Case

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Pontine Necrosis Related with Radiation Therapy, Complicated with Spontaneous Hemorrhage

Highlights

- Radiation therapy (RT) is frequently used for treatment of head and neck cancer.
- RT might induce vascular injury, such as telangiectasia and endothelial cell injury.
- These vascular injuries may result in spontaneous hemorrhage in necrotic brain.
- Physicians should be aware of complication, as brain necrosis with hemorrhage.
ABSTRACT

The brain necrosis induced by radiation therapy (RT) is an uncommon pathology of brain. A case of spontaneous hemorrhage at necrotic brain is also rare. A 52-year-old man who had nasopharyngeal carcinoma and had been treated with RT, presented with gait disturbance, dizziness, ataxia, dysarthria, and dysphagia. Magnetic resonance imaging (MRI) demonstrated progressed radiation necrosis of pons, and spontaneous hemorrhage at the site of necrosis. The hematoma was diminished by conservative treatment. However, the patient's neurologic symptoms did not recover. Two years later, spontaneous bleeding recurred at necrotic brain. His neurologic symptoms worsened. One year later, his neurologic symptoms were more progressed. He showed severe dysphagia, profound weakness and respiratory failure. This case provides the description of relapsed spontaneous hemorrhage and medullary dysfunction caused by pontine necrosis and progressed post-radiation injury, complicated with hemorrhage, and urges caution in that the necrotic brain tissue may be vulnerable to bleeding.

Keywords: Radiation Necrosis; Radiation Therapy; Pontine Hemorrhage

INTRODUCTION

The brain necrosis is an infrequent late complication related with radiation therapy (RT), and usually induces progressive and irreversible process, and requires medical or surgical treatment [1,2]. Most cases are related with cancer and got therapeutic RT. Nasopharyngeal carcinoma, usually treated with RT, were reported by several late complications, and infrequently reported for brain necrosis [3-5]. Thus, for physiatrists, post-radiation brain necrosis is a cause of burdens for disabilities.

In this case report, we describe a patient with pontine demyelination and necrosis, who had been treated with RT for nasopharyngeal carcinoma. Spontaneous bleeding occurred after necrosis, twice. The recovery of patient was significantly impaired and showed poor
prognosis and medullary dysfunction, due to progression of radiation injury and re-bleeding likely caused by brain necrosis.

CASE REPORT

A 52-year-old man was presented with gait disturbance, dizziness, ataxia, dysarthria, and progressed dysphagia in December 2009. The patient had nasopharyngeal carcinoma, stage IV (T4N2M0) involving sphenoid, infratemporal fossa and skull base and was treated with radiation therapy (RT, total dose of irradiation 85GY) and chemotherapy for 2 years ago. After treatment, his cancer was diminished as clinical remission. Magnetic resonance imaging (MRI) showed contrast enhancing lesion with edema (Fig. 1). The lesion was revealed as post-radiation brain injury by magnetic resonance (MR) spectroscopy, for differential diagnosis from metastatic cancer (Fig. 1). And then he got steroid therapy for 1 year. After then, his dysphagia and dysarthria was getting worse. For evaluation of neurologic progression, he underwent MRI study again. The MRI study revealed progressed necrosis of pons, and spontaneous hemorrhage at the site of necrosis (Fig. 2). After diagnosis, he was referred
to rehabilitation department. Manual muscle test showed grossly good grade of muscle strength, however, Berg balance test showed 6 of 56. The score of modified Bathel index was 31. Speech evaluation showed mild impairment of verbal communication (AQ 91.6) and severe ataxic dysarthria. Videofluoroscopic swallowing study (VFSS) revealed direct aspiration of thin barium (Dysphagia Outcome and Severity Scale [DOSS] 4). He got rehabilitation therapy and corticosteroid therapy for 16 months after diagnosis of hemorrhage. The spontaneous hemorrhage was diminished by conservative treatment. However, despite of physical therapy for standing and balance, and occupational therapy for dysphagia, the patient’s neurologic symptoms did not recover. His ataxia, weakness and dysphagia were slowly progressed. Berg balance test showed 4 of 56. Manual muscle test showed grossly fair+ to good− grade of muscle strength in whole limbs. He did not ambulate without wheelchair, diet with dysphagia modification and liquid restriction (DOSS 3). Several months later, He got spontaneous hemorrhage in pons again, and demyelinating lesion was more progressed to cerebellum and medulla (Fig. 3). His mental function was relatively preserved; mini-mental screening test reveal 23 of 30 point. Weakness of whole limb worsened more (fair grade in whole limbs), and his dysphagia also more deteriorate (DOSS 2 on VFSS). He did not maintain oral diet. For management of dysphagia, he was taken percutaneous endoscopic gastrostomy (PEG). One year later after PEG, his neurologic symptoms were getting worse. He suffered from medullary dysfunction, such as respiratory difficulty, and profound weakness of whole limbs (poor grade in whole limb), despite of continuous oral steroid therapy. He used home-ventilator system for respiratory failure.

DISCUSSION

Radiation therapy can cause significant injury to any part of the central or peripheral nervous systems. For brain, several type of complications had been classified acute encephalopathy, early delayed encephalopathy, focal cerebral necrosis, and diffuse cerebral injury [6]. Acute encephalopathy occurs during the first several days of treatment and consists of headache, nausea, fever, and somnolence. Acute encephalopathy was treated by corticosteroids. Early delayed encephalopathy is a broad designation referring to reversible clinical and radiographic worsening occurring from a few weeks up to several months after brain irradiation. The clinical and radiographic changes generally improve over a few months [6]. Focal cerebral radiation
necrosis can occur after treatment of primary or metastatic brain tumors, or following incidental irradiation of the brain during treatment of extraneural tumors such as pituitary adenoma, nasopharyngeal carcinoma [5,7]. Diffuse cerebral injury is most frequent form of post-radiation brain injury and can cause neuro-cognitive deficit [8,9]. Drug for enhancing cognition, such as methylphenidate, donepezil, were used for treatment for diffuse cerebral injury [6].

For classification, radiation-induced brain injury, based on MR findings, are generally regarded as a white matter lesion alone 17.5%, white matter lesion with contrast enhanced lesion 85.8%, white matter lesion with contrast-enhanced lesion and cyst 14.1% [10]. The outcome or complication of brain necrosis is not well known. The necrosis in brain induced by RT for treatment of nasopharyngeal carcinoma were reported several times [3,4,11]. In addition, the necrotic brains after RT were more frequently encountered at considering whole cancer. However, the reports of necrotic complication were diminished in recent period [12]. Moreover, hemorrhagic complication within necrotic brain is rare. These late complications for RT usually occur in several months to several years after RT [13]. The incidence of late brain injury would increase with increment of total dose of radiation, especially more than total dose of 54 Gy, or fractions of 2 Gy/day [14,15]. The higher total doses (85 Gy) might be main causative factor in this case. The possible reasons for poorer prognosis of this case might be the location of necrosis; surgical treatment may be not considered for pontine necrosis, in contrast with temporal lobe necrosis [16].

![Fig. 3. Axial views of the spontaneous hemorrhage within necrotic pons, with more progressed demyelinating lesion, extended to cerebellum and medullar.](https://e-bnr.org)
The RT usually induces vascular injury, such as telangiectasia and endothelial cell pathology [17-19]. Thus, these vascular injuries may result in spontaneous hemorrhage in necrotic brain. These complications often occur in very late period and show continuous progression by several cytokines, such as tumor necrosis factor-alpha, interleukin 6 and vascular endothelial growth factor [20]. The pathologies of radiation necrosis with hemorrhage are gliosis and proliferation of vessels with thin walls with fibrinoid necrosis [6,17]. Blood-brain barrier (BBB) disruption is also early finding of RT [21]. Thus, vascular hypothesis is one of possible pathophysiology of spontaneous hemorrhage in post-radiation necrosis. RT induces injury of endothelial cells and disruption of BBB, chronic vasogenic cerebral edema, ischemia, demyelination, and necrosis [17-19]. Therefore, neo-vascularization and telangiectasia with thin walls might cause spontaneous intracerebral hemorrhage.

Medical treatments for radiation-induced brain injury were well known as corticosteroids for counteracting vascular endothelial damage and blocking the pathogenic inflammatory processes. Long-term therapy is often necessary to provide symptomatic control, which may result in immunosuppression, myopathy, psychiatric disturbances, osteopenia, glucose intolerance, abnormal fat distribution, or poor wound healing. Recent treatment of post-radiation necrosis was introduced by bevacizumab, as an angiogenesis inhibitor, which a drug was inhibiting vascular endothelial growth factor A [5,22]. Usual dosages of bevacizumab are a dose of 5 mg/kg every 2 weeks or 7.5 mg/kg every 3 weeks. These regimens have been shown to reverse neurocognitive deficits, cerebral edema, and enhancement on MRI in patients with malignant gliomas [22].

In this case, during early stage of pontine necrosis, the symptoms of patient responded for corticosteroid. However, the patient did not respond for corticosteroid in late stage. Finally, the patient suffered from medullary dysfunction, typical neurologic progression of brain necrosis induced by RT.

Most clinicians usually know about necrosis, one of serious complication for RT. The RT usually induces vascular injury, such as telangiectasia and endothelial cell pathology. Thus, these vascular injuries may result in spontaneous hemorrhage in necrotic brain. This case report describes pontine necrosis with progressed radiation injury, complicated with hemorrhage, and urges caution in that the necrotic brain tissue may be vulnerable to bleeding. Physicians would be aware of critical side effect such as brain necrosis, and should be cautious about radiation therapy.

REFERENCES


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