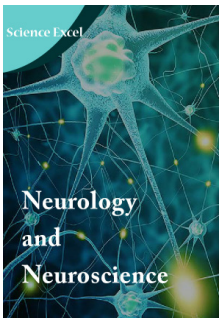
Neurology & Neuroscience

Review Article



Radiation-Induced Cavernoma Progression: Case Report and Literature Review

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- Received Date: May 05 2025
- Accepted Date: May 20 2025
- Publication Date: May 22 2025

Keywords

Cavernoma, Vascular Malformations, Central Nervous System, Adverse Effects, Ionizing Radiotherapy.

Abstract

This article reports a rare case of radiation-induced cavernoma progression in an adult patient following treatment for a brainstem cavernoma. Cavernomas are benign vascular malformations that may occur sporadically or be associated with ionizing radiation. While radiotherapy is effective in treating central nervous system (CNS) tumors and symptomatic cavernomas, it can also induce late adverse effects, such as the formation of new cavernomas. The patient, a 47-year-old man, underwent radiotherapy after experiencing refractory seizures due to a brainstem cavernoma. Initially, clinical improvement was observed, but eight months after treatment, new cavernoma lesions appeared, worsening the clinical picture. Radiotherapy can stabilize existing cavernomas but is also associated with the formation of new ones due to vascular endothelial damage. These effects may manifest years after radiation exposure, with a latency period ranging from 1 to 26 years. Magnetic resonance imaging (MRI) plays a key role in diagnosis and monitoring. Although radiotherapy is a valid option when surgery is contraindicated, long-term follow-up is essential to detect complications and adjust therapeutic strategies.

Introduction

Cavernomas, or cerebral cavernous malformations, are benign vascular lesions composed of clusters of dilated capillaries with thin walls, without interposed neural tissue. These malformations affect approximately 0.01% to 0.5% of the general population and can be of familial origin with autosomal dominant inheritance or sporadic, often related to trauma, vascular anomalies, or prior exposure to ionizing radiation [1,2].

Radiotherapy is an important therapeutic tool in the treatment of CNS tumors and cavernomas that are not amenable to open surgical resection. However, its late adverse effects include vascular changes such as capillary telangiectasias, necrosis, gliosis, demyelination, and even the induction of new cavernomas [3,4].

Radiation-induced cavernous malformations have been described primarily in patients undergoing cranial radiotherapy, especially during childhood, but cases in adults have also been reported. The latency period for their appearance is highly variable, ranging from 1 to 26 years after exposure [5,6].

This article presents a rare case of cavernoma progression induced by radiotherapy in the treatment of a brainstem cavernoma in an adult patient, highlighting the importance of long-term follow-up and imaging surveillance in irradiated patients [7].

Case report

WA 47-year-old previously healthy male began neurological follow-up due to difficult-to-control seizures. A high-field (1.5 Tesla) brain MRI with gadolinium contrast revealed a ring-enhancing lesion within the cavum septum pellucidum, adhered to the left lamina of the septum and the posterior column of the left fornix. A black T2* (WI) ferritin deposit, punctate in the right thalamus, suggested an old hypertensive microhemorrhage. An image consistent with a right ponto-mesencephalic cavernoma was observed, along with hypotrophy of the right medullary pyramid and the anterior right half of the pons (Figure 1).

Given the refractoriness to pharmacological treatment and the significant functional impact of the seizures, fractionated stereotactic radiotherapy was indicated, consisting of 5 consecutive sessions at 4 Gy per fraction, totaling 20 Gy. During the immediate post-treatment period, the patient showed significant clinical improvement with seizure control.

However, eight months after the end of radiotherapy, the patient reported worsening

Citation: Cembraneli PN, Cavalcante JBF, Cembraneli IN, et al. Radiation-Induced Cavernoma Progression: Case Report and Literature Review. Neurol Neurosci. 2025;6(4):016

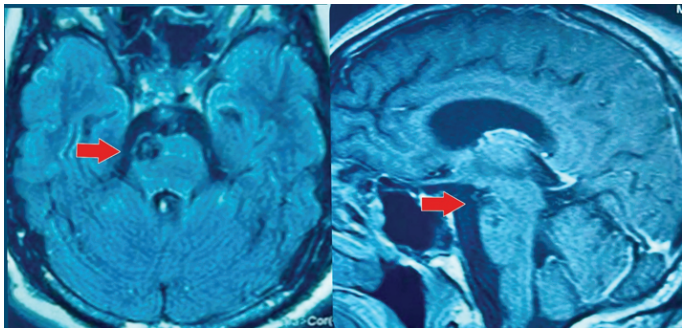

Figure 1. *Axial and sagittal brain MRI showing a hypointense image in the right ponto-mesencephalic region, suggestive of a cavernoma (red arrow).*

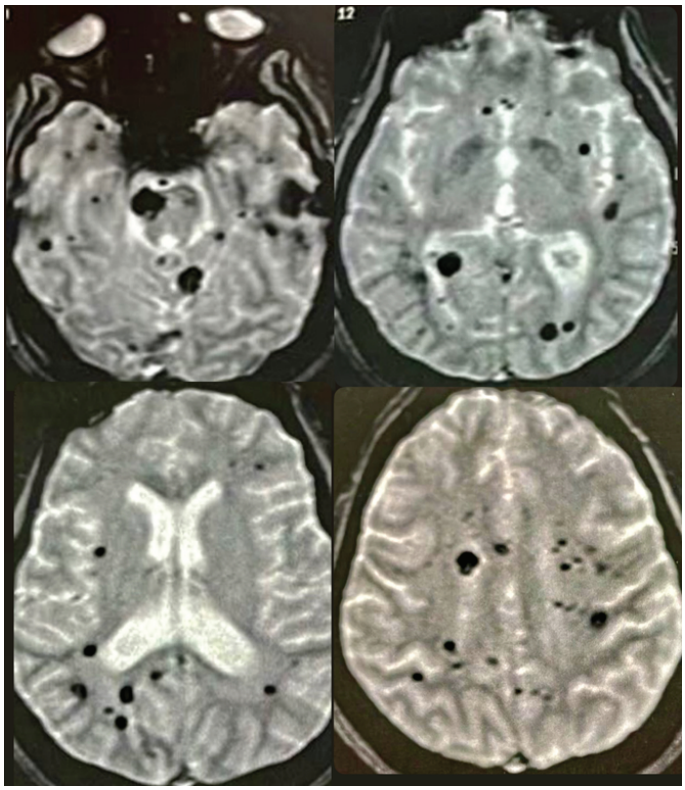

Figure 2. *Axial brain MRI showing multiple isointense lesions without gadolinium enhancement in juxtacortical and deep brain regions, suggestive of multiple cavernomas.*

seizures with increased frequency and intensity, along with the emergence of new neurological deficits.

A follow-up brain MRI revealed multiple lesions suggestive of cavernomas diffusely distributed throughout the brain parenchyma in locations distinct from the initial lesion, consistent with late-onset radiation-induced cavernous malformations (Figure 2).

Discussion

Although radiotherapy is commonly used to treat malignant neoplasms, it can also be indicated for cerebral cavernomas, particularly when they become symptomatic due to refractory seizures or recurrent hemorrhages. It serves as an alternative when surgery is contraindicated due to the cavernoma's location, such as in the brainstem, or when the lesions are multiple and difficult to resect. In selected cases, radiosurgery (such as Gamma Knife or CyberKnife) offers a targeted radiation option with minimal damage to healthy brain tissue [8,9].

Radiotherapy for cavernomas acts via ionizing radiation, which damages abnormal blood vessels, potentially reducing lesion growth, stabilizing the malformation, and preventing further hemorrhagic episodes. However, this approach is associated with significant complications. Notable adverse effects include cerebral radionecrosis due to vascular damage and increased permeability, and the progression or formation of new cavernomas, which may worsen neurological symptoms [10,11]. Neurological deficits, radiation-induced telangiectasias, and even cognitive impairments may also occur depending on the irradiated area [12,13].

Radiation-induced cavernomas are a rare but significant complication of radiotherapy, especially in patients undergoing cranial irradiation. These benign vascular lesions may develop asymptomatically or symptomatically, depending on their size and location. The pathophysiological mechanisms behind their formation are complex and not yet fully understood, but endothelial damage, chronic inflammation, and abnormal vascular proliferation are key factors [14,15].

Ionizing radiation disrupts vascular endothelium, impairing the blood-brain barrier and fostering conditions that promote the abnormal proliferation of blood vessels. Over time, this leads to clusters of dilated, fragile vessels characteristic of cavernomas. Chronic inflammation caused by radiation exposure also plays an important role, with the release of pro-inflammatory cytokines contributing to vascular remodeling [16].

Studies have shown that radiation-induced vascular lesions can be categorized as telangiectasias—dilated vascular formations—and cavernomas—more complex malformations with disorganized growth patterns. Telangiectasias may precede cavernoma formation and often serve as precursors to more severe lesions [17]. In the present case, the increased seizure frequency eight months after radiotherapy suggests lesion progression over time, potentially exacerbated by radiation [18,19].

The latency between radiation exposure and cavernoma development varies widely. Studies report a latency of 1 to 26 years, with an average of 8 to 12 years. This indicates that radiation may have long-term effects, often arising years after oncologic treatment has ended and the patient is in remission [20,21].

Although the presence of cavernomas in adult patients is less common than in children, it is increasingly recognized as patient survival improves. This is especially important as children, with developing neural structures, are more susceptible to long-term radiation effects [22,23].

Radiation-induced cavernomas are well documented in children treated with prophylactic cranial radiation for acute lymphoblastic leukemia. However, adult cases have also been reported, usually linked to high-dose radiotherapy for specific CNS tumors [24].

MRI is essential for diagnosing and monitoring cerebral cavernomas, thanks to its high resolution and ability to highlight specific lesion characteristics. On T2-weighted imaging, cavernomas typically appear hypointense at the center, reflecting old blood or microcalcifications, with a hyperintense rim representing the lesion periphery. T1-weighted images may show a more homogeneous signal depending on recent bleeding. Contrast-enhanced imaging with gadolinium can help

identify active regions or abnormal perfusion and delineate lesion borders, aiding differentiation from other vascular malformations. During follow-up, MRI is vital to detect lesion growth or new hemorrhages, especially using diffusion-weighted imaging (DWI), which provides detailed information for treatment planning [25].

Early diagnosis is crucial to assess lesion severity and initiate appropriate therapy. In this case, worsening seizures and the spread of cavernomatous lesions highlight the need for ongoing monitoring [26].

Treatment approaches vary depending on clinical presentation. Asymptomatic lesions are usually managed conservatively, with regular MRI follow-up to monitor evolution [27,28]. However, symptomatic patients—such as those with refractory seizures or recurrent hemorrhages—may require more aggressive treatment, including surgical resection or radiosurgery, depending on lesion location and hemorrhage risk [29,30].

Surgical treatment of cavernomas must be carefully considered, especially for lesions in eloquent brain regions such as the brainstem, as in this case. The risk of severe neurological complications may limit therapeutic options, necessitating detailed surgical planning [31,32].

Literature has shown that cavernoma development in irradiated patients may remain asymptomatic for years. This underscores the need for long-term follow-up. As seen in this case, new lesions or progression may occur months after completing radiotherapy, reinforcing the importance of continued monitoring [33,34].

Articles suggests that the risk of cavernoma formation increases with higher radiation doses and when irradiation targets particularly vulnerable CNS areas. Therefore, rigorous clinical follow-up with periodic MRIs and ongoing neurological assessments is required [35,36].

Radiotherapy for cavernomas must be carefully planned and used only when benefits outweigh the risks. Long-term follow-up is essential, as radiation's late effects may emerge months or years after treatment. Complications such as new vascular lesions may require additional therapy. Continuous imaging follow-up, especially via MRI, is crucial to assess disease evolution and adjust management accordingly [37,38].

Conclusion

Cavernomas are CNS vascular malformations that, although usually congenital, can arise as a late effect of radiotherapy. This case highlights the importance of ongoing neurological and radiological monitoring in patients undergoing radiotherapy—even in adults—to enable early detection and proper management of these lesions. Early recognition of radiation-induced cavernomas is essential to prevent complications such as seizures and hemorrhages, contributing to improved patient safety and quality of life.

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