Radiotherapy Induced Achalasia-like Esophageal Motor Disorder

Radyoterapiye Bağlı Gelişen Akalazya Benzeri Özofagiyal Motor Bozukluk

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ABSTRACT

Achalasia is known as a neuromuscular disease caused by various reasons. A 59 year-old man was diagnosed with tongue base carcinoma. He underwent tumor excision and lymph node dissection. Due to the close surgical margin and muscle invasion, adjuvant chemoradiation was applied. Fifty Gray (Gy) radiation dose was prescribed to the neck lymph nodes and supraclavicular fossa; and 50 Gy radiation dose was applied to the surgical bed with an additional 10 Gy boost dose. One month after the end of the chemoradiation, the patient came with deglutition disorder. We performed an upper gastrointestinal endoscopy and high-resolution manometric study. High amplitude simultaneous pressure waves which were typical for vigorous achalasia were seen on esophageal manometry. Care should be taken about the possibility of some rare esophageal motility disorders after the chemoradiation therapy especially in the early period.

Key Words: Achalasia, deglutition, deglutition disorder, manometric study, radiotherapy.

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INTRODUCTION

Achalasia is characterized as a failure of relaxation of the lower esophageal sphincter and reduced motor activity in the body of the esophagus, manometrically. If there are nonperistaltic, spastic contractions in the esophageal body, the disease is referred to as vigorous achalasia which was more recently also named as spastic achalasia [1]. Pathophysiologically, it is the degeneration of the plexus myentericus resulting in a lack of inhibitory neurons needed for coordination of lower esophageal sphincter’s relaxation and peristaltic contractions of the body of the esophagus. Histological studies demonstrated the reduction or the absence of the myenteric Plexus consisting of ganglion cells (2). Achalasia can be classified as primary and secondary. The time of onset, age, the duration of symptoms and weight loss are used to differentiate these two entities. There are many causes of secondary achalasia. Radiation therapy is one of the least common of secondary causes. Radiation exposure can denervate ganglionic cells of myenteric plexus and cause achalasia like syndrome (3).

In this context, we report a case to demonstrate an achalasia-like motor disorder of esophageal motility caused by 60 Gy radiation therapy to the neck for tongue base carcinoma. This presentation is extremely rare and unusual. And also we decided to call attention to the point that deglutition disorders caused by motor dysfunction can be seen immediately after radiotherapy as reported in this case.

CASE REPORT

A 59 year-old man was admitted to the hospital with a hard and big tongue base mass. Multiple biopsies were taken from the mass and histopathology revealed a tongue base adenoid cystic carcinoma, which developed from the posterior part of the tongue and progressed anteriorly. The patient underwent wide local excision and neck lymph node dissection. The pathologic specimen showed close surgical margin and muscle invasion. Perineural invasion and angiolymphatic invasion were positive.

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There were 22 reactive lymph nodes and no metastatic lymph node. According to the unfavorable prognostic factors adjuvant concurrent chemoradiation was applied. Three dimensional conformal radiation therapy planning was performed. Surgical bed was irradiated with a total dose of 50Gy and an additional 10 Gy boost was prescribed to the tumor bed. The total dose of neck and supraclavicular fossa was stopped at 50 Gy due to the uninvolved lymph nodes. Daily applied fraction dose was 2 Gy. Esophageal maximum and minimum doses were 1.8 Gy and 48.86 Gy, respectively. The esophageal mean dose was 32.17 Gy. The percent volume of esophagus receiving 45 Gy (V45) and the percent volume of esophagus receiving 40 Gy (V40) were 35% and 56%, respectively. The radiotherapy course continued for one and a half month. By this time he had no deglutition disorder and no local-regional recurrence. One month after the end of the chemoradiation the patient was referred to the department of gastroenterology with the painful deglutition disorder for both liquid and solid foods, and subsequently his condition became more severe by the onset time. His daily-life was restricted by the progressive deglutition disorder. And his quality of life was deteriorated by this disorder. On admission there was an unintentional weight loss despite the patient’s good appetite. An upper gastrointestinal endoscopy was applied. There were normally functioning esophagogastric junction and a mildly dilated esophagus with no evidence of esophagitis, stricture or tumor. Esophageal high-resolution manometry was performed. An achalasia like motor disorder was detected with uncoordinated, high amplitude and simultaneous contractions of the body of esophagus in all of the swallows. However, lower esophageal sphincter pressure and its relaxation were normal as shown in the Figure 1.

The uncoordinated and simultaneous contractions of the body of esophagus and the loss of the normal peristalsism caused deglutition disorder in this patient. We think that radiotherapy acutely denervated ganglion cells of the myenteric plexus. After the end of the chemoradiation, deglutition disorder occurred in only one month. He had no complaint and had a routine endoscopic examination with normal findings before the radiation therapy.

DISCUSSION

Achalasia is a disorder which classically means a failure of relaxation and aperistalsism. Achalasia can be classified as primary and secondary. These can be differentiated based on the onset of symptoms. The combination of onset in older age (50 years), shorter duration symptoms (<1 year), and significant weight loss are important factors for the diagnosis of secondary achalasia. Primary achalasia makes up most of the (nearly 90%) achalasia diagnosed patients. Secondary achalasia consists of Chagas disease, pseudoachalasia, post surgical and autoimmune disorders, infections, malign disease etc.. Clinical features of idiopathic achalasia closely mimic achalasia secondary to radiotherapy and also may have the same manometric features. Secondary achalasia has been reported with a wide variety of tumours such as stomach or pancreatic adenocarcinoma. Also hepatocellular carcinoma can cause secondary achalasia (4).

Mechanisms underlying the pathogenesis of radiation-induced gastrointestinal damage are still under investigation. Epidermal growth factors, interleukins, and tumor necrosis factors have also been implicated in the pathology of the effects of radiotherapy on esophagus [5]. Histologic studies of the esophagus of irradiated patients have demonstrated epithelial thickening, chronic inflammation, fibrosis of the submucosa and muscularis propria, and rarely chronic ulceration (6).

Late term effects of radiation therapy often manifest as dysphagia, altered motility due to fibrosis or muscular damage possibly with accompanying nerve injury. Examination of the esophagus may show strictures as well as disruption of peristalsis at the level of the irradiated esophagus with uncoordinated and non-peristaltic waves above and below the irradiated region. Abnormal peristalsis has been reported 1 to 3 months after the treatment completion (7). Also, as in our case, a high-resolution manometry is used to demonstrate uncoordinated and simultaneous contractions of the body of esophagus caused by radiotherapy in the first month.

Development of radiation-related late complications are dose dependent, and the dose, at which 5% of patients will develop later complications within five years after the end of the radiation therapy, has been estimated to be 60 Gy when one third of the length of the esophagus is irradiated (8). As in this case radiotherapy mainly affected the body of the esophagus.

Regardless of excitatory ganglion neuron impairment, inhibitory ganglion neuron dysfunction is an early manifestation of achalasia, and these neurons mediate inhibition and ordered extension of esophageal peristalsism (9). Reduction of peristalsism is a result of the affected neurons. This can be a clue to explain the physiologic abnormalities of achalasia. Impaired inhibitory innervations of the smooth muscles of the esophagus above the lower esophageal sphincter is difficult to demonstrate because of the absence of resting tone in this region. When smooth muscles are affected, contraction force decreases, but coordination and peristalsism are not impaired. Smooth muscles are not likely to be affected.

We ruled out all the reasons that can cause secondary achalasia by upper gastrointestinal endoscopy and a magnetic resonance imaging (MRI) of the abdomen. And there was no other cause for deglutition disorder. On the other hand our patient was older than those with typical idiopathic achalasia onset and had shorter duration of dysphagia and unintentional weight loss just after the radiation therapy although his primary carcinoma was under control. In the present case, dysphagia due to achalasia like motor disorder was probably caused by 60Gy radiation given for tongue base carcinoma. Irradiation and chemotherapy might denervate myenteric plexus for developing dysphagia in a short time. We thought that the effects of radiotherapy may not reach the lower esophageal sphincter but by that time radiotherapy will subsequently affect lower esophageal sphincter.

CONCLUSION

Through a demonstration of a case we propose that 60 Gy radiation can cause esophageal motor disorder and care should be taken for this condition. Esophageal neurons of myenteric plexus can be denervated from the body to the lower sphincter of the esophagus.

Conflict of Interest

No conflict of interest was declared by the authors.

REFERENCES


