Abstract

Radiation-induced (RI) changes such as radiation-induced cavernous malformations (RICMs) and radiation-induced cranial neuropathy (RICN) manifest as late delayed complications and can be seen on post-treatment imaging. Cavernous malformations (CMs) are vascular malformations that are made up of dilated, thin-walled capillary spaces without intervening brain parenchyma. Cranial nerve damage due to radiation exposure is a rare consequence of radiation therapy (RT). We present a case of intracerebral CMs/hemorrhagic vasculopathy and left seventh and eighth nerve complex cranial neuropathy 14 years following RT to the brain for tectal glioma.

Keywords: Hemorrhagic vasculopathy, neuropathy of seventh and eighth nerve complex, post-radiation

Introduction

Radiation therapy (RT) continues to be a popular treatment for neoplasms of the central nervous system (CNS). Radiation-induced cavernous malformations (RICMs) and radiation-induced cranial neuropathy (RICN) are late-onset complications seen on post-treatment imaging. Incidence of RICMs increases with an increase in latency interval. Incidence is 4% with 10 years latency increasing to 60% with 25 years latency.[1] The median duration from RT to RICM was 10 years if the dosage was <30 Gy and 4 years when >30 Gy. The latency depends on the total RT received in children below 10 years. A shorter latency is observed if the dosage is >3000 cGy.[2]

RICN develops years after ionizing RT. The latency duration from RT to RICN is on a scale of years. The median latent period for the occurrence of radiation-induced (RI) cranial neuropathy was 8 years. Following irradiation for head and neck malignancies, lower-group nerves (IX–XII) were involved more than the upper (II–VI).[1]

Here, we present a case of post-radiation leukoencephalopathy with multiple cavernoma formations and facial and vestibulocochlear nerve complex neuropathy.

Case History

At the age of 10 years, the patient presented with vomiting and headache increasing on exertion. A fundoscopy examination revealed papilledema raising the suspicion of raised intracranial pressure (ICP). Lateral and third ventricle dilation with normal fourth ventricle suggestive of obstructive hydrocephalus was noted in magnetic resonance imaging (MRI). A rounded non-enhancing tectal lesion with narrowing of the aqueduct of Sylvius was seen as suggestive of tectal glioma.

Ventriculoperitoneal shunt was done to relieve ICP. The patient underwent posterior fossa radiation with external beam radiotherapy at a cumulative dose of 50 Gy administered by 25 fractions. A radiation port with opposing lateral fields centered over the brain stem was used. After completion of the radiotherapy, the symptoms subsided.

Fourteen years post-radiation at the age of 24 years, he presented with an inability to walk and reduced hearing in the left ear for the past 2 months. Audiometry findings revealed a sensorineural hearing loss in the left ear.

MRI showed hyperintensity on T2/fluid-attenuated inversion recovery (FLAIR) in bilateral parieto-occipital white matter suggestive of post-radiation leukoencephalopathy [Figure 1].

Multiple non-enhancing T2 and FLAIR hyperintensities with surrounding hypointense rim are noted in the white matter of bilateral temporo-occipital; cerebellar hemispheres; basal ganglia; pons and midbrain without diffusion restriction. They were hypointense on magnitude and hyperintense on phase images of susceptibility-weighted images (SWI) suggestive of RI vascular proliferation with resultant cavernomas [Figures 2–4].
The left seventh to eighth nerve complex was T2 hypointense with smooth thickening in the intracanalicular portion showing post-contrast enhancement suggestive of post-radiation neuropathy/neuritis [Figure 4].

**Discussion**

Complications of radiotherapy are acute, early delayed and late. Late complications occur after 180 days and include RI vasculopathy [RI capillary telangiectasia (RIT), RICMs, RI Moyamoya pattern, RI microhaemorrhages, mineralising microangiopathy and large vessel steno-occlusive vasculopathy], white matter leukoencephalopathy and RI intracranial neoplasms (meningioma and glioma).[^1]

Capillary telangiectasias are dilated capillaries interspersed with normal brain parenchyma T1 isointense, T2 hyperintense with blooming on gradient recalled echo (GRE). RITs are similar to Type IV cavernous malformations (CMs) (seen only on GRE/SWI) and differ pathologically...
in the presence of intervening brain tissue. Hence, it is postulated that both belong to the common pathway and RIT precedes RICM.\[^4\]

CMs are dilated capillaries with no intervening normal brain. It gives a popcorn appearance on T2 with a hypointense hemosiderin rim. Radiation causes hyalinization and fibrinoid necrosis, resulting in reduced flow inducing hypoxia-inducible factors and vascular endothelial growth factors causing angiogenesis. With aging, these factors decline; hence, RICM is more common in young and more likely to arise as multiple lesions.\[^5\]

Cerebral microhemorrhages are tiny focal hemorrhages seen as punctate regions of signal dropout with blooming on GRE and inapparent on other MRI sequences and computerized tomography (CT).\[^6\]

Moyamoya is collaterals formation due to occlusion of the circle of Willis. Mineralizing microangiopathy is parenchymal calcification in the corticomedullary junction and dentate nucleus.\[^1\]

Large vessel vasculopathy is detected on MR angiography and occurs due to increased atherosclerosis and intima hyperplasia. It is rare due to newer carotid sparing intensity-modulated radiotherapy techniques (IMRT).\[^7\]

Delayed effects of radiation result in atrophy of the cerebrum, demyelination, and gliosis.\[^8\]

Conformal three-dimensional radiotherapy (3DRT) is better than two-dimensional radiotherapy (2DRT) in decreasing the dose to normal tissue.\[^9\] 2DRT is comprised of one beam from one-four directions. 3DRT utilized axial plane and varied tissue contours for accurate dose rendering. IMRT enables modulating field number and the radiation intensity of each field and to sculpt radiation.\[^10\]

Table 1 summarizes the characteristics of post-radiation therapy CNS complications reported in previous studies\[^3,4,11-14\].

### Table 1: Clinical profile of post-radiation therapy CNS complications in various studies\[^3,4,11-14\]

| Authors            | Year | Number of patients | Latency period from exposure to RT to the onset of symptoms | Type of CNS complications and their frequency |
|--------------------|------|--------------------|-------------------------------------------------------------|-----------------------------------------------|
| Poussaint et al.\[^11\] | 1995 | 20                 | 8.1 year                                                   | Post-RT sites of hemorrhage                   |
| Kong et al.\[^10\]  | 2011 | 317                | Mean latency 7.6 years                                       | Lower cranial nerve RICN (IX–XII) -81/317-25.5% |
| Peng et al.\[^12\]   | 2012 | 616                | More than 6 months                                           | Mean incidence of RICN - 30.9%                |
| Passos et al.\[^13\] | 2015 | 100                | 16.7 years                                                  | RICN in 2DRT -8.9%                           |
| Cutsforth-Gregory et al.\[^4\] | 2015 | 31                 | 12 year                                                      | RICN in IMRT -3.5%                           |
|                    |      |                    |                                                             | RICN in 2DRT -84.5%                          |
|                    |      |                    |                                                             | RICN in IMRT 24.8%                           |
|                    |      |                    |                                                             | Overall incidence of late cerebrovascular complications 36% |
|                    |      |                    |                                                             | Microbleeds 29/36 (80.6%)                     |
|                    |      |                    |                                                             | RICM 19/36 (19%)                             |
|                    |      |                    |                                                             | Symptomatic RICM -19%                        |

Cranial nerve damage due to radiation exposure is a delayed rare consequence of RT. Demyelination, coagulation necrosis, or fibrotic changes result in loss of nerve–blood barrier which manifests as cranial nerve thickening and enhancement. RICN appears on MRI as smooth thickening of the nerves with enhancement. Enhancement can occur before symptoms appear and can last for months after symptoms occur.\[^14\] Lower cranial nerves (IX–XII) are involved in RT of head and neck cancers.\[^3,15\]

**Conclusion**

Cranial radiation is an established form of treatment for multiple brain neoplasms, but it can induce secondary pathologies in the post-irradiation period. Thus, one needs to consider the possibility of the development of RI complications, including CM, leukoencephalopathy, and cranial neuropathies as seen in our case, in patients who deteriorate neurologically in the follow-up period after cranial irradiation.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other
clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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