CASE REPORT

Necrotising *Candida* oesophagitis after thoracic radiotherapy: significance of oesophageal wall oedema on CTHirotake Saito,¹ Hiroo Sueyama,² Takanori Fukuda,² Kyuma Ota³¹Department of Radiology, Niigata University Graduate School of Medical and Dental Sciences, Niigata City, Niigata, Japan²Department of Radiology, Niigata Prefectural Central Hospital, Joetsu City, Niigata, Japan³Department of Internal Medicine, Niigata Prefectural Central Hospital, Joetsu City, Niigata, Japan**Correspondence to**Dr Hirotake Saito,
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SUMMARY

Although oesophageal candidiasis is usually a superficial mucosal infection, necrotising *Candida* oesophagitis has been reported to cause oesophageal perforation or lung abscess. We report the case of an elderly Japanese man presenting with painless dysphagia after thoracic radiotherapy for oesophageal cancer. Non-contrast CT demonstrated segmental and oedematous thickening of the oesophageal wall. Endoscopy revealed white plaques on the oesophageal mucosa. The patient's oesophagitis responded to systemic antifungal therapy, and did not lead to oesophageal perforation. He died of recurrent oesophageal cancer several months later. The importance of severe radiation-induced oesophagitis without pain, our pathophysiological hypothesis on the local oedema caused by *Candida* infection and the usefulness of CT in evaluating abnormal thickening of the gastrointestinal tract are discussed separately in the article.

BACKGROUND

Candida spp frequently colonise the upper aerodigestive tract and cause infection under several immunosuppressed conditions including diabetes mellitus¹ and the post-radiotherapy state. Oropharyngeal candidiasis has been detected in 29% of patients undergoing head and neck radiotherapy,² and oesophageal candidiasis was detected in 15% of patients undergoing thoracic radiotherapy.³

Oesophageal candidiasis is usually a superficial mucosal infection associated with white exudative plaques on the oesophageal mucosa.⁴ Although these plaques are sometimes visualised with oesophagitis caused by cytomegalovirus (CMV) or herpes simplex virus (HSV),⁵ empirical antifungal therapy is safe and cost-effective for oesophageal candidiasis.⁶

Necrotising *Candida* oesophagitis (NCE) is a life-threatening pathological condition. It is characterised by transmural inflammatory involvement extending to the oesophageal submucosa and muscle as well as mucosa, and leads to oesophageal perforation⁷ or lung abscess.⁸ Appropriate diagnostic techniques have not been well discussed in the literature.

CASE PRESENTATION

A 78-year-old Japanese man was referred to our hospital for the treatment of oesophageal cancer. His medical history included diabetes mellitus, sepsis due to intramuscular abscess and cerebral infarction. He was diagnosed with clinical

T3N1M0 stage IIIA middle thoracic oesophageal squamous cell carcinoma.

To conserve the antitumour effects of treatment⁹ without chemotherapy-induced neutropaenia, we scheduled two times per day hyperfractionated-involved field radiotherapy alone. The prescribed dose was 36 Gy/24 fractions at the isocentre from opposed anterior–posterior fields (figure 1), and 27 Gy/18 fractions from opposed oblique fields. In spite of the patient's mild dysphagia, he was able to eat a regular diet throughout the 36-day treatment period.

Five weeks after the completion of radiotherapy, the patient visited our clinic and reported dysphagia, which had lasted for the prior 7 days. Pain on swallowing and fever were not present.

INVESTIGATIONS

Serum C reactive protein and β -D-glucan were negative. Non-contrast axial CT demonstrated symmetrical thickening of the upper and middle thoracic oesophagus (figure 2A, B). The attenuation of the thickened oesophageal wall was -2.7 HU (Hounsfield units) on average, which suggested

Figure 1 Anteroposterior portal X-ray image of the irradiation field.

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Figure 2 CT images before and after antifungal therapy. (A and B) Non-contrast axial CT showing oedematous thickening of the upper and middle thoracic oesophagus. (C and D) Contrast-enhanced CT at the same level on day 18 of fluconazole treatment. The thickness of the oesophageal wall decreased.

submucosal oedema. Mediastinal fluid collection, pneumomediastinum and pleural effusion were absent.

Two days after the CT scanning, an endoscopic examination revealed ill-defined oesophageal white plaques (figure 3A) and ulceration (figure 3B). A biopsy from the oedematous and fragile oesophageal wall, which was at high risk of perforation, was not performed.

DIFFERENTIAL DIAGNOSIS

White plaques on the oesophageal mucosa are observed in oesophagitis caused by *Candida* spp, CMV or HSV.

The patient's history of sepsis and inflammation extending into the oesophageal submucosa made NCE the most likely diagnosis. Absence of pain when swallowing was associated with diabetic neuropathy.

TREATMENT

On the day of the endoscopy, fluconazole was intravenously administered at a dose of 400 mg, then reduced to 300 mg daily from day 2 on. The dysphagia responded to antifungal therapy and the patient was again able to eat a semisolid diet. Fluconazole was reduced to 100 mg orally on day 7, and the dysphagia returned. Intravenous fluconazole was resumed at a dose of 400 mg on day 9. The patient's symptoms once again resolved, and oral itraconazole (200 mg) was started on day 17. Contrast-enhanced axial CT on day 18 showed a decrease in the oesophageal wall thickness (figure 2C, D). The total antifungal treatment period was 39 days.

OUTCOME AND FOLLOW-UP

The patient's dysphagia had not returned until the oesophageal cancer recurred at the primary tumour and upper mediastinal node outside the irradiation field 9 months after the beginning of radiotherapy. The patient died 20 days after the recurrence.

Figure 3 Endoscopic findings before antifungal therapy. (A) Ill-defined white plaques on the oesophageal mucosa. (B) Ulceration.

DISCUSSION

We searched for case reports relevant to NCE in PubMed and found three articles.^{7 8 10} We also included another report regarding the case of oesophageal perforation due to angioinvasive *Candida glabrata* oesophagitis.¹¹ Cases of concomitant bacterial infection were excluded. These cases are summarised in table 1.

The lessons learned from this case are summarised as follows: first, the pain related to oesophagitis is not always the initial presentation. Second, *Candida* infection causes oedematous thickening of the oesophageal wall. Finally, CT can clearly demonstrate abnormal thickening of the oesophageal wall.

Severe radiation-induced oesophagitis without pain is a major problem, because the destruction of the mural structure progresses without clinical attention. The discordance between symptoms related to oesophagitis and the gross mucosal appearance is reported in patients undergoing thoracic radiotherapy. In 7 of 82 patients, radiation-induced oesophagitis with a thickly coated ulcer or haemorrhage with or without stricture was endoscopically confirmed despite the patient's low symptom score on the radiation therapy oncology group acute radiation morbidity criteria.³

Candida infection causes local oedema of the oesophageal wall, and this seems to reflect the ability of *Candida* cells to adhere to blood vessels. An experimental rat model revealed that the degree of footpad skin oedema paralleled the number of *Candida* cells in the local lesion.¹² A case of oesophageal perforation with angioinvasive *Candida glabrata* oesophagitis was reported; microscopically, fungal pseudohyphae were observed

Table 1 Cases of necrotising *Candida* oesophagitis

Age (years)	Sex	History	Extent of inflammation	Mortality	Reference number
27	M	Autism, renal failure	Pleura	Alive	7
10	M	Cardiac anomaly, Down syndrome, leukaemia	Pleura	Alive	7
34	F	Diabetic nephropathy	Lungs	Dead	8
62	M	Lymphoma	Oesophagus	Dead	10
40	F	Leukaemia	Pleura	Alive	11
78	M	Cerebral infarction, diabetes, oesophageal cancer, sepsis	Oesophagus	Died of cancer	Present case

F, female; M, male.

in the walls and lumina of blood vessels in the resected necrotic oesophagus.¹¹ *Candida albicans* is known to interact with the vascular endothelium and various component proteins of the extracellular matrix.¹³

We hypothesise that injured or irradiated mucosa is prone to *Candida* infection, and that fungi affect the subepithelial venous plexus to cause a local circulatory disturbance and submucosal oedema.

CT is an excellent tool for detecting abnormal wall thickening of the gastrointestinal tract. Stratified, symmetrical and segmental thickening of the bowel wall is often associated with infectious enteritis, intestinal ischaemia or inflammatory bowel disease.¹⁴ This knowledge is applicable to non-neoplastic and oedematous thickening of the oesophageal wall.

Acute mucosal toxicities during head and neck irradiation are often associated with *Candida* infection, and prophylactic use of fluconazole during radiotherapy is reported to prevent severe oral mucositis and treatment interruption.¹⁵ Whether antifungal prophylaxis can prevent severe radiation-induced oesophagitis or oesophageal perforation should be determined in a randomised controlled trial.

Learning points

- Progressive dysphagia in immunocompromised patients arouses suspicion of necrotising *Candida* oesophagitis.
- Pain is not always the initial presentation of oesophagitis.
- *Candida* infection causes oedematous thickening of the oesophageal wall.
- CT can clearly demonstrate abnormal thickening of the oesophageal wall.

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