Acute Ischemic Stroke Following Radiotherapy to Nasopharyngeal Carcinoma: A Case Report

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Abstract—Acute ischemic stroke following radiotherapy is rare but can be encountered as an early adverse event during head and neck radiotherapy. We presented a 45-years-old woman with ischemic stroke after receiving intensity modulated radiation therapy. She was admitted for acute onset of bilateral upper motor neuron paralysis and somnolence during the course of radiation therapy for her recently diagnosed nasopharyngeal carcinoma. Magnetic resonance imaging showed acute infarction and multiple intermittent arterial narrowing on MR angiography. Treated with corticosteroid, she was rapidly recovered. The radiotherapy to the head and neck may have provoked acute intracranial inflammation causing vasculitis and resulting in ischemic stroke in this patient. Treatment with administration of corticosteroid should be considered in radiation-induced ischemic stroke.

Keywords —radiation; ischemic stroke; vasculitis.

I. INTRODUCTION

It is well known that an ischemic stroke can be one of late complications of cranial radiotherapy.¹,² The exact mechanism by which radiotherapy increases the risk of late stroke is not fully understood. Radiation-induced atherosclerosis, vasculitis, vascular malformation, and vasospasm are the primary causes of radiation-induced ischemic stroke. Typically, radiation-related stroke is a late onset complication, however, radiotherapy caused acute stroke is rare. In this report, we presented a case of an acute ischemic stroke in the territory of posterior-circulation occurred during the intensity modulated radiation therapy (IMRT).

II. CASE REPORT

A 45-year-old woman was transferred to our hospital because of acute onset of, and progressively worsening, initially left side then bilateral, limbs weakness and somnolence. She was recently diagnosed with nasopharyngeal carcinoma (undifferentiated nasopharyngeal carcinoma, T2N0M0, Stage II) and receiving IMRT (70Gy to the primary tumor and 64Gy to the lymph nodes, divided into 2Gy per fraction per day, 5 days per week) with Erbitux. During the course of receiving the radiation, she reported blurred vision, which was considered as radiation-induced optic dysfunction. After having received 20-fractions of radiotherapy in 4 weeks, she suddenly developed left-sided weakness. She was initially admitted to a local hospital where a computed tomography (CT) of the head without contrast was taken which showed a hypodensity in the right occipital lobe (Figure 1-A). Brain magnetic resonance imaging (MRI) disclosed bilateral occipital acute infarct (Figure 1-B). Brain MR angiography (MRA) showed significant and intermittent narrowing of bilateral middle cerebral arteries (MCA) and posterior cerebral arteries (PCA) (Figure 1-C). A diagnosis of ischemic stroke was made and clopidogrel (75mg/d) was initiated. However, she also developed right limbs weakness, became somnolent and oxygen desaturation on room air in the following 2 days. She was transferred to our Intensive Care Unit (ICU) on the third day after the onset of symptoms. She was previously healthy without hypertension or diabetes mellitus. She rarely or socially drank alcohol and did not use tobacco or illicit drugs. On examination in ICU, her temperature was 36.7°C, blood pressure 160/82 mmHg, pulse was regular at 87 beats per minute, respiratory rate was 19 breaths per minute and the oxygen saturation 98% with 2 liters per minute oxygen via a face mask. She was somnolent. Her muscle strength was diffusely weak but weaker on the left (1/5 proximally, in the left shoulder and hip, and 3/5 distally in the wrist and fingers, British Research Council) than that on the right (4/5 proximally and 4/5 distally). Tendon reflexes were symmetrically depressed. Babinski’s sign was positive bilaterally.
symptoms and signs suggested the presence of a diffusely acute radiation-induced event. The presenting neurologic examination, and neuroimaging findings that were suggestive of a likely radiation-induced vasculitis. She regained consciousness in six days and her muscle strength was significantly improved. LMWH was stopped. She was extubated and transferred to the neurology floor. The dosage of metyprednisolone was tapered down (120 mg/day for 3 days, followed by 80 mg/day for 3 days and 40 mg/day for 3 days) followed by oral prednisone (30 mg/day for 7 days, 20 mg/day for 7 days and 10 mg/day for 7 days). Follow-up brain CT angiography (CTA) at the 16th day revealed significant improvement of blood flow in MCA and PCA territories. Brain MRI at the 23rd day showed a reduction in the size of hyperintensity on T2-weighted image.

Figure 1. CT, CTA, MRI, and MRA of the brain before and after treatment.

The CT scan in Panel A shows a hypodense area in the right occipital lobe (arrow). A diffusion-weighted image (DWI) in Panel B shows a hyperintense focus in the bilateral occipital lobe, more on the right side than on the left, which is suggestive of acute ischemic infarction. Brain MRA shows an intermittent narrowing in both the MCA and PCA (Panel C), a finding that is suggestive of arterial vasculitis. A CT angiography (CTA) scan taken 16 days later shows significant improvement of blood flow in both MCA and PCA territories (Panel D). MRI at the 23rd day reveals chronic infarction in bilateral occipital lobes (Panel E) with improved blood flow on MRA (Panel F).

Considering her progressively worsening symptoms of bilateral limb weakness and somnolence, she was intubated with mechanical ventilation support. The regimen of Clopidogrel was switched to low molecular weight heparin calcium (LMWH). Additionally, she was started on Edaravone (30mg bid), Gangliosides (100mg qd), Rosuvastatin (10mg qd) and several Chinese patent medicines (Urinary Kallidinogenase for Injection, 0.15PNA qd; Butylphthalide and Sodium Chloride Injection, 100ml bid) to improve brain blood circulation. Administration of intravenous metyprednisolone was also initiated because of her clinical history, symptoms, neurologic examination, and neuroimaging findings that were suggestive of a likely radiation-induced vasculitis. She regained consciousness in six days and her muscle strength was significantly improved. LMWH was stopped. She was extubated and transferred to the neurology floor. The dosage of metyprednisolone was tapered down (120 mg/day for 3 days, followed by 80 mg/day for 3 days and 40 mg/day for 3 days) followed by oral prednisone (30 mg/day for 7 days, 20 mg/day for 7 days and 10 mg/day for 7 days). Follow-up brain CT angiography (CTA) at the 16th day revealed significant improvement of blood flow in MCA and PCA territories. Brain MRI at the 23rd day showed a reduction in the size of hyperintensity on T2-weighted image.

III. DISCUSSION

Acute onset of bilateral upper motor neuron paralysis and somnolence in this 45-year-old woman during radiotherapy, at the time having received 20 fractions, strongly suggested an acute radiation-induced event. The presenting neurologic symptoms and signs suggested the presence of a diffusely severe cerebral dysfunction, or encephalopathy. Neuroimaging studies showed acute infarct in the bilateral PCA territories of the posterior-circulation. The underlying mechanism responsible for her clinical presentation was likely the radiation-induced intracranial inflammation causing vasculitis rather than a simple ischemic stroke.

According to the TOAST classification, there are five major etiologies causing subtypes of ischemic stroke, namely large-artery atherosclerosis, cardioembolism, small-vessel occlusion, other determined etiology, and undetermined etiology. Additionally, hematologic disease, use of illicit-drug or oral-contraceptives, and history of migraine can also be causative. However, these etiologies were unlikely responsible for the development of stroke in our patient because she had no such risk factors. The etiology for stroke in our patient was probably due to her underlying radiotherapy for two reasons: first, our patient did not have conventional risk factors for stroke including hypertension, diabetes mellitus and smoking; second, her initial blurry vision may suggest optic nerve dysfunction, which was commonly seen in radiation to the head and neck, may suggest that she is susceptible to radiation. Laboratory and animal studies showed that radiation causes endothelial damage, smooth muscle cell proliferation and migration, fibrosis, and also accelerates atherosclerosis.

Clinical studies showed that patients who have received radiotherapy for head and neck cancer are subject to an increased risk of the late onset of cerebrovascular disease. Radiation-induced atherosclerosis has been thought to be the most common pathogenesis for stroke after radiation, but it is limited to the irradiated area with little correlation to atherogenic risk factors. Radiation-related stroke, typically a late-occurring complication, commonly occurs approximately 5 years after radiation in elderly or 20 years in younger individuals. Thus, the acute radiation-induced atherosclerosis is less likely to occur in our patient after receiving 20-fractions of IMRT. Notably, blood flow in bilateral MCA and PCA was significantly improved on CTA after receiving the 16-days of anti-inflammatory treatment; while it is impossible to restore radiation-induced atherosclerosis in a short period of treatment.

The history of the onset of symptoms, clinical presentation, and response to anti-inflammatory treatment with rapid clinical improvement of reperfusion of intracranial circulation evidenced by CTA and MRA strongly suggested that a mechanism causing ischemic stroke in our patient was likely to be radiation-induced vasculitis than atherosclerosis. Vasculitis, typically present with characteristic “string-of beads” pattern, can be caused by radiation-induced inflammation and is sensitive to corticosteroid treatment. Our recent study demonstrated that radiation activates microglia and stimulates generation of inflammatory cytokine in the brain in the acute phase which may, in turn, cause acute inflammatory reaction and vasculitis. Digital subtraction angiography is a useful tool in evaluating intracranial vasculitis but its sensitivity is low. The golden standard for the diagnosis of vasculitis is pathological confirmation via tissue biopsy, which was not performed in our patient.

This case highlights a patient, who received head and neck radiotherapy, had an increased risk for acutely developing
ischemic stroke, likely caused by radiation-induced intracranial vasculitis. Prophylactic administration of corticosteroid against inflammation during radiotherapy may be beneficial and is recommended.

REFERENCES


Questions:

1. Which symptom is not included in the diagnostic criteria for reversible cerebral vasoconstriction syndromes?

   A. Severe and acute headache.
   B. Angiography showing multifocal segmental cerebral artery vasoconstriction.
   C. Normal or near-normal CSF
   D. Reversibility of angiographic abnormalities within 6 weeks after onset.
   E. no evidence of aneurismal subarachnoid hemorrhage.

2. Complication of head and neck radiotherapy includes all of the following EXCEPT:

   A. Brain Necrosis.
   B. Nerve Injury.
   C. Vasculitis.
   D. Seizure.
   E. Cardiac failure.

3. Radiation-induced vascular injury includes all of the following EXCEPT:

   A. Vasculitis.
   B. Moyamoya Disease
   C. Stroke
   D. Cerebral hemorrhage
   E. Mitral valve relapse.

Answers:

1. D; 2. E; 3. E.
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