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Neuroimaging Highlight

Very Delayed SMART Syndrome

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A 52-year-old man presented with 3 days of a migraine-like headache and several days of word-finding difficulties. He was found to be profoundly aphasic and with a right homonymous hemianopsia. He had a history of migraine well controlled with duloxetine. He was treated with cranial radiotherapy at age 9 due to a diagnosis of a medulloblastoma. He had developed post-radiation complications, including a right frontal asymptomatic meningioma and an anterior communicating aneurysm that was coiled 2 years prior due to a subarachnoid hemorrhage.

MRI revealed evolving left temporo-occipital-parietal areas of T2 hyperintensities and cortical enhancement (Fig. 1). Cerebrospinal fluid revealed elevated protein, but infectious, neoplastic, paraneoplastic and autoimmune workup was negative. An Electroencephalogram (EEG) revealed left temporo-occipital slowing but no epileptiform discharges. A positron emission tomography (PET) scan 3 weeks after presentation revealed hypometabolism over the affected regions (Fig. 1). He was diagnosed with stroke-like migraine attacks after radiation therapy (SMART) syndrome.

SMART syndrome is a delayed complication of whole-brain irradiation associated with subacute attacks of myriad neurological symptoms, including headaches, seizures or focal neurological deficits.[1,2] These deficits may improve over several weeks but may persist. Classical MRI findings include increased T2 signal within temporal, parietal or occipital cortices and cortical thickening and enhancement.[1,2] The proposed pathophysiology is delayed radiation-induced endothelial dysfunction and neuronal hyper-excitability.[1,2] We diagnosed SMART syndrome on the basis of a consistent clinic-radiologic presentation and the exclusion of alternative diagnoses.

A history of brain or whole-body radiation therapy is required for diagnosis. Radiotherapy timing has been reported to range from a few years to several decades.[1,2] In this case, radiotherapy was administered more than 40 years before presentation. This is the longest time reported to the best of our knowledge. Further, there are reports of PET findings that range from hypermetabolism to hypometabolism in affected brain regions.[3] It is hypothesized that hypermetabolism may be an early and seizure activity-related phenomenon, while hypo-metabolism may be seen in later phases, which would be consistent with our findings.

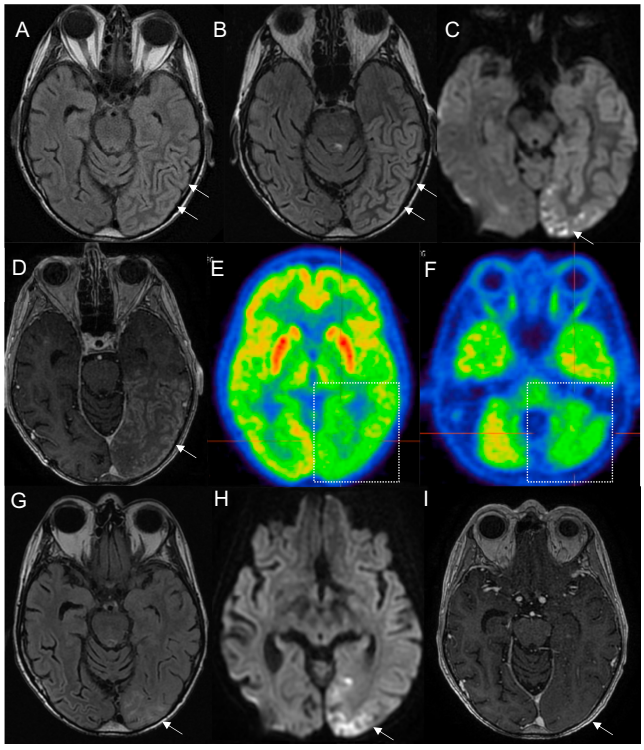


Figure 1. Neuroimaging findings. Initial MRI (day 3) revealed subtle cortical thickening and T2-hyperintensities in the left occipitotemporal-parietal regions (A). These findings progressed over 1 week (B). At 3 weeks after presentation, diffusion restriction and cortical enhancement were seen (C, D). PET findings at this time revealed hypometabolism in the same affected regions (E, F). At 3 months after presentation, MRI revealed decreased conspicuity of left parietal and occipital T2-hyperintensities and diffusion restriction and resolution of cortical enhancement (G, *H*, I).

There is no established management, and steroids and verapamil have been suggested.[1,2] One retrospective study indicated that steroids could be associated with incomplete recovery, but steroids were likely prescribed in more severe cases.[4] In our case, we tried a short course of steroids, verapamil and a combination of vitamin E and pentoxifylline (proposed treatments for radiation-induced necrosis).[5] Levetiracetam and

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lacosamide were used in the acute phase as seizure preventives. Over the following months, our patient recovered from the standpoint of aphasia and right homonymous hemianopsia. At 2 months after presentation, repeat MR brain demonstrated improvement. At 3 months after presentation, he was nearly back to baseline and was discharged home with further outpatient rehabilitation.

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Dr McLeod: revision of the first draft and obtaining clinical information.

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