcinoma.A prospective study on the frequency of gastro-esophageal candidiasis in 465 patients who underwent endoscopy, showed that candidiasis was more frequent in patients with esophageal carcinoma (27%) than in patients with other forms of mucosal injury, such as oesophagitis (15%)[2].

Although candidiasis can develop secondary to malignancy, possibly due to impaired antifungal host defense due to mucosal damage, there is increasing evidence that Candida infection itself has carcinogenic properties and several reports have been published of increased incidence of oral and esophageal squamous cell carcinoma in patients with chronic candidiasis.

Aims and objectives of the study

- To evaluate the pattern of oesophageal candidiasis in patients with ca esophagus.

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- To know the prevalence of oesophageal candidiasis in ca oesophagus.

Methodology

Study design - Case series study
Sample size -50 patients
Study duration - 3years
Study participants - All patients of ca esophagus coming to OPD and In-patients in the Department of General Surgery, HIMS, hassan.

Inclusion criteria

All patients of ca esophagus coming to OPD and In-patients in the department of general surgery will be included in this study.

Exclusion criteria

- Diabetes
- Immunocompromised state
- Age<15 years
- Age>65 years
- CKD

Method

All patients of ca esophagus coming to OPD and In-patients in the Department of General Surgery, HIMS, hassan were included in the study. Clearance from ethical committee was taken before starting the study. All patients underwent routine blood investigations and upper GI endoscopy. Biopsy of the specimen for histopathological examination done.

Statistical analysis

The study is a hospital based case series study. Data obtained from these patients will be systematically recorded and analysed using statistical package for social services (SPSS), chi square will be used to assess statistical significance.

Results

Distribution of patients according to their characterstics

	No of patients	Percentage (%)
Age		
<50years	30	60
>50years	20	40
Sex		
Male	35	70
Female	15	30
Smoking		
Yes	36	72
No	14	28
Alcohol		
Yes	32	64
No	18	36

Distribution of patients according to dysphagia

Dysphagia grade	No of patients	Percentage (%)
1	01	2
2	03	6
3	06	12
4	22	44
5	18	36

Anatomical site, Macroscopic appearance, Histopathological grade

Variable	Frequency	Percentage (%)
Anatomical site		
Upper third esophagus	3	6
Middle third	28	56

esophagus		
Lower third esophagus	19	38
Macroscopic appearance		
Ulcerative	24	48
Infiltrative	18	36
stricture	2	4
polypoid	1	2
Fungoid	1	2
mixed	4	8

Histopathological type	Frequency	Percentage (%)
Squamous cell carcinoma	48	96
Adenocarcinoma	2	4
Well differentiated	16	32
Moderately differentiated	28	56
Poorly differentiated	6	12

Incidence of candidiasis

Esophagitis (Candidiasis)	No of patients	Percentage (%)
Patch	5	10
Plaque	3	6
None	42	84

Discussion

Esophageal cancer is typically manifested at an advanced stage and current survival rate is 19%, with majority of patients dying of thier disease. Adenocarcinoma is the most common histology in western countries. There has been concomitant decline in the incidence of squamous cell carcinoma(SCC) both worldwide and and in the united states. Increasing incidence of adenocarcinoma is due to increasing obesity and GERD and global reductions in cigarette smoking contribute to its decreased incidence of SCC. Tobacco and alcohol are strong risk factors for SCC. Other risk factors are HPV, plummer-vinson syndromes, history caustic ingestion, achalsia, herediatry cancer syndromes associted with SCC include tylosis and fanconianemia.SCC arise in any part of esophagus, majority arise in the proximal and middle esophagus. Adenocarcinomas arise in the distal esophagus and GEJ. Dyshagia is the most common symptom which is progressive initially for solids progressing to liquids. Other symptoms include heart burn, regurgitation, fatigue, retrosternal pain, anemia, weight loss.

Esophagitis was evaluated by endoscopy. The gross appearance of the esophageal mucosa was graded grade 0, normal; grade 1, few raised white plaques - 2 mm in diameter without ulceration; grade 2, multiple raised white plaques - 2 mm in diameter without ulceration; grade 3, conflfluent, linear, nodular elevated plaques with superfiicial ulceration; and grade 4, grade 3 findings plus narrowing of the esophageal lumen[5].

Candida is known to predispose to oral and oesophageal squamous cell cancer (SCC). Permissive factors that lead to immune deficiencies can underlie persistent or recurring candidiasis, called chronic mucocutaneous candidiasis (CMC).CMCD, particularly those with the GOF-STAT1 mutation, have a broad clinical phenotype, signifificantly reduced life expectancy and an increased incidence of SCC.patients who develop oesophageal SCC on a background of CMCD present at a younger age. Delsing et al. reported a 25-year-old female who presented with dysphagia on a background of CMCD and GOF-STAT1 gene mutation, where the initial gastroscopy revealed only candidiasis, but the cytology confirmed malignant epithelial cells.The pathogenic mechanisms leading to SCC in the presence of CMCD are not fully understood, but it is believed to be due to chronic inflflammation caused by the infection, as well to candidial catalytic activity leading to the production

of nitrosamines such as nitroso-N-methylbenzylamine (NBMA) which is carcinogenic. is involved in mediating antibacterial, antiviral and antifungal immune responses, suppression of cell growth, and apoptosis as well as tumourgenesis and tumoursuppression. transfection of STAT1c into oesophageal squamous cell carcinoma cells resulted in apoptosis and cell cycle arrest, while the absence of STAT 1 was associated with poorer outcomes. Patients should have an endoscopy if they have any upper gastrointestinal symptoms. They should also have regular surveillance endoscopy with chromoendoscopy using Lugol's iodine or narrow band imaging to detect squamous dysplasia or early cancers[13].

In a large study evaluating risk factors for esophageal candidiasis in 281 non–human immunodefificiency virus patients, corticosteroids, antibiotic use, herbal medicaions, and heavy drinking were identifified as risk factors[12].

Hideyuki Ogiso et al. study shows that EC was observed in 184 of 7736 cases (2.4% morbidity rate). Multivariate analysis revealed that signifcant risk factors for the development of EC were: diabetes mellitus {odds ratio (OR): 1.52}, proton pump inhibitor (PPI) use (OR: 1.69), atrophic gastritis (AG) (OR: 1.60), advanced gastric cancer (OR: 4.66), and gastrectomy (OR: 2.32). When severe EC (Kodsi grade ≥ II) was compared to mild EC (grade I), the most signifcant risk factors were advanced gastric cancer (OR: 17.6) and gastrectomy (OR: 23.4)[15]

In our study 60% of patients are below 50years and 40% are above 50 years of age. Esophagel cancer was more common in males(70%). 72% of patients with esophageal cancer are smokers and 64% had habit of alcohol consumption. Esophageal cancer was more common in mid part of esophagus(56%) followed by lower esophagus(38%) and upper esophagus(6%). In 24 patients growth was ulcerative, infiltrative in 18 patients. Stricture noted in 2 patients.

In our study 96% of patients had squamous cell carcinoma, 4% had adenocarcinoma of esophagus. Histopathological examination showed 32% patients had well differentiated, 56% moderately differentiated, 12% had poorly differentiated morphology. Among 50 patients candidiasis is seen in 8 patients of which 5 patients had white patches and 3 patients had white plaques.

Esophageal candidiasis usually responds well to antifungal therapy. The treatment of esophageal candidiasis is usually systemic. The most commonly used medication for the treatment of esophageal candidiasis is the systemic antifungal with oral fluconazole 200 to 400 mg per day for 14 to 21 days.. For patients who may not be able to tolerate oral medication, the alternative is 400 mg of fluconazole intravenously daily. Itraconazole 200 mg per day orally or voriconazole 200 mg twice daily for 14 to 21 days are other treatment options. Amphotericin B deoxycholate 0.3 to 0.7 mg/kg per day may also be used in patients with nonresponsive candida esophagitis, but it has serious medication side effffects, and clinicians should avoid routine use. Treatment with posaconazole 400 mg twice a day orally for patients with severe and refractory esophageal candidiasis appears to be signifificantly efficient. Patients experiencing fluconazole-refractory esophageal candidiasis (B-II) should be treatedwith itraconazole solution (200 mg/day Po), voriconazole (200 mg B.I.D), or caspofungin (50 mg/day) (A-II). Or intravenous amphotericin B deoxycholate (0.3–0.7 mg/kg/day) can be considered[14].

Conclusion

Esophageal candidiasis has strong assosiation with esophageal cancer. Esophageal candidiasis is also the risk factor for development of esophageal cancer in addition to other risk facors like smoking, alcohol, GERD.

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