

## CASE REPORT

# Chondroradionecrosis of the trachea after definitive radiotherapy for cervical esophageal cancer: A case report

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## Abstract

Chondroradionecrosis (CRN) is an infrequent phenomenon after definitive RT. The clinical manifestation is usually difficult to distinguish from that of tumor recurrence; however, clinicians should be aware of the possibility of CRN.

## KEY WORD

oncology

## 1 | INTRODUCTION

We describe the case of chondroradionecrosis (CRN) of the tracheal cartilage after definitive RT for cervical esophageal cancer. After completing RT, imaging studies showed the lesion regarded as a recurrence. The patient underwent esophagectomy and pathology revealed no residual cancer, with ischemic necrosis and fibrosis of the trachea.

Chondroradionecrosis (CRN) is a rare but serious complication<sup>1</sup> that can be fatal if not managed aggressively. It is a known complication of laryngeal cancer treatment and occurs months to years after the conclusion of radiotherapy (RT).

The symptoms of CRN include hoarseness, dryness, severe pain, and edema; however, these symptoms are similar to those of tumor recurrence.<sup>2</sup> In addition, RT-induced inflammation and tissue fibrosis can be misinterpreted as recurrent tumors on imaging studies, leading to incorrect

diagnosis and management of CRN. Here, we report the case of a cervical esophageal cancer (CEC) patient with CRN of the trachea after 66 Gy of RT, which was misdiagnosed as a tumor recurrence.

## 2 | CASE REPORT

After a thorough review of the medical records of patients treated with definitive RT for CEC, a patient who received concurrent chemoradiotherapy (CCRT) was identified and selected for the study. This study was approved by the institutional review board (IRB #4-2020-1272) at our institution.

A 66-year-old man visited the hospital for dysphagia lasting for 3 months and a weight loss of 4–5 kg in November 2019. The patient had a history of heavy alcohol consumption and a smoking history of 30 pack-years. Initial esophagogastroduodenoscopy (EGD) revealed a protruding mass at the

cervical esophagus, 17–21 cm from the upper incisor (UI). Biopsy was performed, and the patient was diagnosed with squamous cell carcinoma. Positron emission tomography-computed tomography (PET-CT) revealed a hypermetabolic lesion in the cervical esophagus.

The patient received definitive CCRT with two cycles of systemic chemotherapy (1000 mg/m<sup>2</sup> 5-fluorouracil and 60 mg/m<sup>2</sup> cisplatin). The initial RT prescription dose was 60 Gy in 1.8–2 Gy fractions. The RT dose distribution is shown in Figure 1. PET-CT performed after 58 Gy of

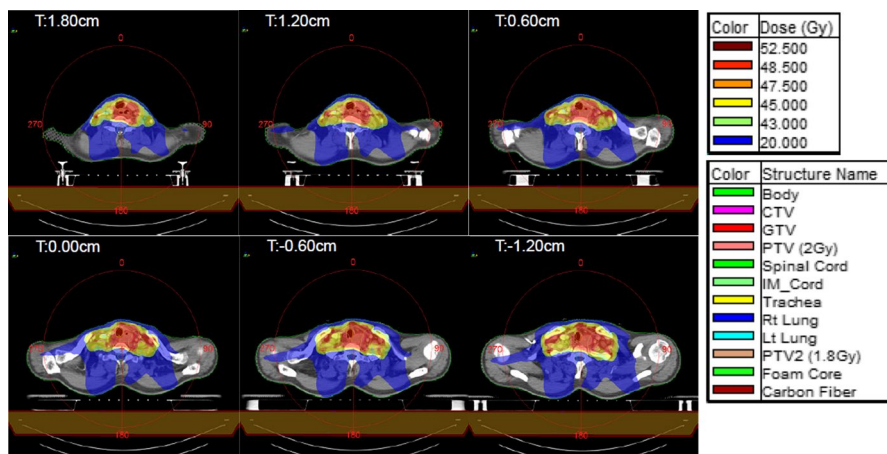


FIGURE 1 Radiotherapy dose distribution for the primary esophageal lesion

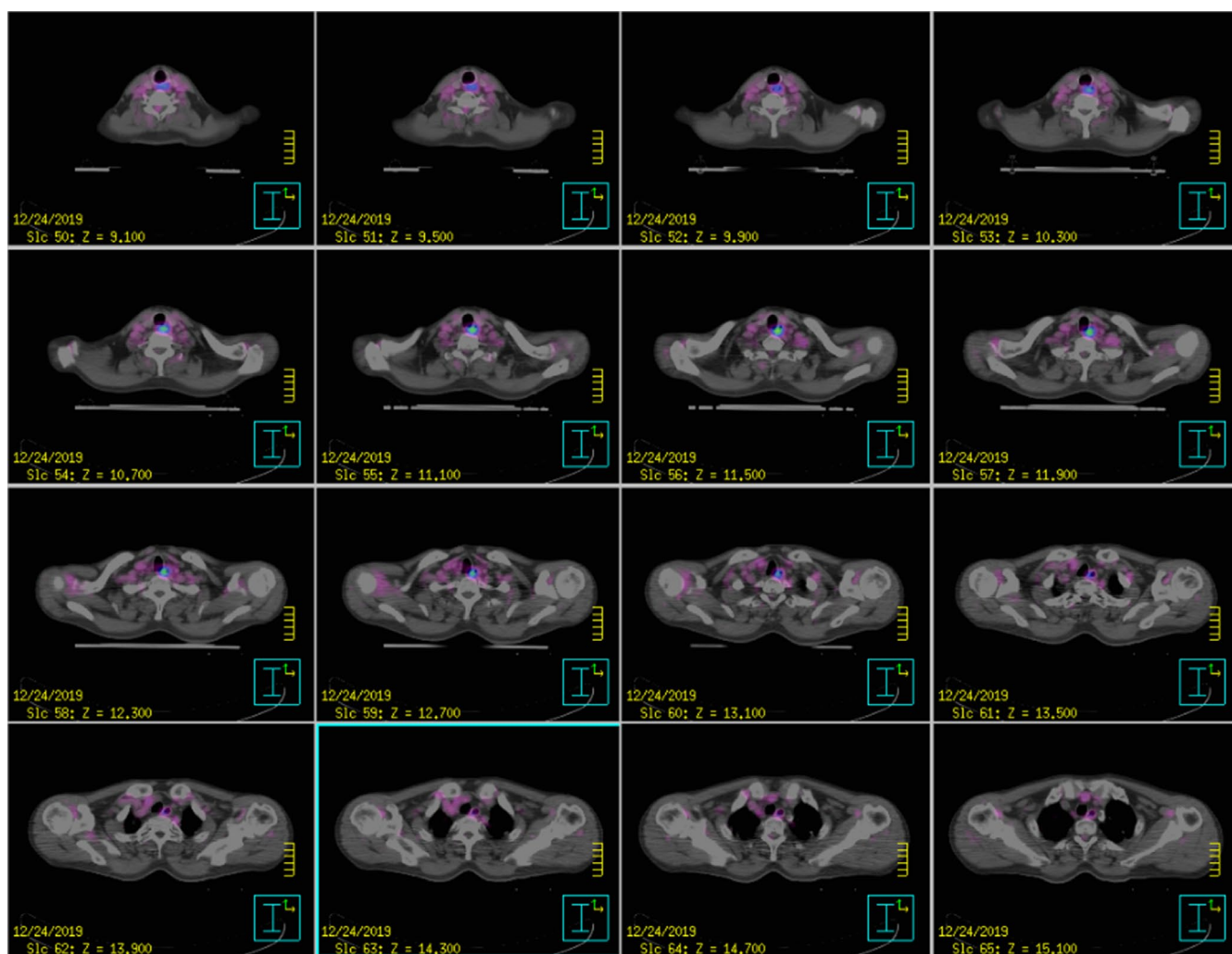


FIGURE 2 Positron emission tomography (PET) image taken after 58 Gy of irradiation showing a residual tumor with fluorodeoxyglucose (FDG) uptake

irradiation revealed a residual tumor with focal fluorodeoxyglucose (FDG) uptake (Figure 2). While the initial intent was 60 Gy of RT in 30 fx, additional irradiation of 6 Gy in 3 fx was prescribed since the patient desired the most all aggressive treatment possible.

Chest CT performed 2 months after the conclusion of CCRT showed mild esophageal wall thickening in the thoracic inlet. PET-CT showed markedly decreased FDG uptake in the cervical esophageal tumor but showed a focal hypermetabolic lesion in the upper esophagus (Figure 3). Although an EGD biopsy showed ulceration with chronic non-specific inflammation of the ulcerative lesion located 17–21 cm from the UI, the lesion was clinically regarded as a viable residual lesion and the patient was recommended to undergo total laryngectomy for the assumed residual lesion. However, the patient feared losing his voice and was hesitant in making a decision.

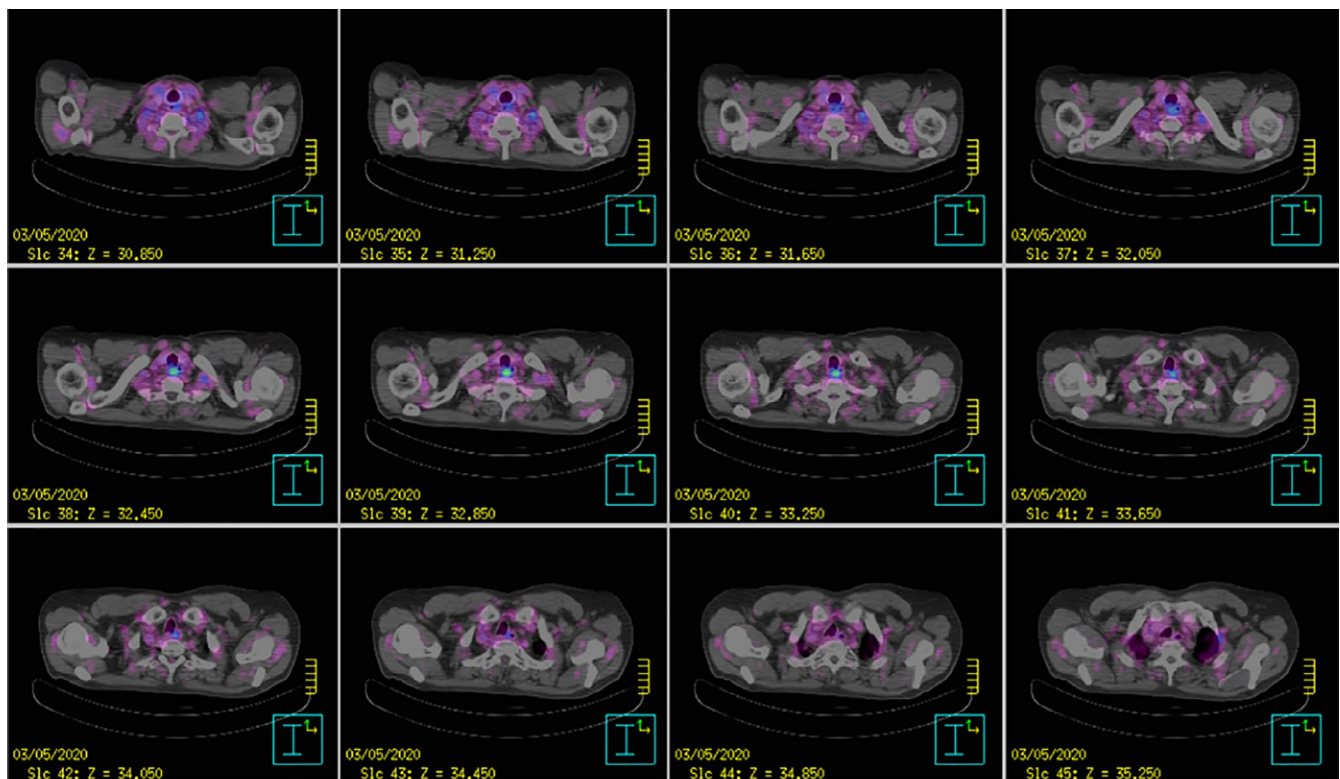
In April 2020, the patient visited the emergency room for throat pain, fever, and dyspnea. Chest CT showed the localized cervical esophageal rupture with abscess formation at the C6-T1 spine level (Figure 4). He underwent emergency esophagectomy with total laryngectomy and hypopharyngectomy, along with mediastinal tracheostomy. The pathology report showed no residual cancer, with ischemic necrosis and fibrosis of the trachea (Figure 5).

The latest follow-up in November 2020 showed no evidence of tumor recurrence or any unusual findings.

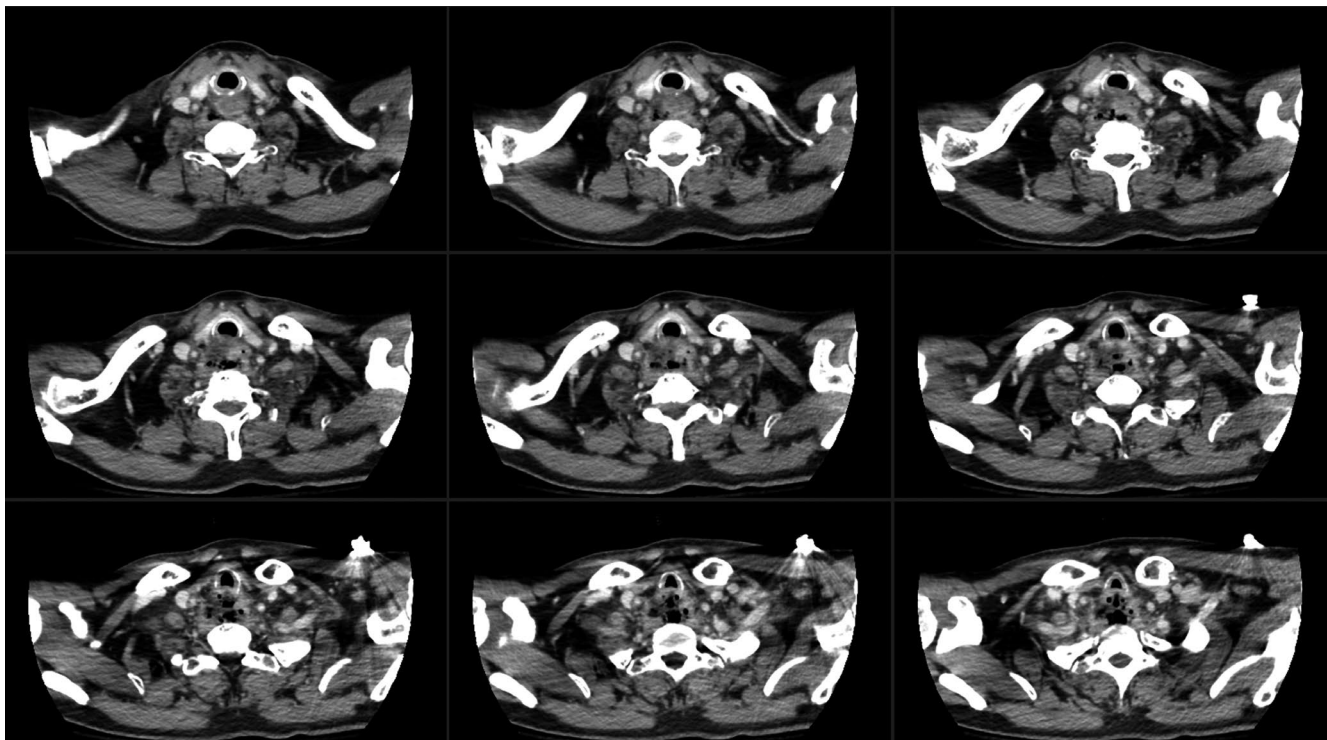
### 3 | DISCUSSION

Here, we report the case of a CEC patient who developed CRN after 66 Gy of RT, which was misdiagnosed as a recurrent tumor. As our patient had a history of heavy alcohol and tobacco consumption, he might have experienced more severe RT-induced inflammation than other patients. Moreover, the patient had a higher risk of developing CRN because the delivered irradiation dose (66 Gy) was higher than the standard RT dose. Nonetheless, clinicians regarded the focal lesion showing FDG uptake to be a recurrent tumor, excluding the possibility of CRN. Such misjudgment resulted in inappropriate early treatment that eventually led to the requirement of surgical treatment due to progressive CRN. If the clinicians had suspected CRN and offered appropriate medical treatment, the patient might have had a different clinical prognosis.

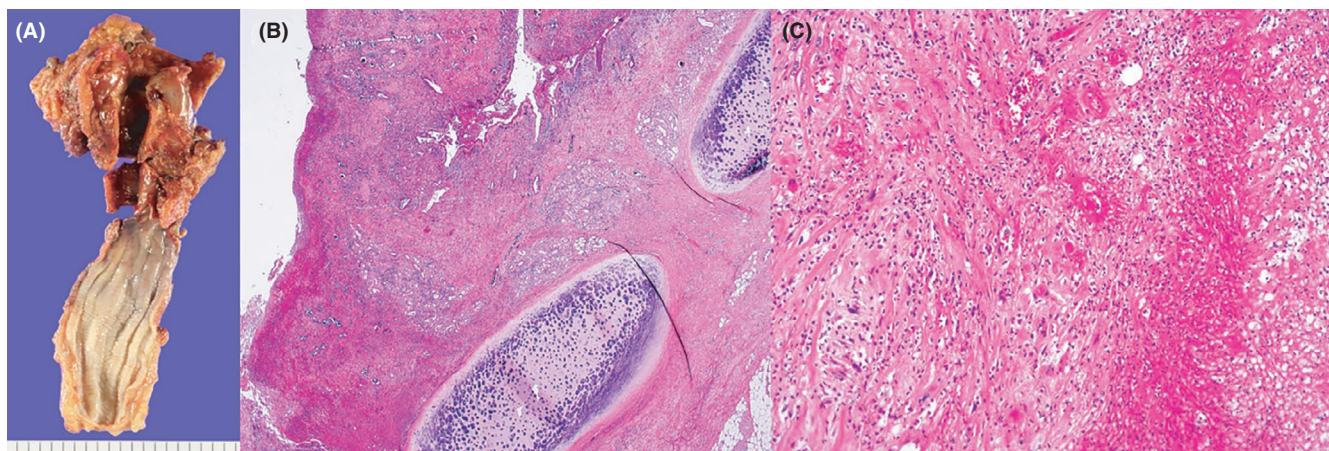
Despite the negative results of the Radiation Therapy Oncology Group dose-escalation trial for esophageal cancer,<sup>3</sup> dose-escalation for CEC is an issue of ongoing debate in radiation oncology. A previous study on CEC showed that high-dose RT (>59.4 Gy) improved local and locoregional control without increasing severe toxicities.<sup>4</sup> Despite an RT dose-escalation, no case of CRN was reported. Therefore, CRN is a consequence of not only high-dose RT but also a combination of both high-dose RT and other patient conditions. Other risk factors of CRN include prior surgical intervention,



**FIGURE 3** Positron emission tomography (PET) image taken 2 months after the conclusion of concurrent chemoradiotherapy (CCRT) revealing a hypermetabolic lesion in the upper esophagus



**FIGURE 4** Chest computed tomography (CT) image taken at the day of emergency room admission showing esophageal rupture with abscess formation at the C6-T1 spine level



**FIGURE 5** (A) Gross image of surgical pathology. (B) Low-power view of the surgical specimen ( $\times 40$ ). The laryngeal tissue with inflammation and fibrosis is shown. The surface epithelium is degenerated due to diffuse inflammatory process. (C) Coagulative necrosis showing acute inflammation and predominant neutrophil infiltration. The infiltration of band segmented neutrophils with eosinophils is shown ( $\times 200$ )

history of endotracheal intubation, comorbidities such as diabetes mellitus, and smoking history.<sup>1,5</sup> Nonetheless, we should carefully monitor for treatment-related toxicities after high-dose irradiation since dose-escalation can result in severe toxicities such as CRN and esophageal stricture.<sup>6</sup>

Imaging studies may provide a means for distinguishing recurrent tumors from CRN. The typical CT findings of CRN include sloughing of dead cartilage fragments, resulting in defects in the cartilage and cartilage collapse, and the presence of

gas bubbles around the cartilage; however, these changes also occur as inflammatory changes after RT.<sup>7</sup> PET can also be used to distinguish CRN from tumor recurrence, showing a sensitivity and specificity of 80% and 81%, respectively.<sup>8,9</sup> Tissue confirmation with biopsy is eventually necessary; however, due to the uncertainty of biopsy findings, clinicians often misdiagnose CRN as tumor recurrence even when pathology reports show inflammation or tissue necrosis. Although the diagnosis of CRN is clinically challenging, its clinical value is high

since early diagnosis of CRN can prevent unnecessary salvage treatment such as chemotherapy and RT, which may result in a graver prognosis. Long-term regular follow-up of high-risk patients by radiation oncologists is thus necessary.

The management of CRN can differ according to the Chandler criteria.<sup>10</sup> In most cases, CRN presents as grade IV disease, which eventually requires surgical intervention such as tracheotomy and laryngectomy. However, non-surgical treatments, including antibiotics, corticosteroids, and hyperbaric oxygen (HBO) therapy, have also been used for the management of CRN.<sup>11,12</sup>

In summary, CRN is an infrequent phenomenon after definitive RT. The combination of high-dose RT, chemotherapy, and other patient conditions may affect the prevalence of CRN. The clinical manifestation of CRN is usually difficult to distinguish from that of tumor recurrence; however, clinicians should be aware of the possibility of CRN to provide proper management.

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## CONFLICT OF INTEREST

None declared.

## AUTHOR CONTRIBUTION

JK: collected data, analyzed data, and prepared the manuscript. SIK: performed the histological evaluation and provided pathology image. JSC: reviewed the manuscript. CGL: reviewed the manuscript. THK: conceptualized the study, collected data, and prepared the manuscript.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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