

Introduction

- Historically, esophageal candidiasis (EC) in patients with malignancy had been a common infection in the pre-azole era, and it was associated with thrush, cytopenia, and chemotherapy. [1]
- However, the presentation and outcomes of EC in cancer patients in the current era of new cancer treatments and frequent use of azoles as antifungal prophylaxis are scarcely studied.

Objectives

- To investigate the epidemiology, risk factors, and clinical outcomes of EC in cancer patients.

Materials and Methods

Retrospective cohort study

Jan 2017–Oct 2021
(4 years)MD Anderson Cancer Center, TX, USA
(743-beds, cancer hospital)

323 patients with EC*



*Confirmed by biopsy

Risk factors,
clinical features,
and outcomeIndependent risk
factors for
treatment failure

Binary logistic regression analysis

Treatment failure:

Those who needed to extend the treatment over 2 weeks because of a poor clinical response to initial treatment [2], or those who needed to restart anti-fungal treatment because of relapse of endoscopy-confirmed EC within 1 year after a previous treatment

Results

1. Patient characteristics

Characteristics	N=323	%
Sex, male	215	66.6
Age (years), median (IQR)	67	59-73
BMI, median (IQR)	24.6	21.8-29.2
History of smoking	185	57.3
History of alcohol use	129	39.9
Hematological malignancy	34*	10.5
Solid tumor	294*	91.0
Esophageal cancer	95	29.4
Lung cancer	35	10.8
Gastric cancer	33	10.2
Others	161	9.3
Diabetes mellitus	66	20.4
Chronic kidney disease	27	8.4
Chronic liver disease	20	6.2
Esophageal disease	183	57.0
History of esophageal surgery	54	16.7
History of radiation**	74	22.9
Malnutrition	94	29.1
Recent antibiotics use	66	20.4
Recent steroid use	65	20.1
Recent chemotherapy	229	70.9
Recent proton pump inhibitors	215	66.6
Asymptomatic	105	32.5
Odynophagia	47	14.6
Dysphagia	126	39.0
Retrosternal pain	29	9.0
Oral thrush	7	2.2
Co-infection	3	0.9
Endoscopy severity grade [3] (The Kodsi classification)		
1	121	37.5
2	146	45.2
3	43	13.3
4	13	4.0
Treatment failure	28	8.7
ID consultation	20	6.2
Treatment	206	63.8
Fluconazole	202	62.5
Voriconazole	1	0.3
Caspofungin	3	0.9
No active treatment	117	36.2
Fluconazole duration, median (IQR)	14	10-14

2: Comparing EC patients with and without failure of fluconazole treatment

Characteristics, N (%)	Non-Failure (N=175)	Failure (N=27)	p-value
Sex, male	107 (61)	22 (81)	0.04
Age (years), median (range)	67 (30-89)	68 (38-84)	0.88
BMI, median (IQR)	25.3 (21.8-29.5)	24.0 (21.6-27.4)	0.49
History of smoking	94 (52)	13 (48)	0.86
History of alcohol use	66 (38)	13 (48)	0.30
Malignancy type			0.07
Hematological malignancy	21 (12)	0 (0)	
Solid tumor	150 (86)	26 (96)	
Both	4 (2)	1 (4)	
Type of solid tumor			
Esophageal cancer	42 (24)	12 (44)	0.03
Lung	21 (12)	1 (4)	0.32
Gastric	13 (7)	2 (7)	> .99
Diabetes mellitus	34 (19)	7 (26)	0.43
Chronic kidney disease	17 (10)	0 (0)	0.14
Chronic liver disease	10 (6)	1 (4)	> .99
Esophageal disease	83 (47)	21 (78)	0.003
History of esophageal surgery	21 (12)	7 (26)	0.07
History of radiation	32 (18)	9 (33)	0.07
Malnutrition	56 (32)	8 (30)	0.81
Recent antibiotics use	44 (25)	2 (7)	0.04
Recent steroid use	41 (23)	4 (15)	0.32
Recent chemotherapy	127 (73)	17 (63)	0.30
Recent proton pump inhibitors	113/174 (65)	18 (67)	0.86
Asymptomatic	57 (33)	7 (26)	0.49
Odynophagia	28 (16)	4 (15)	> .99
Dysphagia	66 (38)	14 (52)	0.16
Retrosternal pain	16 (9)	3 (11)	0.72
Oral thrush	3 (2)	0 (0)	> .99
Endoscopic severity grade			0.20
Grade 1 or 2	142 (81)	19 (70)	
Grade 3 or 4	33 (19)	8 (30)	
Dose/body weight x days, median (IQR)	27.9 (14.8-45.6)	20.5 (10.5-39.4)	0.11
ID consultation	13 (7)	2 (7)	> .99

3: Multivariable logistic regression analysis of fluconazole treatment failure

Independent predictor	aOR	95% CI	p-value
Esophageal disease	3.88	1.49 to 10.07	0.005

*5 patients had both of hematological and solid tumor

** Sites of radiation included esophagus, lung, thyroid, breast, larynx, and tongue.

Discussion

- To our knowledge, this is the largest study of EC identifying characteristics, clinical manifestations, treatments, and outcomes in cancer patients
- 91% of EC were seen in patients with solid tumor, predominantly esophageal cancer
- Talukdar A, et al. found that 57% (75/132) patients of esophageal cancer had culture positivity for *Candida* species [4]
 - The role of *Candida* in esophageal cancer remains unknown, whether risk factor promoting carcinogenesis
- Importantly, 32.5% patients with EC were asymptomatic and EC was only an incidental finding, concurrent with previous study [5]
 - Cancer patients can have silent EC with a wide variety of endoscopic severity
- Concomitant oral thrush was uncommon (2%), in sharp contrast to a previous small study from our institution (96%) [6],
- Fluconazole was most commonly used as per guidelines but dose was diverse from 100-800 mg and duration was also diverse from 7-28 days
 - However, body weight/dose x treatment days did not significantly differ between failure vs non-failure group
- As *Candida* species and susceptibilities were not identified for most patients, it remains unclear whether the patients' clinical failure was due to resistance to antifungals

Conclusion

- EC is predominantly encountered in patients with solid tumors on no antifungal prophylaxis, especially those with underlying esophageal disease, which is a predictor of azole treatment failure.
- In one-third of patients, EC was asymptomatic, seen only as an endoscopic finding.

References

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