Recognizing SMART Syndrome: Imaging Evolution, Pitfalls, and Differentiation from Recurrence

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Disclosures

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- None

Clinical Background

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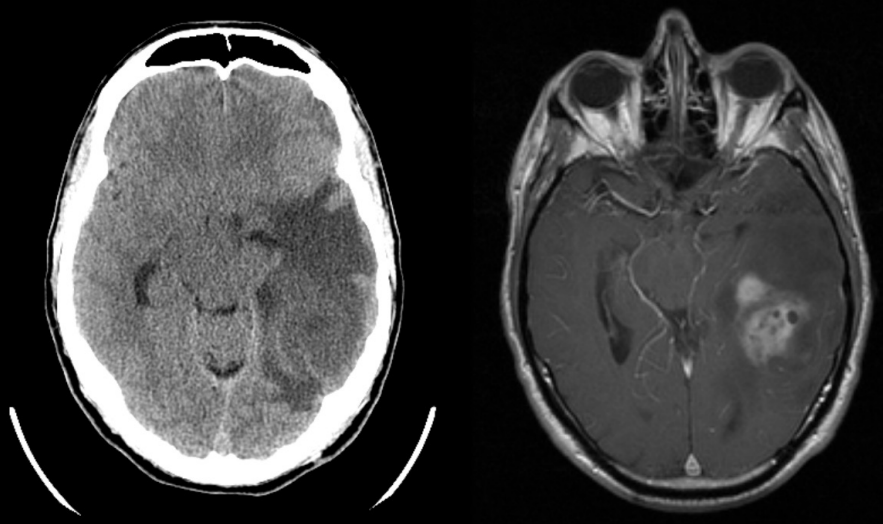
- 62-year-old-male
- Remote history:
  - Left temporo-occipital GBM
  - Gross total resection, temozolomide, radiation (60 Gy)
  - Good response without further treatment for 19 years
- Recent presentation:
  - Dysarthria, confusion, headaches, recurrent falls
  - Recurrent focal seizures during admission
  - MRI: new unilateral cortical/leptomeningeal enhancement in prior RT field



Recent Imaging Findings

Treatment with corticosteroids and verapamil

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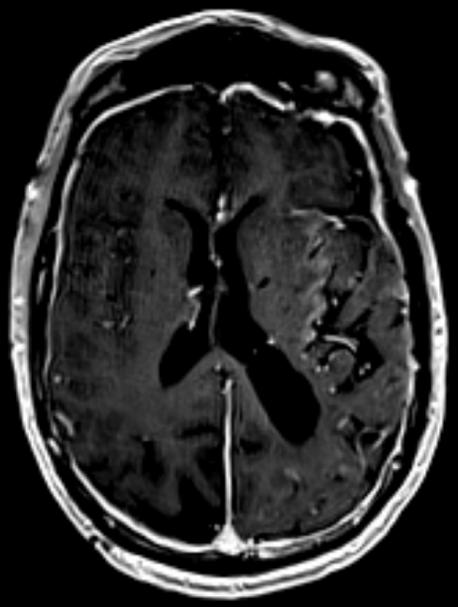
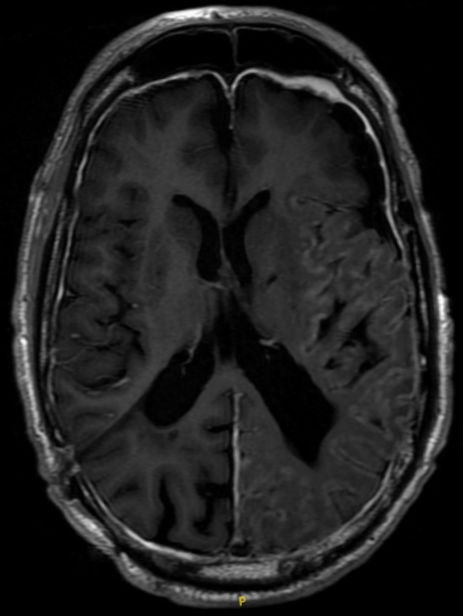
ONSET



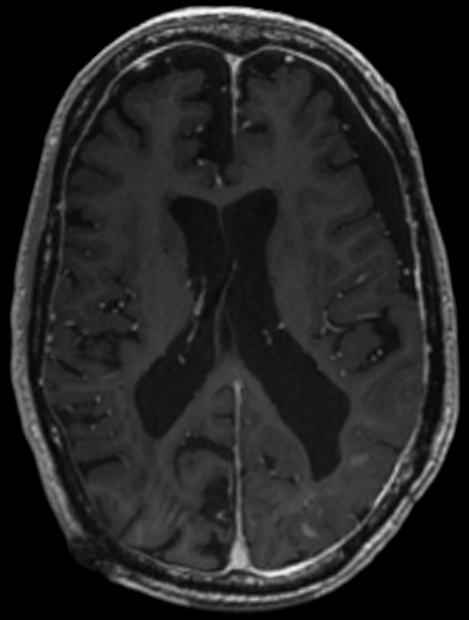
Day 1

PROGRESSION



Day 19

RESOLUTION



Day 43

New Unilateral Enhancement in Prior RT Field

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- Mimics:
  - Recurrence/leptomeningeal disease
  - Infection
  - Patient had focal seizures ⟶ peri-ictal mimic considered
- SMART discriminator:
  - Unilateral gyriform cortical ± leptomeningeal enhancement confined to RT field
  - Improvement/resolution on follow-up imaging
- Recognition can prevent unnecessary biopsy/therapy

Imaging phenotype & reversibility: [1,2,4]

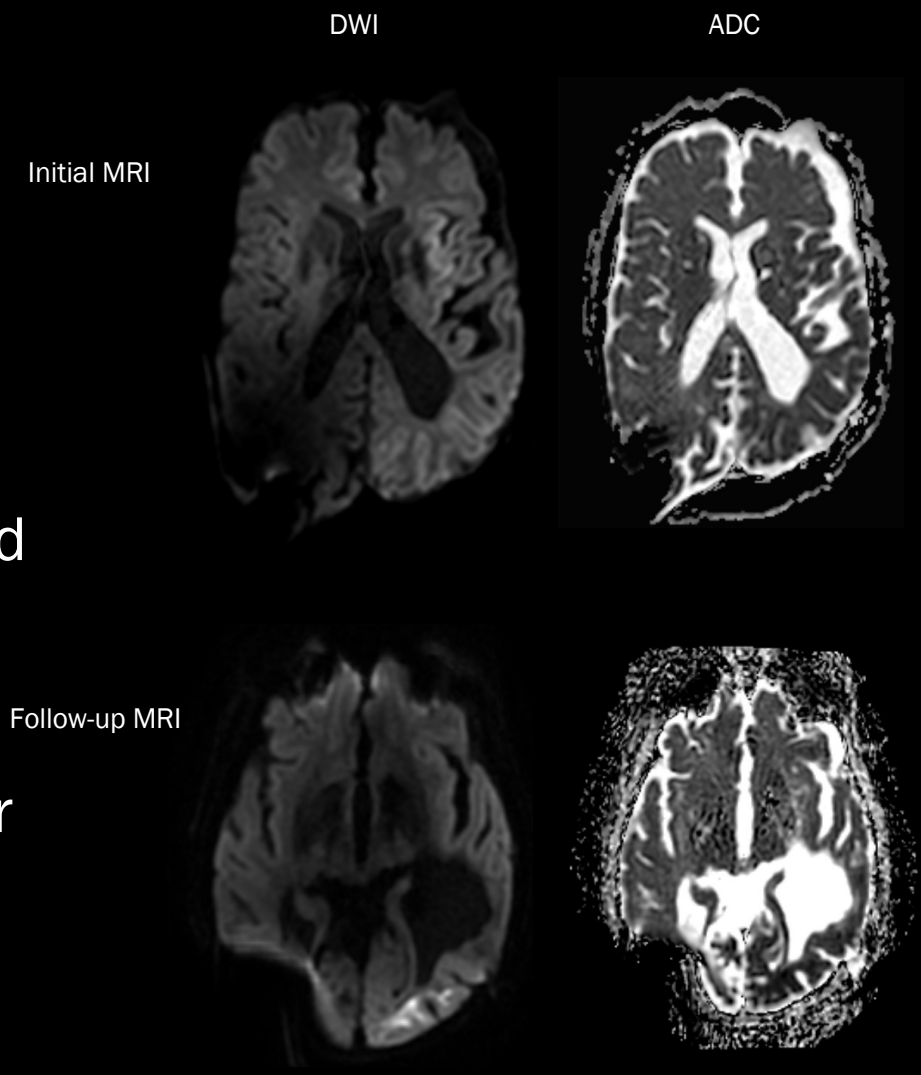
Findings Against Malignancy

- No mass/ nodular solid component
- Enhancement **confined to irradiated territory**
- CSF cytology negative; spine MRI negative
- Non-masslike pattern + confinement favors SMART over recurrence

Imaging pattern & RT field confinement: [1,2,4]

Diffusion Findings

- Initial MRI: Diffuse mild cortical DWI hyperintensity with equivocal ADC (not a discrete territorial infarct)
- Follow-up MRI: New focal left occipital restricted diffusion consistent with superimposed infarct
- Interpretation: Supports SMART-related neurovascular dysregulation with possible progression to infarction (PRES-like spectrum)



Typical DWI pattern: [2,4]

SMART Syndrome

Stroke-like Migraine After Radiation Therapy

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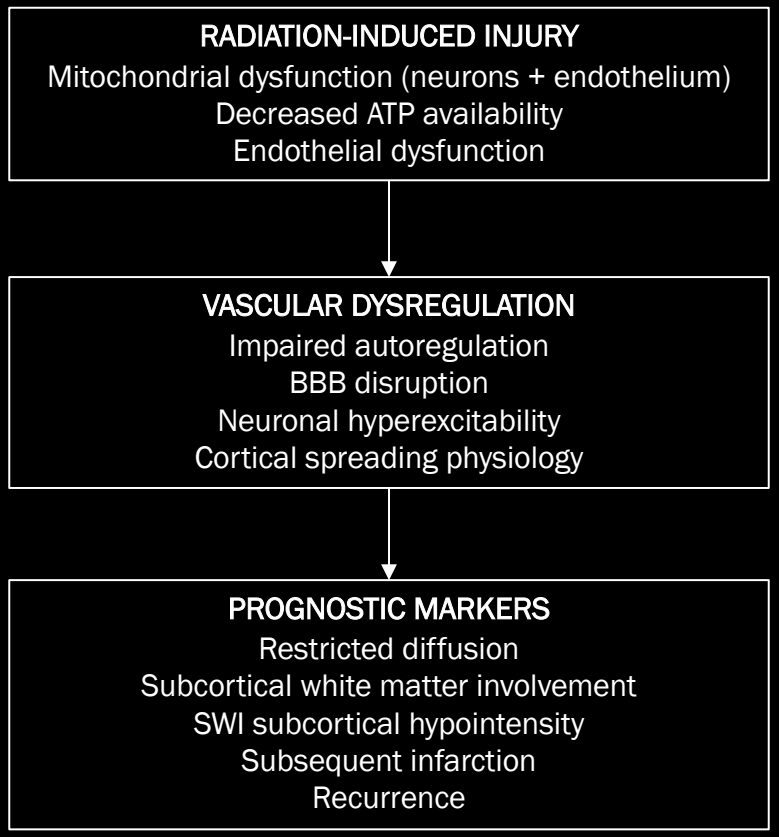
Delayed radiation-induced neurovascular dysfunction
Years–decades after cranial irradiation; often reversible



[4]

SMART Syndrome

Imaging Findings

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- Unilateral gyriform cortical ± leptomeningeal enhancement
- Confined to prior RT field
- Does not respect vascular territories
- Predominantly cortical involvement; subcortical white matter involvement may occur and is associated with worse recovery
- Cortical T2/FLAIR hyperintensity and swelling; typically resolves on follow-up

Diagnostic imaging features: [1,2,4]

Stepwise Assessment of New Enhancement in Prior RT Field

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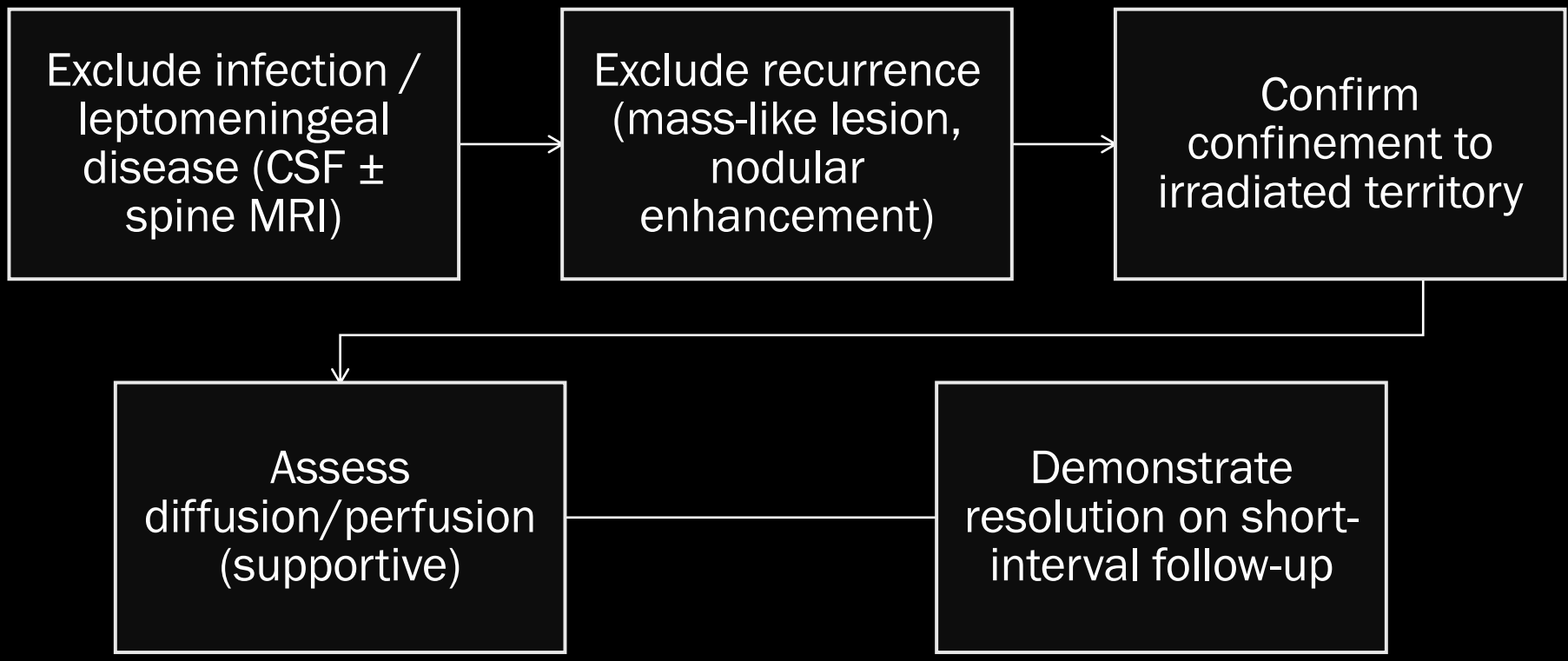

Avoid unnecessary biopsy and misdirected therapy

SMART Syndrome

Treatment

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- Corticosteroids to empirically treat acute inflammatory changes and cerebral edema
- Calcium channel blocker such as verapamil to treat vascular dysfunction, reduce cerebral vasospasm, manage migraine-like symptoms, and prevent long-term recurrence
- Antiplatelet agents such as aspirin and blood pressure medications in cases with superimposed infarction
- Antimigraine and antiepileptic medications such as carbamazepine to control migraines and seizures
- L-arginine has been proposed to improve endothelial function and stroke-like episodes

Steroids / clinical management: [2,4]. Verapamil / aspirin / recurrence reduction: [1,4]. L-arginine (MELAS analogy): [4]

Summary

- SMART can present decades after cranial irradiation
- Hallmark: unilateral cortical ± leptomeningeal enhancement confined to RT field
- Often reversible; incomplete clinical or imaging recovery reported
- Steroids + verapamil; clinical improvement with near-resolution on follow-up

Natural history & reversibility variability: [2,4]. Imaging hallmark: [1,2,4]

References

[1] Black DF, Bartleson JD, Bell ML, Lachance DH. SMART syndrome: stroke-like migraine attacks after radiation therapy. *Cephalalgia.* 2006;26(9):1137-1142. doi:10.1111/j.1468-2982.2006.01184.x

[2] 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;34(12):2298-2303. doi:10.3174/ajnr.A3602

[3] Zheng Q, Yang L, Tan L-M, Qin L-X, Wang C-Y, Zhang H-N, et al. Stroke-like migraine attacks after radiation therapy syndrome. *Chin Med J (Engl).* 2015;128(15):2097-2101. doi:10.4103/0366-6999.161393

[4] Ota Y, Nemoto M, Gyoten T, Liao E, Shah G, Capizzano AA. Comprehensive update and review of clinical and imaging features of SMART syndrome. *AJNR Am J Neuroradiol.* 2023;44(6):626-639. doi:10.3174/ajnr.A7859