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Metamorphopsia with SMART Syndrome: A Case Report

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Metamorphopsia · Visual distortion · Complex visual hallucinations · SMART syndrome

Abstract
Introduction: SMART syndrome is a rare complication of brain radiotherapy. This is the first described presentation of SMART syndrome with metamorphopsia, which responded to aspirin, verapamil, and high-dose L-arginine therapy. ***Case Presentation:*** A 43-year-old man presented with 3 weeks of migraine headaches with metamorphopsia and complex visual hallucinations affecting the left lower quadrant of both visual fields. This occurred on a background of high-dose radiotherapy for right cerebellar astrocytoma 32 years ago. MRI brain demonstrated unilateral gyriform enhancement and FLAIR hyperintense cortical swelling in the right occipital lobe consistent with SMART syndrome. ***Conclusion:*** Unusual presentations of SMART syndrome exist and require consideration in all patients with focal neurological deficit post-brain radiotherapy. Validated diagnostic and treatment modalities for SMART syndrome are urgently required.

Introduction

Stroke-like migraine attacks after radiation therapy (SMART) syndrome is a rare complication of brain radiotherapy. Typical presentations involve headaches, seizures, and focal neurological deficits. This is the first described presentation of SMART syndrome with persistent metamorphopsia and transient complex visual hallucinations, which were fully resolved with aspirin, verapamil, and high-dose L-arginine therapy.

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Case Presentation

A 43-year-old man presented with 3 weeks of new-onset holohemispheric headache with migraine characteristics, associated with subacute-onset, persistent, and progressive metamorphopsia affecting the left lower quadrant of both visual fields. This was described as non-distressing visual distortion exclusively affecting human faces, without prosopagnosia, micropsia, or macropsia. There were associated recurrent intermittent brief periods of complex visual hallucinations of "rotating fans" and "smoke" lasting seconds within the same visual field. There was no visual loss with Humphrey visual field testing to suggest Charles-Bonnet phenomena and visual acuity was preserved. Optical coherence tomography was deemed unnecessary due to presence of binocular metamorphopsia consistent with cortical pathology. Neurological examination demonstrated abnormalities with complex shape perception; however, shape discrimination and facial perception testing were normal. Fundoscopy did not demonstrate retinal pathology. His current symptoms occurred on a background of high-dose (over 50 Gy) right posterior cerebellar field radiotherapy for right cerebellar peduncle astrocytoma 32 years ago. He had no other known medical comorbidities and never had previous migraine headaches.

MRI brain performed 3 weeks post-symptom onset demonstrated unilateral gyriform enhancement with T2 and FLAIR hyperintense cortical swelling in the right occipital lobe, without evidence of tumour recurrence (Fig. 1). Cerebrospinal fluid assessment demonstrated a high protein of 0.70 g/L but was otherwise acellular. Electroencephalography was normal (Fig. 1–3).

A diagnosis of SMART syndrome was made. The patient was commenced on aspirin, verapamil, as well as high-dose (0.5 g/kg) L-arginine therapy. High-dose glucocorticoid therapy was initially delayed due to influenza A pneumonia but ultimately not required due to rapid resolution of his symptoms after the other therapies were administered. There was no recurrence of his symptoms at 3-month follow-up.

Discussion

SMART syndrome is a complex and rare neurological disorder characterised by migrainous headaches and stroke-like symptoms. It can affect both adult and paediatric populations with a tendency to affect males to a great proportion [1]. Due to the rarity of the condition, there have been no true prevalence rates within published literature. There is large variability in age of onset, with studies highlighting individuals between 3.5 and 88 years, with a mean time of symptom development post-radiation of 14 years [2]. This patient developed SMART syndrome 32 years after cranial irradiation, highlighting the need for clinical vigilance when diagnosing individuals with a remote history of cranial irradiation. Previous studies have suggested a radiation dose of greater than or equal to 50 Gy for the individual to be susceptible to its development [3].

The pathophysiology of SMART syndrome is poorly understood; however, a multifactorial cause has been the most agreed upon aetiology. It is suspected that irradiation to the brain tissue leads to white matter necrosis, damage to the vascular endothelium, and subsequent demyelination and gliosis. Recent evidence has also suggested that radiation-related mitochondrial dysfunction may be responsible; however, this remains unclear [4].

Current methods of diagnosis rely on clinical history taking with MRI, CT perfusion, and PET-FDG imaging. Characteristic findings on MRI include gyriform cortical enhancement with associated T2 and FLAIR hyperintense cortical swelling. Modified diagnostic criteria have been proposed by Black et al. [5] that consisted of a combination of imaging and clinical

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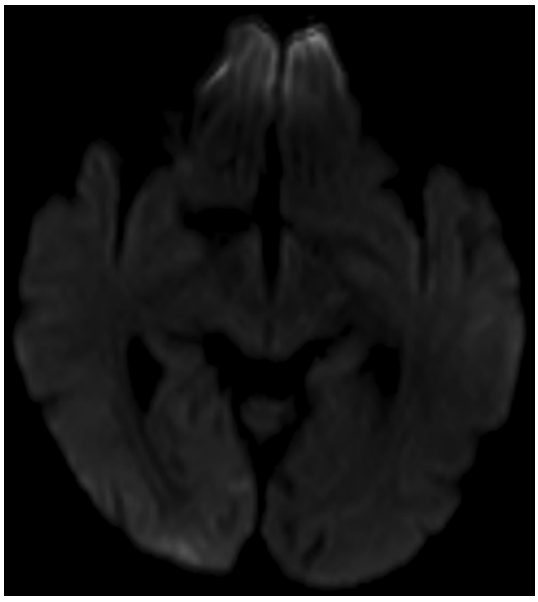

Fig. 1. Right occipital gyriform DWI hyperintensity.

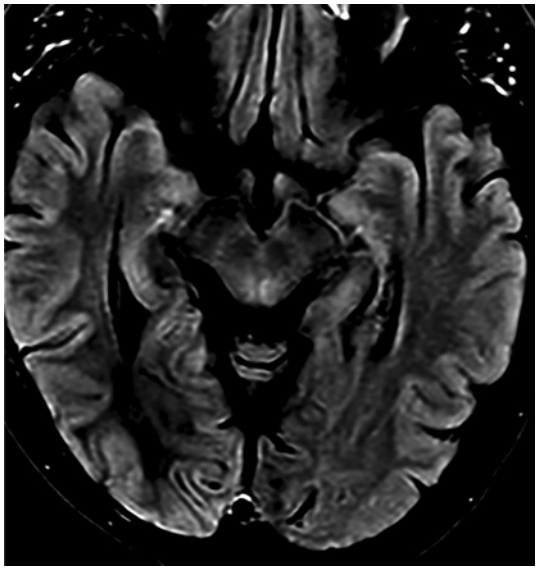

Fig. 2. Right occipital gyriform enhancement with FLAIR hyperintense cortical swelling.

diagnostic criteria, although no validated tool is currently within circulation. These criteria include prolonged but reversible unilateral cortical signs and symptoms beginning years after cranial radiation associated with transient, diffuse, unilateral cortical grey matter enhancement on MRI (sparing white matter), which is not attributable to any other disorder.

To our knowledge, this is the first case report to describe metamorphopsia as a sign of unilateral focal cortical dysfunction due to SMART syndrome. Metamorphopsia is a symptom of visual disturbance characterised by binocular or monocular perceptual distortions of the shapes and sizes of objects. It classically presents as straight lines appearing warped, distorted, or bent, but it can also present in other forms such as micropsia and macropsia, which affect a patient's quality of vision and face perception [6]. Micropsia is a visual disturbance where objects are perceived to be smaller than they objectively are and macropsia is the perception of objects being larger than they objectively are [6].

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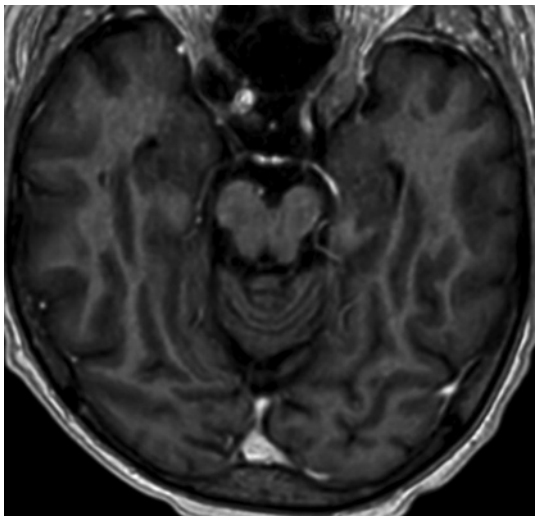

Fig. 3. Normal post-contrast T1 MRI sequences.

Many theories regarding the pathophysiology of metamorphopsia in different conditions have been developed over the years. In patients with metamorphopsia attributable to retinal pathology, it was postulated that the thickening of inner retinal layers led to disruption in the level of the photoreceptors resulting in mislocation of light on the retina, subsequently causing metamorphism. Associated retinal pathology include age-related macular degeneration, diabetic and non-diabetic macular oedema, vitreoretinal interface disorders, retinal detachment, central serous chorioretinopathy, and conditions that can cause macular serous elevation. However, this patient with binocular metamorphopsia meeting SMART syndrome diagnostic criteria had radiologically proven right occipital lobe pathology, which supports the theory by Wiecek et al. [7] that any disruption to cortical processing may cause this visual phenomenon [6].

Conclusions

SMART syndrome can present unusually with binocular metamorphopsia after 30 years post-high-dose cranial irradiation. This highlights the need for clinicians to be vigilant regarding its diagnosis, especially in patients presenting with unusual neurological symptoms on a background of remote high-dose brain radiotherapy. Future studies aimed at establishing validated diagnostic criteria and treatment modalities for SMART syndrome are urgently required to improve patient outcomes.

Statement of Ethics

Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images. Ethical approval is not required for this study in accordance with national guidelines. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000540417).

Conflict of Interest Statement

The authors declare that there is no conflict of interest.

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Author Contributions

Luke Flain and Aisha Lay: literature review, manuscript drafting, and manuscript review; Eden Gadil, Karlie James, and Sanchayan Thanachayan: manuscript drafting and manuscript review; Stephen Bacchi: supervision and manuscript review; and Rudy Goh: supervision, conceptualisation, literature review, manuscript drafting, and manuscript review.

Data Availability Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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