



Case Report

SMART Syndrome (Stroke-like migraine attacks after radiation therapy): When to suspect it?

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ABSTRACT

Background: Stroke-like migraine attacks after radiation therapy (SMART) syndrome is a benign complication of brain radiation therapy, which presents circa a decade after radiation treatment. Symptoms are stroke-like deficits, epileptic seizures, and migraine. Cranial magnetic resonance imaging is characteristic for alterations in the form of unilateral cortical hyperintensities and gyriform enhancement, most prominent in the parieto-occipital regions. Prompt diagnosis is essential to avoid unnecessary investigations (e.g., brain biopsy and angiography).

Case Description: We describe a 51-year-old female patient treated initially with cranial irradiation for a left-sided occipital metastatic lung adenocarcinoma. Five years later, she presented with migraine headache, aphasia, and a right sided hemiparesis.

Conclusion: The triad of migraine, seizure, and hemiparesis within the context of a prior brain radiotherapy should promptly raise the suspicion of SMART syndrome. Prompt diagnosis is essential to avoid unnecessary invasive investigations.

Keywords: Diagnostic work-up, Epileptic seizure, Migraine, Radiation therapy, Stroke

INTRODUCTION

Stroke-like migraine attacks after radiation therapy (SMART) syndrome is a late, but benign complication of brain radiation therapy.^[1] Onset of symptoms presents 1–37 years (in general a decade) after radiation treatment^[4] and consists of neurological deficits resembling stroke-like deficits, epileptic seizures, and migraine.^[2] Characteristic imaging findings (magnetic resonance imaging [MRI] T2-weighted and FLAIR images) consist of unilateral cortical hyperintensity and gyriform enhancement, most frequently seen in the parieto-occipital regions.^[4] Black *et al.*^[1] showed that the characteristic SMART cortical enhancement findings appear within the 1st week of symptom onset, resolve within 1 month, but may also last up to 3 months. The pathophysiology of SMART is not fully elucidated.^[4] Delayed radiation-induced neurotoxicity appears to be one of the most important factors leading to radiation induced necrosis, myelopathy, and leukoencephalopathy.^[4] The neuronal dysfunction may cause neuronal cortical hyperexcitability, endothelial damage, and altered autoregulation, ultimately resulting in a reduced threshold value for cortical spreading

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depression. This mechanism is thought to be the underlying phenomenon in migraine headaches and seizures.^[3,4] Although SMART is generally considered to be a self-limiting condition,^[4] Black *et al.*^[1] reported permanent neurological as well as long-term imaging sequela. Treatment is symptomatic. We present a female patient with SMART syndrome occurring 11 years after radiation therapy for brain metastases.

CASE DESCRIPTION

In 2009, a 51-year-old female patient was treated with cranial irradiation for a left-sided occipital metastatic lung adenocarcinoma. Four years later, in 2013, a further surgical intervention was necessary to remove a radiation-induced tumor necrosis. One year later, she presented with migraine headache, aphasia, and a right-sided hemiparesis. An electroencephalogram showed nonconvulsive status epilepticus. Treatment with lacosamide and levetiracetam was initiated. In 2020, hospitalization was necessary due to hip fracture. The patient again presented during this latter hospitalization with aphasia and a right-sided hemiparesis, which possibly caused a fall and consequently the hip fracture. Due to the patient's aphasia, no conclusive anamnesis was available.

Based on her previous history, an epileptic event was suspected. Her antiepileptic medication was increased without improving her clinical status. Cranial MRI (cMRI) was performed to rule out an ischemic or hemorrhagic event. Instead, cMRI showed gyriform contrast enhancement within the left parieto-occipital regions. These changes were exclusively localized in the areas irradiated in 2009. Based on her clinical presentation (migraine, seizure, and hemiparesis), as well as on the morphology and location of the MRI alterations [thick gyriform enhancement, Figure 1a and b], the diagnosis of SMART was made. In addition to her antiepileptic medication, steroid treatment was initiated under which her symptoms improved gradually. A control MRI showed regressing signal alterations in the affected areas [Figure 1c and d]. The patient gave permission to publication of her case.

DISCUSSION

SMART syndrome presents with a plethora of symptoms ranging from migraine and seizures to hemiparesis. Other conditions may present with similar symptoms, such as hemiplegic migraine,^[3] posterior reversible encephalopathy syndrome,^[5] epilepsy, and stroke. However, the main difference between these latter conditions and SMART lies within the patient's history; SMART patients present with a history of brain radiation therapy. In our patient, diagnosis was delayed as seizure, aphasia and hemiparesis were suspected to be a presentation of Todd's paresis (without

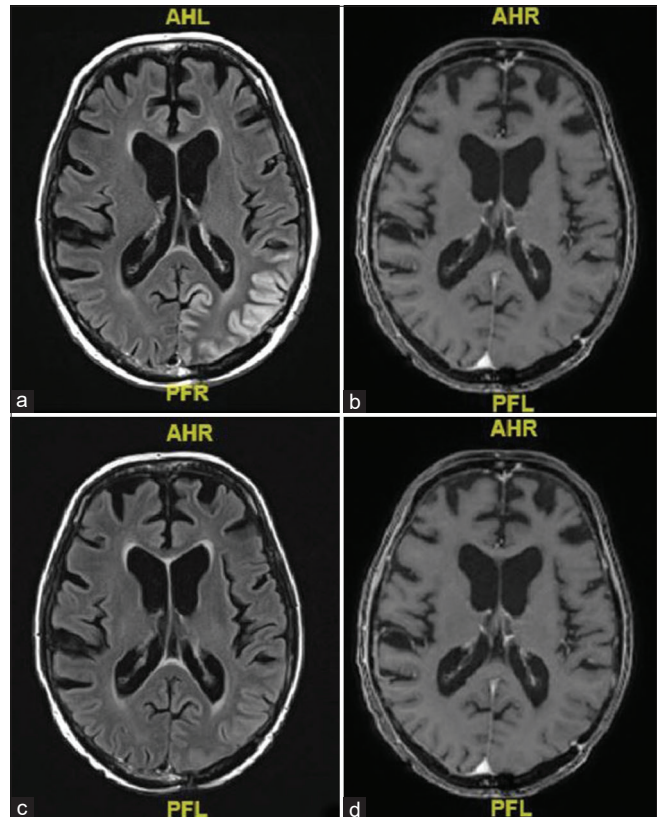


Figure 1: Brain MRI at presentation and after 10 days of SMART syndrome. Gyral enhancement of the left parietooccipital region with mild swelling on axial postcontrast FLAIR MRI (a) and on postcontrast T1-weighted imaging (b). Complete resolution of findings 10 days later on postcontrast FLAIR (c) and postcontrast T1-weighted imaging (d).

considering her previous brain radiation therapy) focusing initially solely on adaptation of her antiepileptic medication. Only after performing cranial imaging, the diagnosis of SMART was made and treatment supplemented with steroid administration, which improved her neurological status within weeks. Retrospectively, it can be argued that her symptoms (aphasia, hemiparesis, and epileptic seizures) presenting 5 years after brain radiation therapy, were already signs of SMART syndrome. At that stage, however, no MRI was made to establish the diagnosis. Awareness and a high degree of suspicion for SMART syndrome are necessary for prompt diagnosis, to avoid further potentially invasive tests, such as brain biopsy.^[4]

Take-home points

1. SMART syndrome is a clinicoradiologic diagnosis based on a history of brain irradiation, clinical symptoms, and characteristic MRI findings (see points 2 and 3).
2. The triad of migraine, seizure, and hemiparesis within the context of a prior brain radiotherapy should promptly raise the suspicion of SMART syndrome.

3. cMRI shows characteristic alterations in the form of unilateral cortical hyperintensities and gyriform enhancement, most prominent in the parieto-occipital regions.
4. SMART syndrome can be self-limiting.
5. Treatment is symptomatic (e.g., seizure control). Supplemental steroid therapy may prove beneficial.
6. Prompt diagnosis is essential to avoid unnecessary investigations (e.g., brain biopsy and angiography).

Data availability statement

All data analyzed for this case report are included in this article and its supplementary material files. Further enquiries can be directed to the corresponding author.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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