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LETTER TO THE EDITOR

Delayed radiation myelopathy after concurrent chemoradiation for hypopharyngeal-esophageal carcinoma

LAM CHAN[1], WINNIE YEO[1], SING F. LEUNG[1], JAMES GRIFFITH[2], ENDERS K.W. NG[3] & ANTHONY T.C. CHAN[1]

[1]*Department of Clinical Oncology,* [2]*Department of Diagnostic Radiology and Organ Imaging, and* [3]*Department of Surgery, Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong*

To the Editor:

History

A 73-year-old man presented to us in May, 2000 because of progressive dysphagia for 3 months. Upper gastrointestinal endoscopy revealed a tumor mass resulting in tight stricture of the lower hypopharynx and upper esophagus. Biopsy of the tumor mass showed it to be a poorly differentiated squamous cell carcinoma. Computed tomography revealed that the tumor was large (8 cm long $\times$ 4 cm deep $\times$ 5 cm wide) and extended from the lower hypopharynx to the upper-thoracic oesophagus (Figure 1). No neck, thoracic or abdominal metastases were evident. Pre-treatment stage was T3/T4 N0 M0 carcinoma of cervical to upper thoracic esophagus with hypopharyngeal extension. The patient was reluctant to acccept surgery, and opted for chemoradiation.

Radiation therapy was delivered with 10 MV photons through a pair of anterior and posterior opposing radiation ports to a planned total dose of 50 Gy in 2 Gy fractions, in two phases. In phase I, the radiation port spanned from the C3 vertebral level down to T5 level, and 30 Gy was delivered. In phase II, despite the use of 3-dimensional conformal radiation therapy planning, it was found that lateral-oblique ports could not be used to avoid the spinal cord satisfactorily, owing to the broad lateral and posterior extent of the tumor. Instead, radiation with a similar setting to phase 1 was used. A final dose of 44 Gy was delivered in 2 Gy fractions, 5 fractions per week, to the target volume. The radiation dose was lower than the usual dose (of 50 Gy) used in curative-intent chemoradiation for esophageal carcinoma, in order to minimize injury to the spinal cord. Concurrent chemotherapy comprised cisplatin 60 mg per m^2 on Day 1 and Day 22, and 5-fluorouracil 200 mg per m^2 per day by continuous intravenous infusion on Days 1–5 and Days 22–26. The patient defaulted follow-up 4 weeks after completing chemoradiation therapy, at which time his swallow function had not shown improvement.

In July 2002 (26 months after chemo-radiotherapy), he presented to us with a month's history of progressive bilateral lower limb weakness, which was associated with urinary retention. The symptom of dysphagia had completely resolved. Examination showed bilateral spastic paraparesis with pin-prick sensation diminished from the T8 level downwards. Magnetic resonance imaging (MRI) revealed a long segment of intense edema (similar to cystic myelomalacia) centrally in the spinal cord from C5 to T4 (Figure 2a). Small foci of contrast enhancement were present at the C7 and T1 levels (Figure 2b). A diagnosis of delayed radiation myelopathy was made. Despite transient improvement of his lower limb power to grade 3/5 after a course of rehabilitation, 8 months later his power progressively deteriorated again to grade 0/5, and he became chair-bound. Follow-up MRI in December 2003 showed moder-

Correspondence: Prof. Anthony T.C. Chan, Department of Clinical Oncology, Prince of Wales Hospital, 30–32 Ngan Shing Street, Shatin, Hong Kong SAR, China. Tel: (852)-2632 2118. Fax: (852)-2648 7097. E-mail: anthony@clo.cuhk.edu.hk

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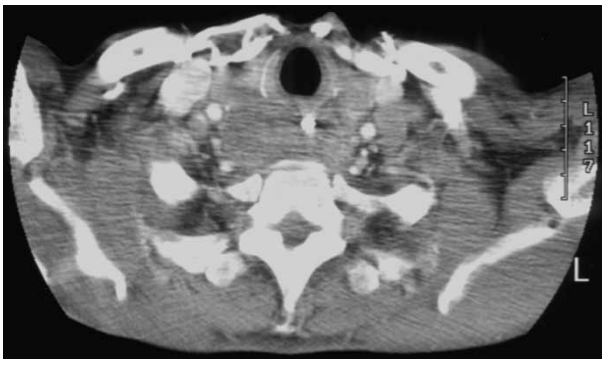

Figure 1.

ate severity focal cord atrophy (Figure 3). Esophagoscopy showed no residual tumor in the hypopharynx and esophagus.

Discussion

Delayed radiation myelopathy, also known as chronic progressive radiation myelopathy, is a rare but recognized late complication of radiation therapy [1–2]. The condition had been reported following radiotherapy treatment of nasopharyngeal carcinoma, oropharyngeal, esophageal, and lung carcinoma. Time of onset of symptoms following radiation therapy is variable, and ranges from 12 months to 8 years. Typical symptoms are those of a slowly progressive ascending sensorimotor disturbance. MRI has enabled both an early and specific diagnosis of radiation myelitis. The imaging reveals central cord swelling confined to the irradiated field (the latter being reflected by fat accumulation within the irradiated vertebrae). Confinement of the abnormality solely to the irradiated area helps distinction from the main differential diagnosis of segmental transverse myelitis. MRI also facilitates exclusion of other diseases that may give rise to similar symptoms such as vertebral metastases, leptomeningineal infiltration or degenerative canal stenosis.

Figure 2.

Figure 3.

According to one series of radiation myelopathy [3] comprising seven patients after treatment of nasopharyngeal carcinoma, MRI performed 1–4 months following onset of neurological symptoms showed similar abnormalities in all patients. Follow-up imaging revealed discernible cord atrophy as early as 10 months following onset of symptoms. Cord contrast enhancement was not apparent after 22 months. As radiation myelitis is a rare condition, the prognostic relationship between the severity of MRI changes and clinical progress has not been determined.

The mechanism of radiation-induced myelopathy is not known. According to one radiological-pathological study [4], cord injury was most pronounced in the lateral corticospinal tracts and posterior columns. Although the MRI findings initially resemble syringomyelia and cystic myelomalacia, the initial prompt resolution suggests the radiological appearance to be most likely due to intense central cord

edema as a result of increased vascular permeability brought along by radiation-induced endothelial damage.

As regards the question of whether the risk of myelopathy is increased in the setting of concomitant chemo-irradiation, in the literature there is another similar case report concerning development of unexpected radiation myelopathy in a patient with non-Hodgkin's lymphoma treated with high-dose chemotherapy with autologous hematopoietic cell transplantation and involved field radiation [5]. In our patient, no special predisposing factor for radiation injury (e.g. diabetes, hypertension, vascular insufficiency) was apparent. The radiation dose level and planning administered was reviewed and confirmed to be within the safe limit for spinal cord tolerance [6]. Apart from reporting an uncommon complication of treatment in a cancer patient, our case can provide further evidence that concurrent application of chemotherapy (especially cisplatin and 5-fluorouracil, which have both been associated with neurotoxicity) could have enhanced radiation injury to the spinal cord.

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