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Smart Syndrome in ALL: An Ugly Reality of Cranial Irradiation

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Introduction

Stroke-like migraine attacks following radiation therapy (SMART) is a rare syndrome that occurs as a late complication of brain radiotherapy.[1] The overall incidence is unknown but there are about 100 cases of SMART syndrome reported in the literature since it was first described in 1995.[2] The usual presentation consists of recurrent headache attacks associated with seizures and paroxysmal focal neurological deficits (e.g., aphasia, hemianopsia, and negligence), usually regarded as reversible or partially reversible, but this is not always the case as seen in the clinical case discussed herein.[3-6]

A typical magnetic resonance imaging (MRI) pattern of SMART presents transient unilateral cortical gadolinium enhancement, increased T2 signal within temporal, parietal, and occipital cortices with gyriform enhancement resolving as the symptoms subside.[4] We hereby report the case of a long term survivor of acute lymphoblastic leukemia (ALL) who was treated with chemotherapy and irradiation twice to brain due to isolated CNS relapse in 1996 developing SMART syndrome after 26 years of brain irradiation in 2022.

Case Report

In 1988, a 12-year-old girl developed ALL. She completed initial treatment on Prof Ian Magrath et al driven NCI MCP 841 program. Achieved complete remission status (CR). She tolerated the treatment well but for severe pains due to intramuscular injections of L-asparginase and fewer episodes of inter current infections needing conservative management and occasional hospitalisation. Her remission lasted for 8 years. Then she presented in 1996 with severe headaches, uncontrolled projectile vomiting, difficulty in walking with left sided weakness. She was diagnosed

with a solitary CNS (pons) relapse 8 years after initial diagnosis in Feb 1988 (Figure 1) It was treated unconventionally with re- irradiation (after initial cranio-spinal prophylaxis for treatment consolidation) with 3000 cGr in 15 fractions as patient refused subsequent chemotherapy. To everyone's surprise she achieved a second remission leaving permanent alopecia over occipital region due to re-irradiation (Figure 2) for which she underwent scalp refashioning to minimise the social handicap accompanying her cosmetic disfigurement. Life has not been easy for her thereafter, she developed uncontrolled Diabetes Mellitus post Covid-19 infection in 2021 and disseminated tuberculosis requiring intensive treatment and leading to temporary colour blindness due to Ethambutol, which she could successfully combat. That was not the end as she presented in 2022 with frequent headaches and altered mental functions and status. A contrast enhanced MRI of brain revealed mild to moderate cortical thickening and gyriform enhancement in left temporal and parieto-occipital lobes with effaced sulci, leading to the diagnosis of SMART syndrome (stroke like migraneous attacks after radiotherapy) with no obvious cortical laminar necrosis (Figure 3). She was treated symptomatically with Carbamezapine, antidepressants and low dose prednisolone in view of her comorbidities. She partially recovered with mild symptomatic relief. She then defaulted for two years. She recently visited us with residual altered mental functions, mild aphasia and left hemiplegia as sequelae.

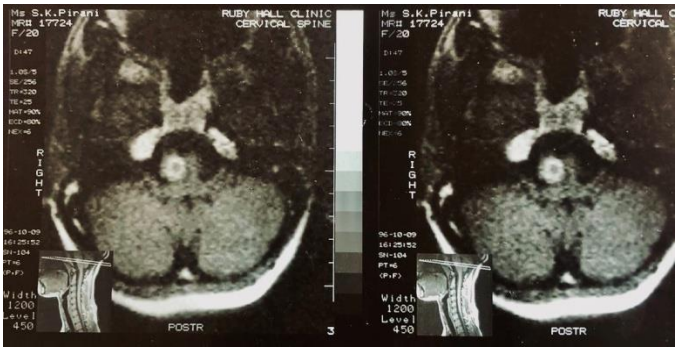

Figure 1: Contrast Enhanced MRI showing isolated PONS relapse in 1988.

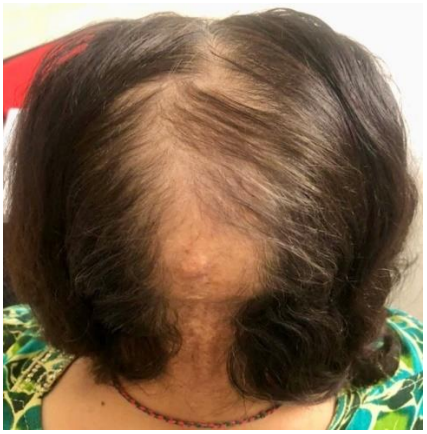

Figure 2: Permanent alopecia over occipital region due to re-irradiation for isolated CNS relapse.

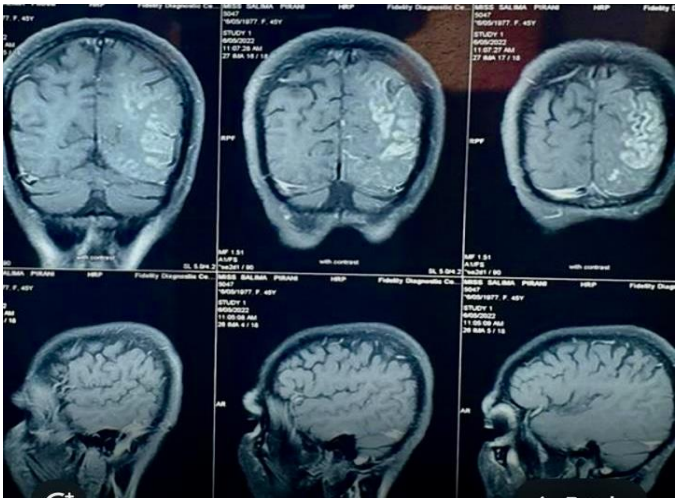

Figure 3: Contrast enhanced MRI of brain revealing mild to moderate cortical thickening and gyriform enhancement in left temporal and parieto-occipital lobes with effaced sulci leading to the diagnosis of SMART

syndrome (stroke like migraneous attacks after radiotherapy) with no obvious cortical laminar necrosis.

Discussion

SMART is a rare syndrome with just about 100 cases reported in the literature till now, the overall incidence is unknown.[2] A history of prior brain radiation along with CNS decline symptoms are needed to make a diagnosis. Dose of around 50 Gy radiation are associated with the syndrome, but lower dose regimens are also reported to cause symptoms.[6,7] MRI is the investigation of choice to confirm diagnosis and to rule out other common etiologies and identify gyriform contrast enhacement on T2 weighted images and FLAIR sequences as hallmark feature confirming SMART syndrome.[8] SMART syndrome is a diagnosis of exclusion. Continued surveillance for other causes remains important. CSF examination, EEG, Magnetic Resonance Angiography (MRA), serum lactic acid level and blood pressure monitoring should also be considered. [9]

The most common complications of brain radiation include focal necrosis, progressive leukoencephalopathy and progressive decline in cognitive and neurological function.[8]

The differential diagnosis from other complications of cerebral radiotherapy with contrast enhancement requires careful analysis of the clinical presentation. The diagnoses to exclude are peri-ictal pseudoprogression (in glioma patients), acute late-onset encephalopathy after radiotherapy and focal radionecrosis, acute infarction, posterior reversible encephalopathy syndrome, viral encephalitis, hemiplegic migraine, mitochondrial disorders, for example, mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes, and other metabolic conditions, for example, urea cycle disorders, post seizure cortical swelling and hemiplegic migraine.[10,11,12] All of these diagnoses were excluded in our patient. The current literature suggests that in approximately 83% of patients, the natural course of SMART syndrome leads to a complete recovery.[12] However, Black et al reported an incomplete neurological recovery in 5 of their 11 patients, with permanent imaging sequelae (cortical laminar necrosis) developing as early as 17 days after the onset of symptoms in 27% of patients, suggesting that recovery can be partial or complete.[4]

Corticosteroids, antiplatelet agents, propranolol and verapamil have all been used without clear benefit.[10] While the usual (or early stage) form of SMART syndrome improves spontaneously, even in cases with dramatic deficits, such as impaired level of consciousness, there is no effective treatment for the more severe form.[11]

Awareness of this syndrome is diagnostically very important as it can obviate the need of invasive investigations such as brain biopsy or cerebral angiography which can have both a psychological and financial toll on patients.

Conclusion

Stroke-like migraine attacks after radiation (SMART) syndrome is a rare, late-onset complication of brain irradiation. Increased cancer survival rate have resulted in an increase in its frequency.[2] The diagnosis of SMART syndrome should be considered whenever gyriform enhancement is noted in the parieto-occipital region in a patient with migraine-type headaches, seizures and stroke-like symptoms with a remote history of brain radiation.[2] Awareness of this syndrome is important to make a proper diagnosis and avoid unnecessary interventions or therapies. There are no specific treatments for SMART syndrome. Despite the

uncertain benefit of the current treatment options, it is important to obtain a rapid control of seizure activity. Steroids are frequently administered on empirical grounds, as they are thought to accelerate recovery. The prognosis is mostly favourable.[13] The recognition of this syndrome will avoid unnecessary invasive investigations and thereby lightening the psychological and financial burden of patients and their families who are already troubled by the diagnosis, treatment course and recovery from these dreadly diseases.

Prophylactic cranial irradiation (PCI) has been largely abandoned in the modern pediatric ALL (Acute Lymphoblastic Leukemia) protocols and its use is decreasing in adult protocols also. It is now replaced by intensified chemotherapy regimens including intrathecal Methotrexate &/or Cytarabine, which prevent CNS relapse while avoiding long term neurocognitive and endocrine risks.

References

1. Shuper A, Packer RJ, Vezina LG, Nicholson HS, Lafond D. 'Complicated migraine-like episodes' in children following cranial irradiation and chemotherapy. Neurology. 1995 Oct;45((10)):1837–40. doi: 10.1212/wnl.45.10.1837.
2. Di Stefano AL, Berzero G, Ducray F, Eoli M, Pichiecchio A, Farina LM, et al. Stroke-like events after brain radiotherapy: a large series with long-term follow-up. Eur J Neurol. 2019 Apr;26 ((4)):639–50. doi: 10.1111/ene.13870.
3. Kerklaan JP, Lycklama á Nijeholt GJ, Wiggenraad RG, Berghuis B, Postma TJ, Taphoorn MJ. SMART syndrome: a late reversible complication after radiation therapy for brain tumours. J Neurol. 2011 Jun;258((6)):1098–104. doi: 10.1007/s00415-010-5892-x
4. Black DF, Morris JM, Lindell EP, Krecke KN, Worrell GA, Bartleson JD, et al. Stroke-like migraine attacks after radiation therapy (SMART) syndrome is not always completely reversible: a case series. AJNR Am J Neuroradiol. 2013 Dec;34 ((12)):2298–303. doi: 10.3174/ajnr.A3602.
5. Haller V, Dashti D, Peters N. SMART - Not Always Only "Stroke-Like". Headache. 2018 Oct;58 ((9)):1465–8. doi: 10.1111/head.13415.
6. Singh AK, Tantiwongkosi B, Moise AM, Altmeyer WB. Stroke-like migraine attacks after radiation therapy syndrome: case report and review of the literature. Neuroradiol J. 2017 Dec;30((6)):568–73. doi: 10.1177/1971400917690009.
7. Bartleson JD, Krecke KN, O'Neill BP, Brown PD. Reversible, strokelike migraine attacks in patients with previous radiation therapy. Neuro-oncol. 2003 Apr;5((2)):121–7. doi: 10.1215/S1522-8517-02-00040-6.
8. Zheng Q, Yang L, Tan L-M, et al. Stroke-Like migraine attacks after radiation therapy syndrome. Chin Med J 2015;128:2097–101. 10.4103/0366-6999.161393
9. Black DF, Bartleson JD, Bell ML, et al. Smart: stroke-like migraine attacks after radiation therapy. Cephalalgia 2006;26:1137–42. 10.1111/j.1468-2982.2006.01184.x
10. Lim SY, Brooke J, Dineen R, et al. Stroke-Like migraine attack after cranial radiation therapy: the smart syndrome. Pract Neurol 2016;16:406–8. 10.1136/practneurol-2016-001385
11. Bompaire F, Zinchenko L, Lahutte M, et al. Smart syndrome: classic transient symptoms leading to an unusual unfavorable outcome. Rev Neurol (Paris) [Internet] 2016:1–7http://linkinghub.elsevier.com/

retrieve/pii/S0035378716300765%5Cnhttp://www.ncbi.nlm.nih.gov/pubmed/27919464

12. Rigamonti A, Lauria G, Mantero V, et al. Smart (stroke-like migraine attack after radiation therapy) syndrome: a case report with review of the literature. Neurol Sci 2016;37:157–61. 10.1007/s10072-015-2396-6
13. Jia W, Saito R, Kanamori M, Iwabuchi N, Iwasaki M, Tominaga T. SMART (stroke-like migraine attacks after radiation therapy) syndrome responded to steroid pulse therapy: report of a case and review of the literature. eNeurologicalSci. 2018 May;12:1–4. doi: 10.1016/j.ensci.2018.05.003.