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Case Report

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Stroke-like Migraine Attacks after Radiation Therapy (SMART) Syndrome Decades after Cranial Irradiation for Pineal Germinoma: A Case Report

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Abstract

We present a case of a 48-year-old man with SMART syndrome occurring decades after cranial irradiation for pineal germinoma. He developed recurrent episodes of confusion, aphasia, and blurred vision, which had increased in frequency over recent months and was initially confused for recurrent transient ischemic attacks. MRI brain showed multiple cortical and deep microhemorrhages and two macrohemorrhages without acute ischemia. Vessel imaging showed no relevant intracranial or extracranial stenosis to explain his symptoms. CSF analysis revealed elevated protein without pleocytosis or infection, and EEG was unremarkable. Given his history of whole-brain radiation and characteristic imaging findings, he was diagnosed with stroke-like migraine attacks after radiation therapy (SMART) syndrome and referred for migraine management. SMART syndrome is a rare, delayed complication of cranial irradiation that can mimic transient ischemic attack or seizure. This case underscores the importance of recognizing late-onset radiation-induced neurovascular syndromes to ensure accurate diagnosis and appropriate management.

Keywords: *radiation therapy, transient ischemic attack, migraine, ischemic stroke, microbleed.*

Introduction

Stroke-like migraine attacks after radiation therapy (SMART) syndrome is a rare, delayed complication of cranial irradiation, observed in both pediatric and adult patients treated for intracranial tumors or metastases[1]. Clinically, it presents years to decades after radiation exposure with transient focal neurological deficits (e.g., aphasia, hemiparesis, visual disturbances) accompanied by migraine-like headaches[2]. Although most reported cases have a benign course, SMART syndrome remains a diagnostic challenge because it can mimic transient ischemic attack (TIA), seizure, or tumor recurrence[3]. Here, we present a patient with recurrent episodes initially diagnosed as TIAs, later found to have radiation-induced vasculopathy and imaging/clinical features consistent with SMART syndrome, with an unusually long latency and recurrence pattern spanning more than three decades.

Case Presentation

A 48-year-old male was referred to the stroke clinic after multiple episodes of confusion, blurry vision, and aphasia. During these events, he developed difficulty speaking and following commands, accompanied by alternating monocular blurry vision and anterograde amnesia. His blood pressure remained stable during episodes, typically ranging from 140–160 mmHg systolic without significant fluctuations. In the preceding two months, both the frequency and duration of his episodes had increased. He presented to the emergency department several times and was repeatedly diagnosed with TIA.

CT head was unremarkable, while CTA head and neck showed no significant stenosis or occlusion to explain his presentation. MRI brain demonstrated no acute ischemia but revealed multiple cortical and deep microhemorrhages which were initially attributed to hypertension. Laboratory evaluation showed LDL 183 mg/dL and HbA1c 5.0%. Cerebrospinal fluid (CSF) analysis revealed elevated protein[4] (140 mg/dL), 36 RBCs, and 3 nucleated cells/cubic mm (reference ranges <6 cells per cubic mm), with a negative infectious panel. EEG was normal. Upon discharge from the hospital, the patient was started on valproic acid for possible seizure activity, without reported improvement in frequency or duration of episodes over the next few weeks.

He then presented to our Cerebral Vasculopathy Clinic for a second opinion after multiple emergency room visits for recurrent episodes labeled as TIAs or seizures, without improvement after initiation of antiplatelet therapy or anti-seizure medication. A detailed medical history revealed that he was diagnosed with pineal germinoma as a teenager and was treated with whole-brain radiation at age 17. He reported experiencing sporadic, recurrent episodes of aphasia and occasional headaches, five to six in total over the past 30 years, each lasting several hours before resolving spontaneously. The episodes began a few years after cranial irradiation, initially rare but increasingly frequent over the past year. Careful evaluation of his MRI brain scans demonstrated both deep and cortical microhemorrhages, as well as two macrohemorrhages in the right periventricular area (Figures 1 & 2), which were suggestive of radiation-induced vasculopathy[5-6]. Given the remote history of cranial irradiation, recurrent transient neurological episodes, characteristic imaging findings of radiation vasculopathy with subsequent hemorrhagic markers, and exclusion of other etiologies, his clinical presentation was felt to be most consistent with Stroke-like migraine attacks after radiation therapy, a condition abbreviated as “SMART syndrome”.

Discussion

Stroke-like migraine attacks after radiation therapy (SMART) syndrome is a rare, delayed complication of cranial irradiation, first described in 1995[5]. It is characterized by reversible, recurrent episodes of focal neurological dysfunction that may occur years to decades after radiation exposure, with reported latency ranging from 1 to 39 years. The exact pathophysiology remains uncertain, but cumulative evidence implicates radiation-induced endothelial injury, chronic impairment of the blood–brain barrier, altered cerebrovascular autoregulation, and cortical spreading depression as key mechanisms underlying the syndrome[3].

Radiation-related endothelial damage disrupts vascular integrity and autoregulatory capacity, resulting in focal hypoperfusion and cortical hyperexcitability[6]. Over time, these processes lead to radiation-induced vasculopathy, characterized by microangiopathy and microhemorrhages, which may coexist with SMART-related cortical dysfunction. The clinical manifestations are transient and diverse, including hemiparesis, aphasia, behavioral change, amnesia, and visual or sensory disturbances. Episodes typically resolve spontaneously over hours to days, although recurrence is common[3]. Such episodes are treated symptomatically with migraine treatment, although the use of vasoconstrictive substances e.g. triptans should be avoided. Repeated TIA workup for an alternative cerebrovascular cause is not usually needed[3].

The differential diagnosis is broad and includes ischemic stroke, transient ischemic attack, autoimmune or infectious encephalitis, transient focal neurological episodes of cerebral amyloid angiopathy (in the right age group), hypertensive arteriopathy, and traumatic microbleeds[7]. In this case, the coexistence of cortical and deep microhemorrhages, in the absence of diffusion restriction or significant white matter disease, along with the age of the patient helped exclude cerebral amyloid angiopathy and hypertensive arteriopathy. CSF analysis showed elevated protein without pleocytosis or pathogens, arguing against infectious or autoimmune etiologies. The absence of acute ischemia on MRI, normal EEG and the patient's history of whole-brain irradiation supported the diagnosis of SMART syndrome over ischemic or epileptic causes.

Accurate recognition of SMART syndrome requires careful history-taking and meticulous review of neuroimaging. Importantly, radiation-induced vasculopathy can manifest 2–30 years after exposure, meaning that many individuals irradiated during adolescence in the 1980's - 1990's are now reaching the age when these delayed complications become clinically evident. Distinguishing SMART syndrome from other causes of cerebral microbleeds prevents misdiagnosis and avoids unnecessary antithrombotic treatments, especially given that radiation induced vasculopathy already has an increased risk of causing hemorrhages. In such cases, management should focus on symptomatic control, migraine prophylaxis, and long-term neurologic surveillance.

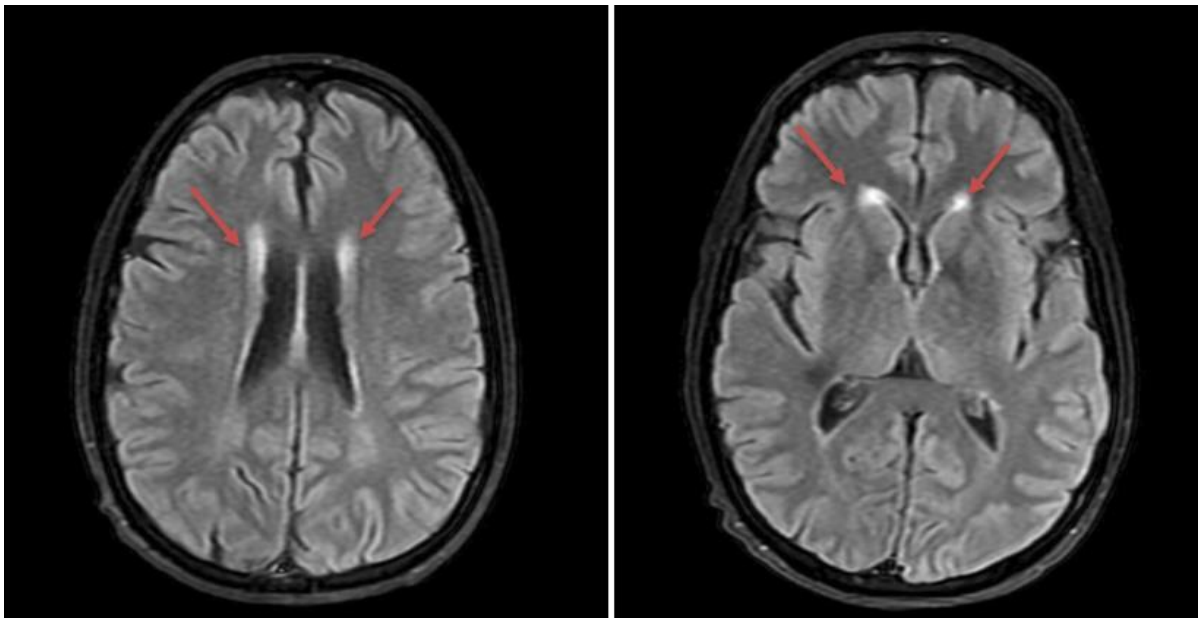

Image 1: T2 FLAIR Axial images demonstrating minimal white matter changes (red arrows)

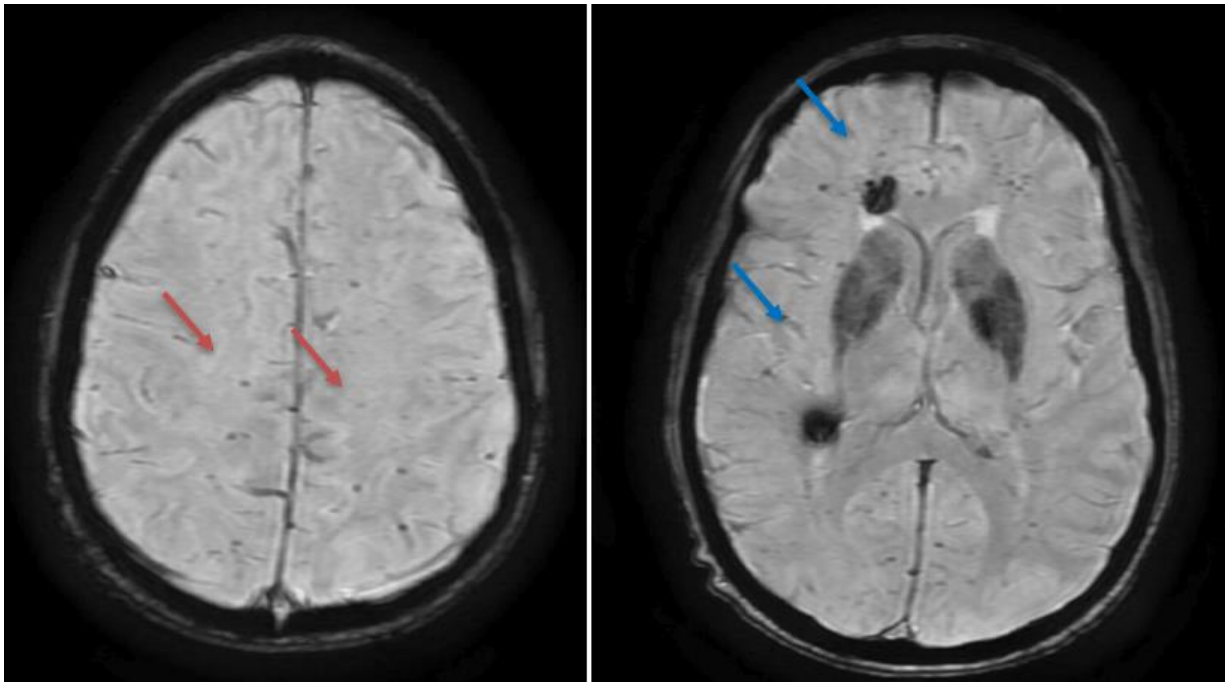

Image 2: Axial T2 Susceptibility Weighted images demonstrating cerebral cortical and deep microbleeds (red arrows) and 2 macrobleeds (blue arrows) in periventricular area in the right hemisphere.

References

1. Black DF, Bartleson JD, Bell ML, Lachance DH. SMART: stroke-like migraine attacks after radiation therapy. *Cephalalgia Int J Headache*. 2006;26(9):1137-1142. doi:10.1111/j.1468-2982.2006.01184.x
2. Black DF, Morris JM, Lindell EP, et al. Stroke-Like Migraine Attacks after Radiation Therapy (SMART) Syndrome Is Not Always Completely Reversible: A Case Series. *AJNR Am J Neuroradiol*. 2013;34(12):2298-2303. doi:10.3174/ajnr.A3602
3. Ota Y, Liao E, Shah G, Srinivasan A, Capizzano AA. Comprehensive Update and Review of Clinical and Imaging Features of SMART Syndrome. *Am J Neuroradiol*. Published online May 4, 2023. doi:10.3174/ajnr.A7859
4. Seehusen DA, Reeves MM, Fomin DA. Cerebrospinal Fluid Analysis. *Am Fam Physician*. 2003;68(6):1103-1109.
5. Shuper A, Packer RJ, Vezina LG, Nicholson HS, Lafond D. "Complicated migraine-like episodes" in children following cranial irradiation and chemotherapy. *Neurology*. 1995;45(10):1837-1840. doi:10.1212/wnl.45.10.1837
6. Angelidis P, Saleh C, Jaszczuk P, Seyam M, Ebner KA, Hund-Georgiadis M. SMART Syndrome (Stroke-like migraine attacks after radiation therapy): When to suspect it? *Surg Neurol Int*. 2021;12:561. doi:10.25259/SNI_893_2021
7. Goldfinch AI, Kleinig TJ. Stroke-like migraine attacks after radiation therapy syndrome: a case report and literature review. *Radiol Case Rep*. 2017;12(3):610-614. doi:10.1016/j.radcr.2017.05.007