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Imaging Findings Of Intracranial Injuries Post Radiotherapy

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São Paulo - SP
BRAZIL
2021

PURPOSE

01	INJURIES	• Illustrate most common post radiation injuries to brain.
02	IMAGING FINDINGS	• Review the imaging findings in acute, early delayed and late delayed radiation-induced brain injuries.
03	ADVANCED MRI TECHNIQUES	• To emphasize the role of Advanced MRI techniques and its implications in management.
04	PATHOPHYSIOLOGIC BASIS	• Review the pathophysiologic basis of radiation-induced injury and discuss the timeline and expected imaging appearances after RT, including the characteristic imaging features after RT with concomitant chemotherapy.

DISCLOSURES

Nothing to disclosure.

CONTENT

1 INTRODUCTION

2 BACKGROUND

3 IMAGING

4 CONCLUSION

INTRODUCTION

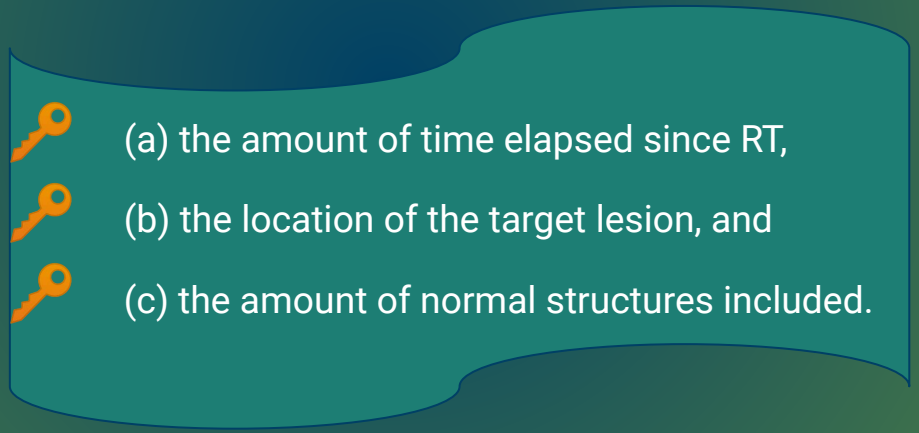
Intracranial Injuries Post Radiotherapy

- In the central nervous system (CNS), the effects of radiation can be roughly divided into effects on vascular endothelial cells and direct effects on neuroglial cells, in particular the oligodendroglial cells.

- three phases: acute, early delayed, and late delayed.
  - Acute and early delayed injuries are usually transient and reversible, whereas late delayed injuries are generally irreversible.

BACKGROUND

3 KEYS to recognizing radiation-induced changes at follow-up imaging are knowledge of:

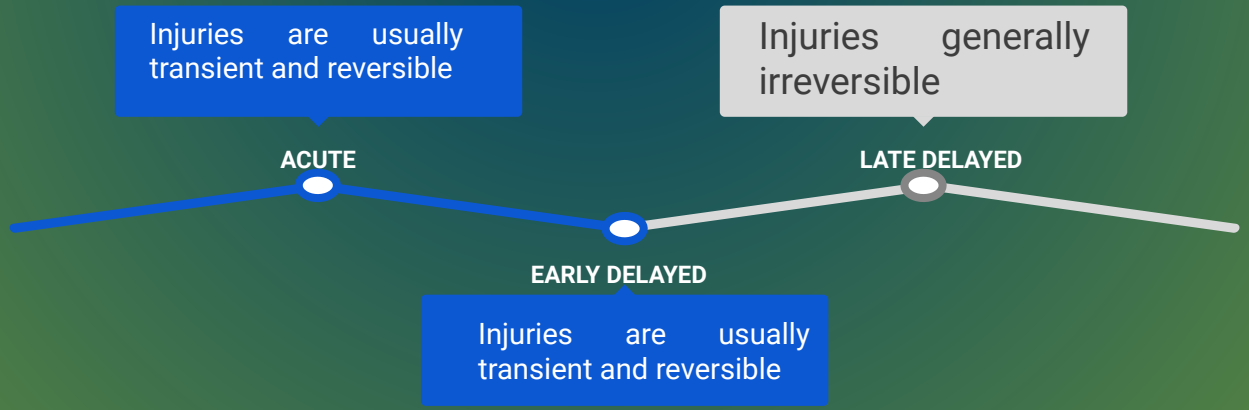


BACKGROUND

- In the central nervous system, the effects of radiation can be roughly divided into effects on:

1. Vascular endothelial cells and
2. Neuroglial cells, in particular the oligodendroglial cells.

- On the basis of the time of expression, radiation-induced injury can be divided into



BACKGROUND

Vascular Endothelial Damage

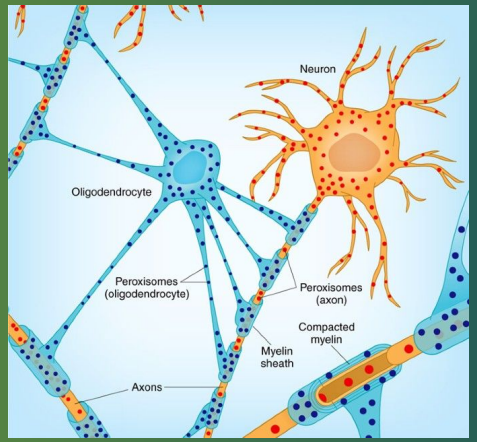
- Causes altered permeability, leading to vasogenic edema and disruption of the blood-brain barrier (BBB) or blood–spinal cord barrier.
    - *May occur within the first 24 hours after irradiation.*

- Can lead to other late vascular effects, such as telangiectasia, thrombosis, occlusion of small vessels, fibrinoid deposits, and hyaline thickening of vessel walls.
    - *As a result, ischemic stroke or hemorrhage may occur months to years after RT.*

https://promocell.com/cells-in-action/endothelial-cells-for-vascular-research/

BACKGROUND

Oligodendrocytes

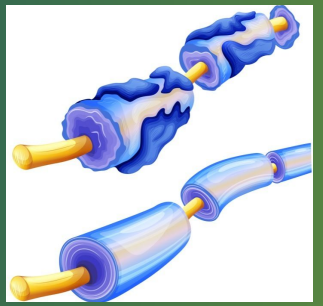


https://www.nature.com/articles/ng0807-936

- Are the most radiosensitive type of glial cell, with cell death occurring rather early after relatively low doses of irradiation.

Demyelination

- Related to the failure to replace normally turned over oligodendrocytes, with the eventual consequence being demyelination.



https://multiplesclerosisnewstoday.com/2019/01/03/high-levels-of-single-factor-halt-oligodendrocyte-progenitor-cells-ability-to-repair-myelin/

CLINICAL RESULT

Chronic damage may play a major role in late delayed radiation-induced neurotoxic effects, including cognitive impairment and white matter disease.

BACKGROUND

RADIOTHERAPY DELIVERY TECHNIQUE

- To correctly interpret imaging studies, the radiologist should be acquainted with the RT delivery technique and RT plan for each patient.

Conventional Multifractionated RT and Stereotactic Techniques

1. ***Conventional multifractionated RT:*** refers to repeated administration of small doses of radiation to a relatively large target, as in *whole-brain RT or focal (involved-field) RT*.
2. ***Stereotactic RT/radiosurgery:*** Emerging evidence indicates that high-dose irradiation used in stereotactic RT/radiosurgery may induce indirect tumor cell death via vascular damage and antitumor immunity, in addition to directly killing tumor cells via DNA damage.

IMAGING

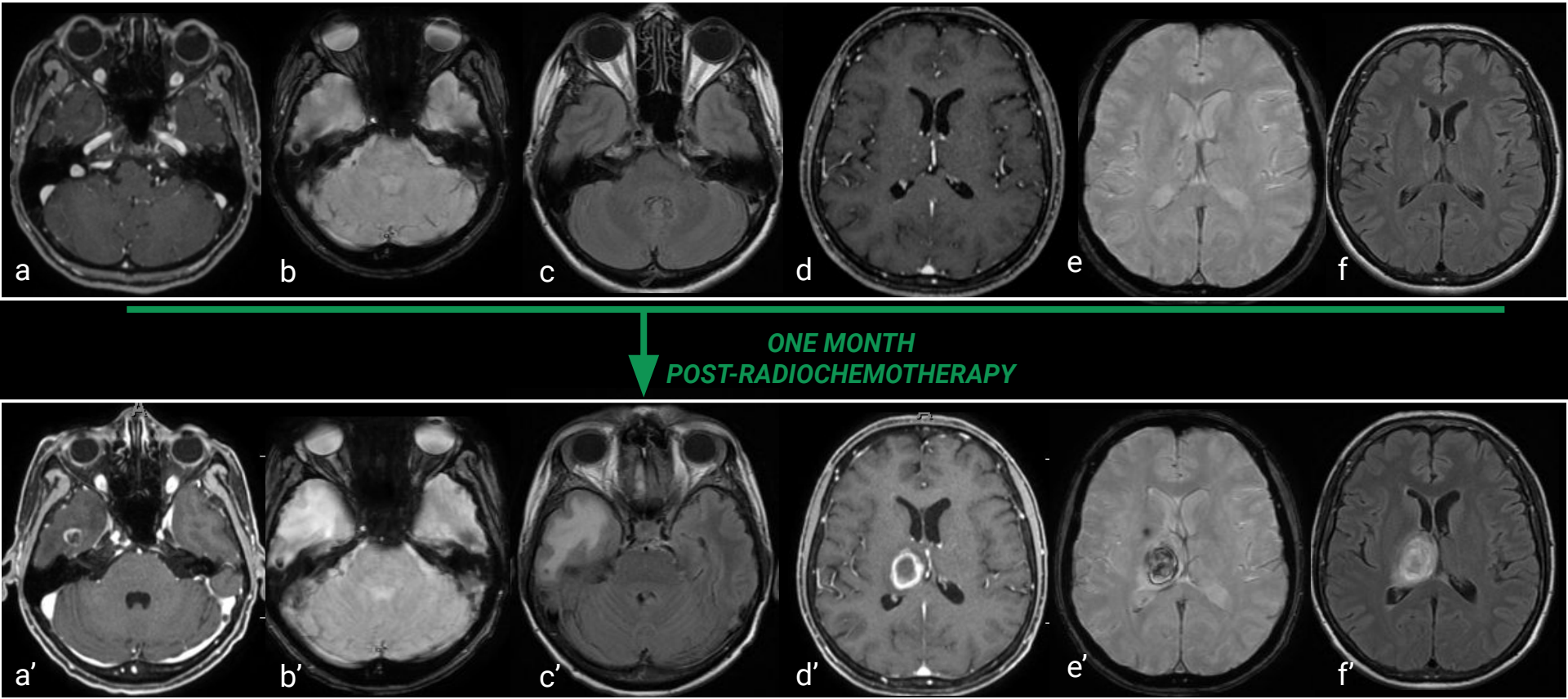
Imaging during ACUTE (1 month after irradiation**) and EARLY DELAYED (**1–6 months after irradiation**) phases related to vascular endothelial damage:**

Vascular endothelial damage causes altered permeability, leading to

- ***Vasogenic edema*** and
- ***Disruption of the blood-brain/spinal cord barrier***.
- ***Hemorrhage and ischemic stroke may occur months to years after RT.***

In addition to vasogenic edema and disruption of the BBB or blood–spinal cord barrier, transient demyelination is thought to be responsible for early delayed radiation-induced injury.

MRI findings can vary from nonenhancing white matter hyperintensity on T2-weighted images to new or increased size of enhancing lesions in the immediate vicinity of the irradiated tumor volume.



50-year-old woman who received whole brain radiotherapy (RCT) for melanoma brain metastases, besides chemotherapy. Returns one month after chemoradiotherapy with mental confusion. The follow up images show growth of enhancing nodular lesions, on axial contrast enhanced T1 weighted images (a, a', d, d'); intralesional hemorrhage in the right thalamic lesion, characterized by susceptibility artifact on SWI (e'); and worsening of the perilesional vasogenic edema, characterized by high FLAIR signal in the white matter adjacent to the lesions (c' and f').

IMAGING

Radiation-induced Leukoencephalopathy

- Generally recognized as a late delayed adverse effect and is thought to develop more than several months after RT.
- May be subclinical, at least initially, although it can result in cognitive deficits.
- Sparing of the hippocampus has recently become an important point during the treatment planning process.

- Use of concurrent or sequential chemotherapy, particularly methotrexate, may significantly increase the incidence and severity of radiation induced leukoencephalopathy.

IMAGING

Radiation-induced Leukoencephalopathy

- At imaging, it is characterized by cerebral white matter high signal intensity on T2-weighted or fluid-attenuated inversion-recovery (FLAIR) images, usually without enhancement or significant mass effect.
- It typically exhibits diffuse and symmetric involvement after whole-brain RT, with relative sparing of the subcortical U-fiber, corpus callosum, and gray matter.
- White matter lesions usually develop around the periventricular white matter at the beginning and progress to diffuse white matter changes with varying degrees of cerebral atrophy over months or years.

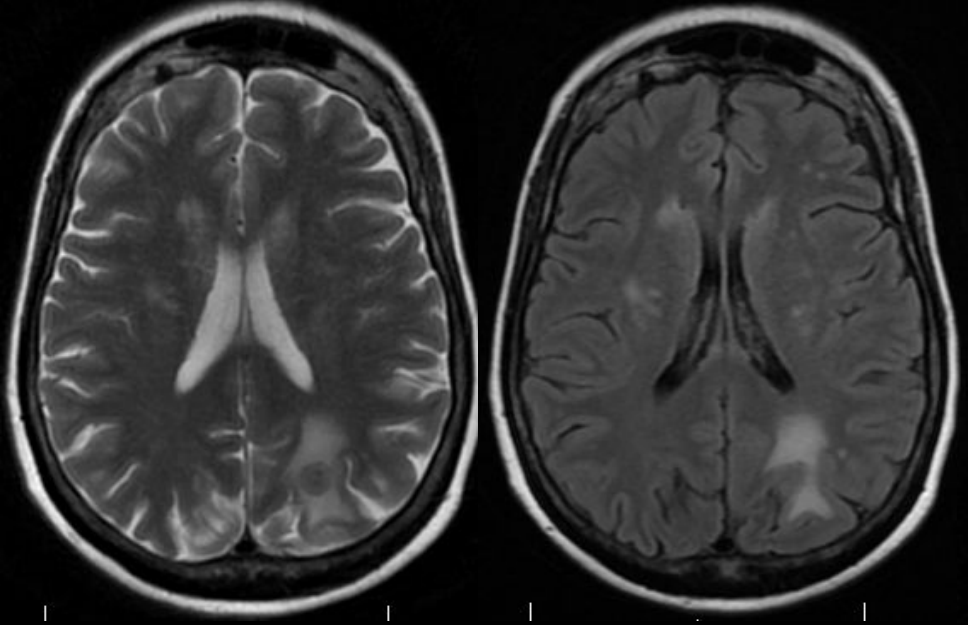
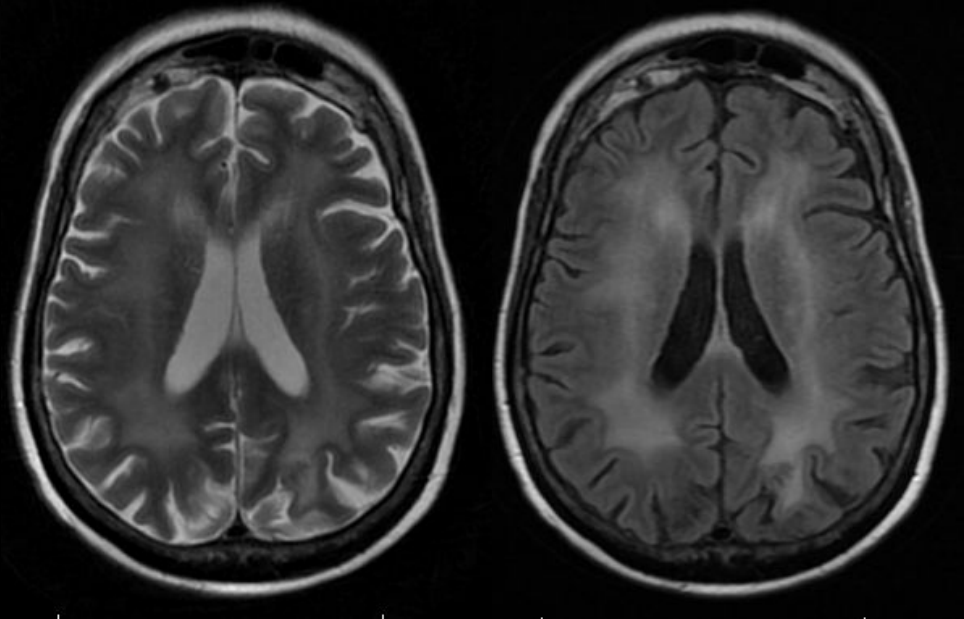


Figure 1. Radiation-induced leukoencephalopathy in a 70-year-old woman who received whole-brain radiation therapy (RT) for brain metastasis related to breast cancer. Axial T2-weighted and FLAIR images before (a and b) and 18 months (c and d) after treatment show the onset of symmetric and diffuse white matter hyperintensity and atrophy (c and d).

18 MONTHS LATTER



IMAGING

Cerebral Radiation Necrosis

- A serious late delayed complication that manifests after a latency period of several months, although the range is broad and cases have been reported more than 10 years after irradiation.
- The reported incidence of radiation necrosis after RT for brain tumors ranges from 3% to 24%.
- Radiation necrosis is more likely to occur when high doses per fraction are administered, and combined use of chemotherapy with RT may play a role in development of treatment-related necrosis.

IMAGING

Cerebral Radiation Necrosis

Radiation necrosis typically develops at or adjacent to the original site of the tumor, the location that received the highest radiation dose.

IMAGING

Cerebral Radiation Necrosis

- Conventional MRI typically demonstrates an enhancing mass lesion with central necrosis and reactive edema. Consultation with the radiation oncologist and radiation dose map should be encouraged whenever feasible.

- Imaging findings of radiation necrosis are not always irreversible and progressive but can be static, decrease, or even resolve at follow-up.

IMAGING

Conventional Imaging for Distinguishing Radiation Necrosis from Tumor Recurrence

Although not always reliable, some clinical or imaging features have been suggested in previous reports and may aid in diagnosis of radiation necrosis and tumor recurrence:

1. Radiation necrosis usually manifests after a latency period of many months. Although the range can be broad, radiation necrosis typically develops within 2 years after RT in glioma patients, and a new or worsening abnormality starting 3 years after RT is unlikely to be due to pure radiation necrosis.
2. Corpus callosum involvement in conjunction with multiple enhanced lesions — with or without crossing of the midline and subependymal spread — were statistically significant, favoring predominant glioma recurrence.
3. Recognize the common involvement of the temporal lobe after RT for nasopharyngeal cancer.

IMAGING

Advanced Imaging for Distinguishing Radiation Necrosis from Tumor Recurrence

- Several advanced imaging techniques have been investigated in an attempt to differentiate radiation necrosis from tumor recurrence:

  1 - Restricted diffusion suggests increased cellularity, and low apparent diffusion coefficient (ADC) typically favors the diagnosis of tumor recurrence.

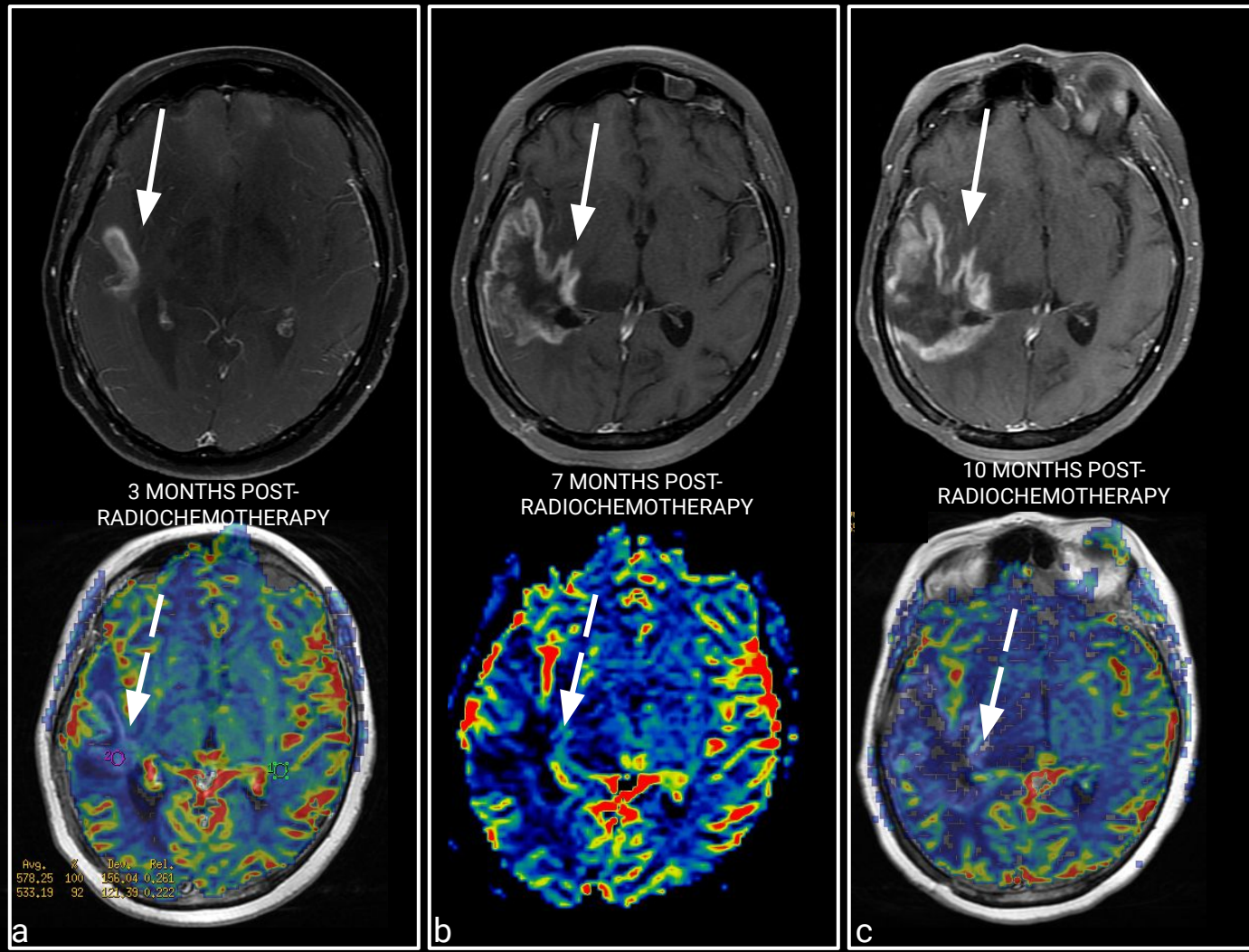
  2 - MR spectroscopy: recurrent brain tumors exhibit high ratios of choline/creatine (Cho/Cr) and choline/Nacetylaspartate (Cho/NAA), whereas radiation necrosis exhibits increased lactate and lipid peaks.

  3 - Dynamic susceptibility contrast (DSC) MRI: the most widely used perfusion technique for brain tumors. Radiation necrosis typically causes hypoperfusion with reduced rCBV, whereas high-grade tumor recurrence results in high rCBV.

  4 - An alternative but less commonly employed perfusion technique is dynamic contrast-enhanced (DCE) MRI. It helps in cases where DSC images are uninterpretable owing to susceptibility artifact, such as that due to hemorrhage or surgical clips. In addition to evaluation of blood volume in a lesion, DCE MRI enables assessment of vascular permeability.

Radionecrosis in an 65-year-old asymptomatic man who received radiochemotherapy (RCT) after resection of the enhancing component of a glioblastoma in the right temporal lobe.

Axial contrast enhanced T1 weighted images and perfusion T2 maps (with relative cerebral blood volume values - rCBV) 3 months post RCT (a), 7 months post (b) and 10 months post RCT. Images show progressive increased enhancement around the resection cavity (arrows) with no increase in rCBV (dashed arrows).



IMAGING

Pseudoprogression

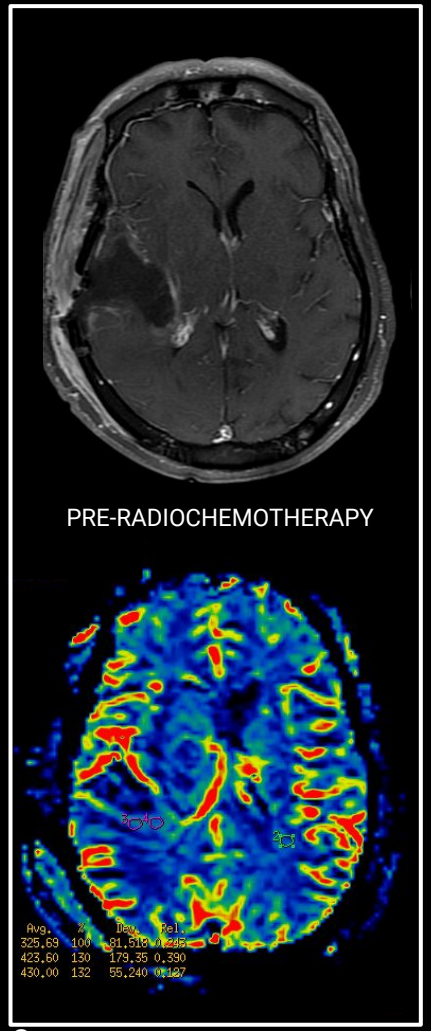
It is a subacute treatment-related effect with MRI features mimicking those of tumor progression.

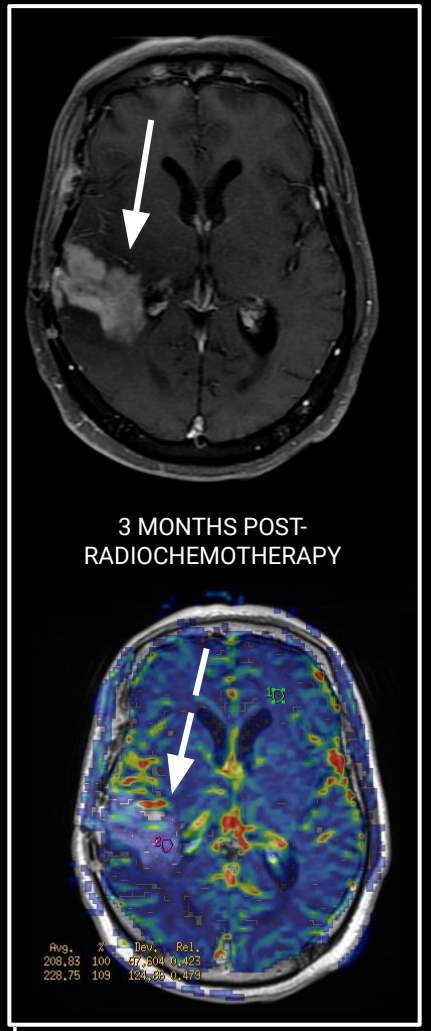
- Patients can present with an increase in contrast enhancement and peritumoral edema at MRI.
- The diagnosis of pseudoprogression is typically made retrospectively on the basis of spontaneous improvement or stabilization of imaging findings without intervention.

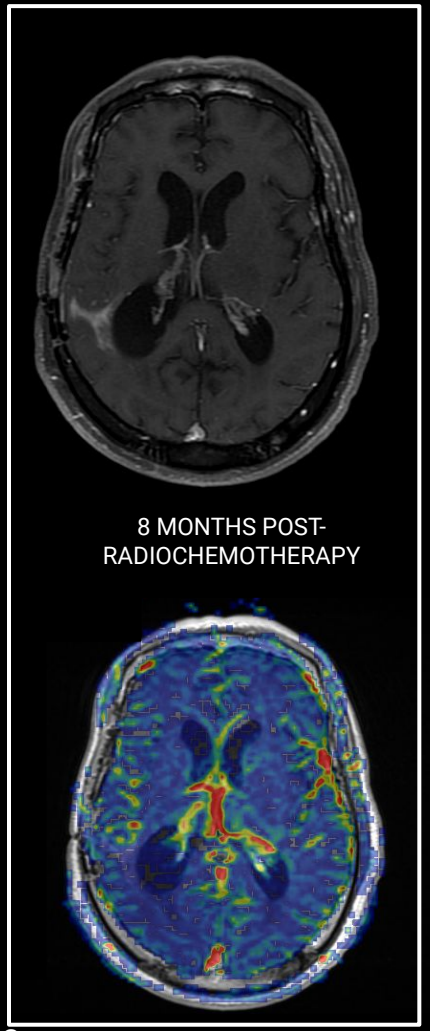
- Typically develops in the setting of combined RT and temozolomide therapy for high-grade or low-grade glioma.
- Pseudoprogression usually develops within 3 months after completion of chemoradiation therapy (CRT) and is often clinically asymptomatic.
- The timing of pseudoprogression is earlier than the typical period in which radiation necrosis is described after RT alone; therefore, it is often classified as an early delayed reaction to radiation.
- The incidence of pseudoprogression is likely to increase with a higher dose of RT. Pseudoprogression may represent an exaggerated response to effective therapy.
- Pseudoprogression is often asymptomatic, whereas true tumor progression is more likely to be associated with clinical decline.

Pseudoprogression in a 60-year-old asymptomatic woman who received radiochemotherapy (RCT), standard-fractionation type, with temozolomide after resection of the enhancing component of a glioblastoma in the right parietal lobe.

Axial contrast enhanced T1 weighted images and perfusion T2 maps (with relative cerebral blood volume values - rCBV) pre radiochemotherapy (a), 3 months post (b) and 8 months post RCT show increased enhancement (arrow in b) involving the resection cavity with no increase in rCBV (dashed arrow in b). Follow-up corresponding images 8 months after RCT show spontaneous reduction of the lesion (c).







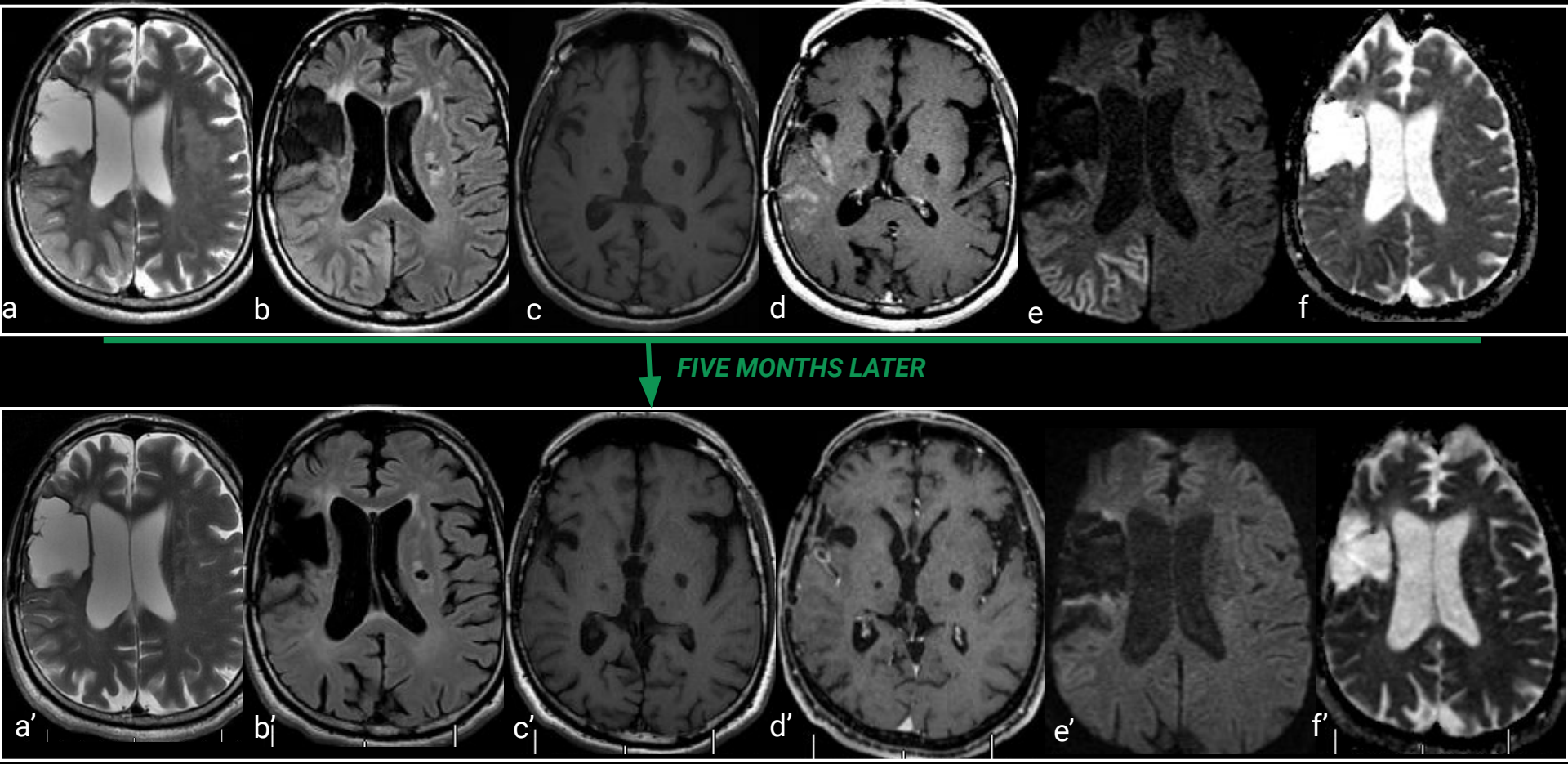
IMAGING

Strokelike Migraine Attacks after RT (SMART Syndrome)

Is an uncommon delayed complication of cranial irradiation. Patients usually present years after RT with migraine like headaches, seizures, and subacute strokelike episodes with symptoms such as hemiplegia, aphasia, and hemianopia. Attacks are typically subacute in onset and resolve after weeks in most cases.

- The combination of radiation-induced vascular damage and clinical and subclinical seizure activity could explain cortical edema and impaired BBB integrity with persisting contrast enhancement for days to weeks and, at times, becoming permanent with evidence of cortical laminar necrosis.

- Imaging findings include transient, unilateral, gyriform abnormal T2 and fluid-attenuated inversion-recovery (FLAIR) signal intensity with mild mass effect and cortical enhancement with minimal leptomeningeal enhancement, usually in an area included in the radiation ports. Diffusion restriction is variably seen. Imaging findings may appear 2–7 days after onset of symptoms and typically resolve in 2–5 weeks.



55-year-old man with history of whole brain radiotherapy and surgical resection of a right frontoparietal Gesmistocytic Astrocytoma 10 years ago. The patient comes with focal motor crisis in hemiface and left upper limb. First MRI exam shows on axial T2 (a) and FLAIR (b) a right occipitoparietal region with cortical thickening and hypersignal associated with gyral enhancement pattern and restricted diffusion (d, e and f). On follow up 5 months later, it was observed clinical improvement of the patient as well as resolution of the mentioned image findings - evolution compatible with stroke like migraine attacks after radiotherapy (SMART Syndrome).

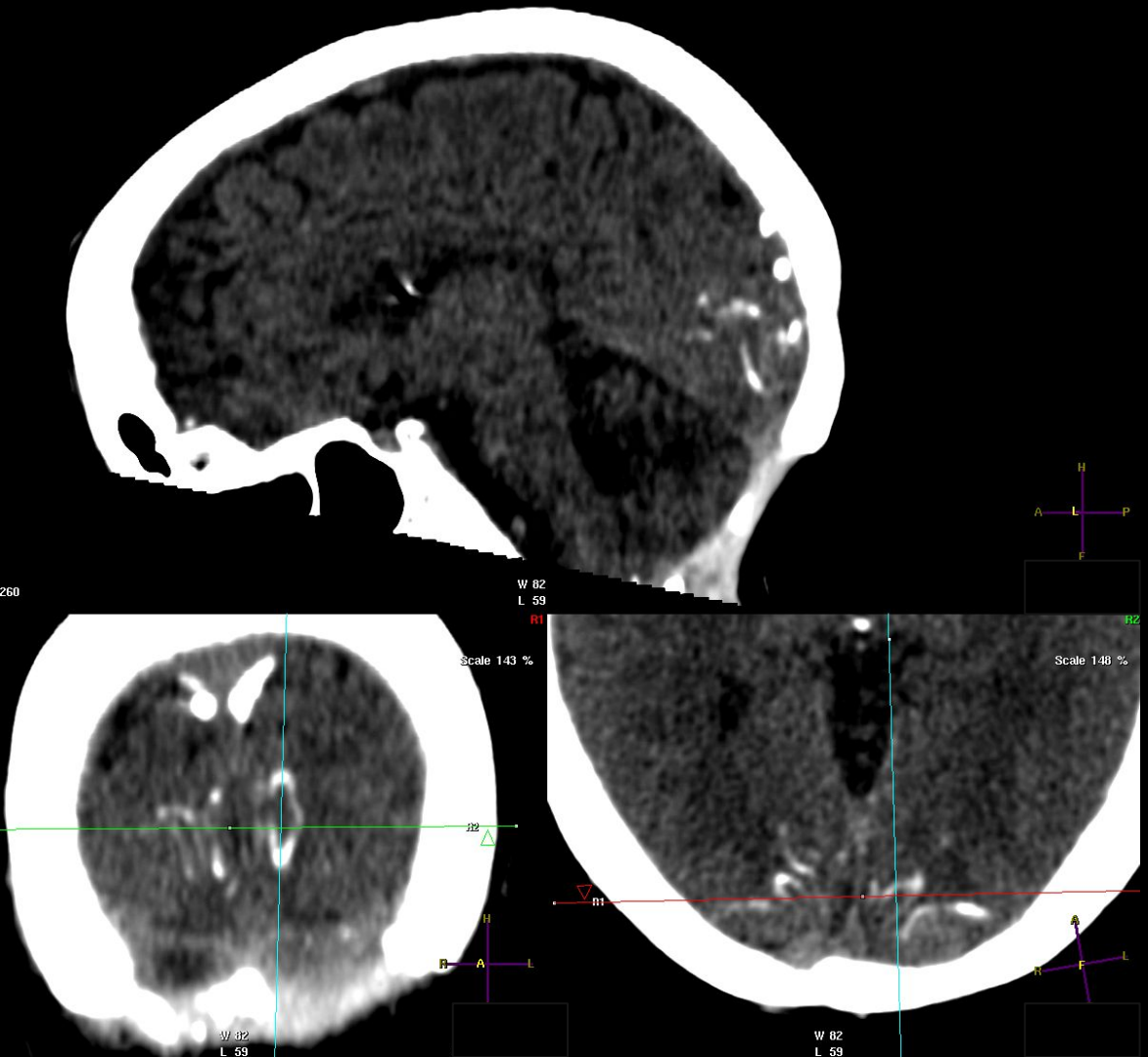
IMAGING

Mineralizing Microangiopathy (Dystrophic Calcification)

It is a distinctive histopathologic process involving the microvasculature of the CNS. It usually develops after combined CNS irradiation and chemotherapy in childhood, although it may develop after RT alone.

- Histologically, the calcification found in mineralizing microangiopathy is present in the walls of precapillary arterioles, capillaries, venules, and smaller arteries such as the lenticulostriate artery. Dystrophic calcification also develops in the perivascular neural tissue secondary to mineralization of plasma fluids, which leak out of the damaged vessels, and regional ischemia resulting from circulatory impairment.

- Can be detected on nonenhanced CT as calcifications in the affected region, typically multiple punctate foci of calcification in basal ganglia and subcortical white matter.
- In most cases, mineralizing microangiopathy is asymptomatic and is an incidental finding at follow-up CT.



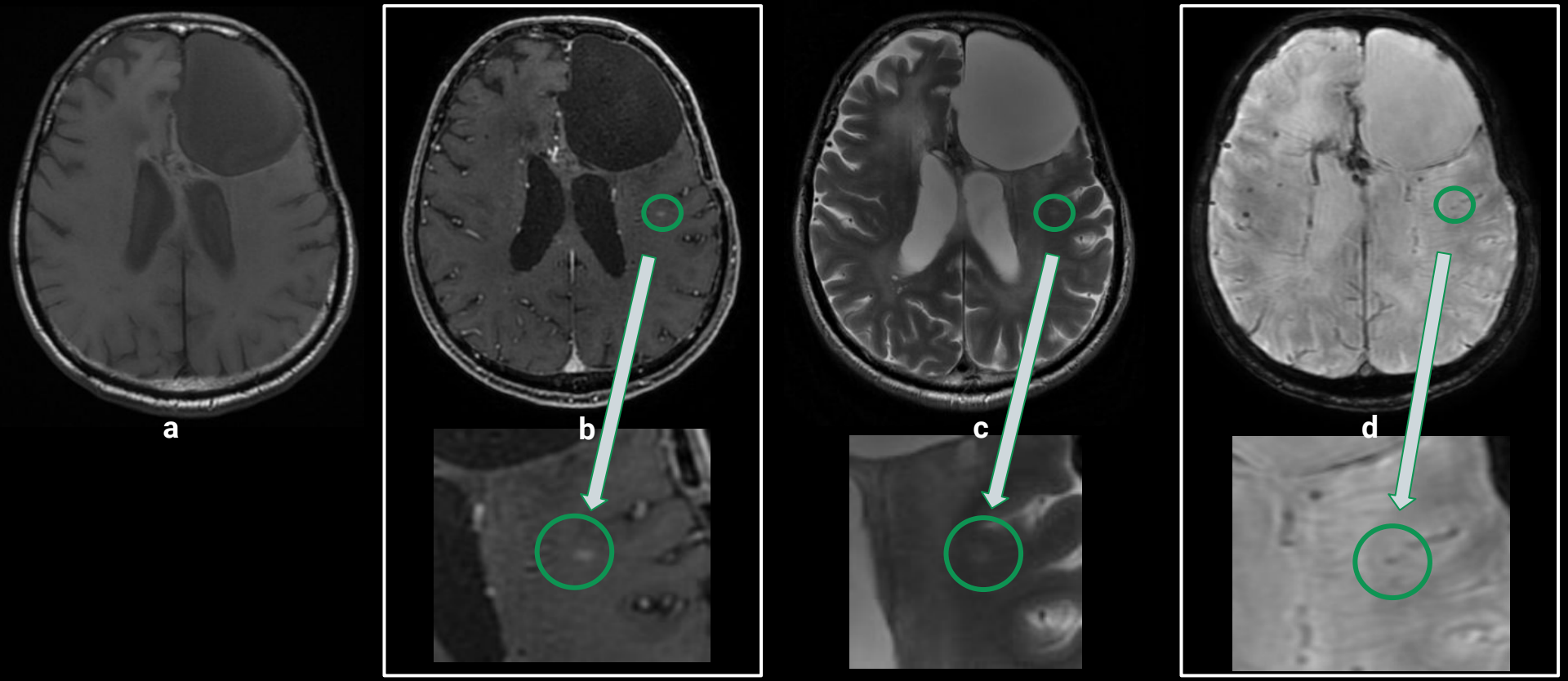
Multiplanar reformats nonenhanced CT images of a 38-year-old man, treated for medulloblastoma 15 years before with surgery and whole-brain RT and ChT, show linear subcortical calcifications in both occipital lobes related to mineralizing microangiopathy (dystrophic calcification).

IMAGING

Capillary Telangiectasia

Radiotherapy may induce capillary telangiectasias - small, asymptomatic low flow vascular lesions of the brain.

On MRI images, they appear as subtle lesions with no mass effect, on T2 with normal or slightly increased signal intensity, low signal intensity on T2* and may demonstrate stippled enhancement on T1.



Axial MRI images of a 65-year-old male treated for frontal left anaplastic oligodendroglioma 8 years before with surgery, whole-brain RT and ChT. Images show a focus with contrast enhancement on T1WI (b), low signal on SWI (d), hypersignal on T2WI (c), with no correspondence on T1WI without contrast (a) - pattern compatible with radioinduced capillary telangiectasia.

IMAGING

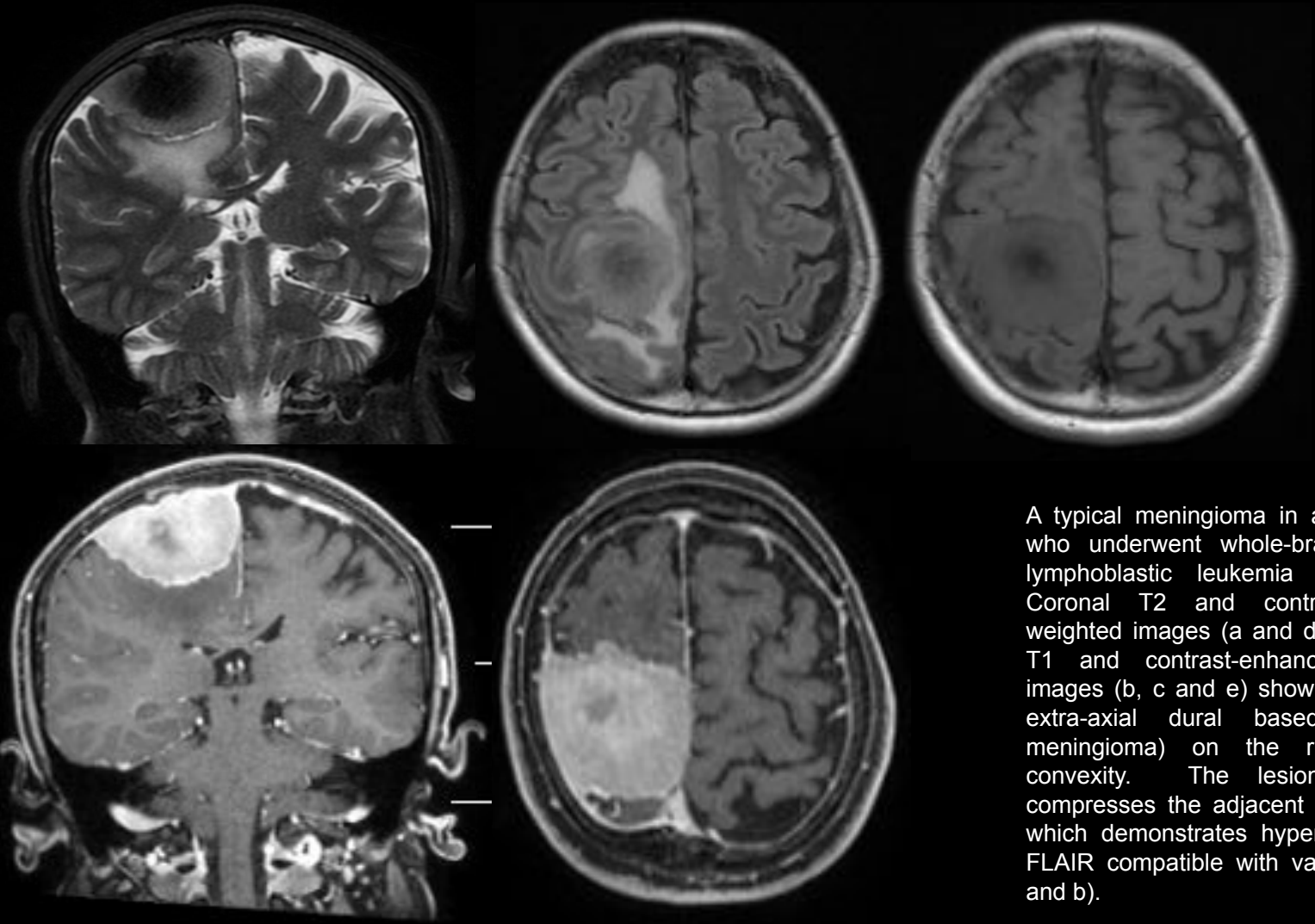
Radiation-induced Brain Tumors

Cranial irradiation has been established as a cause of brain tumors, including meningiomas, gliomas, sarcomas, and nerve sheath tumors.

As longer survival has been achieved with improvements in medical management of primary brain tumors, there is a higher incidence and a larger number of secondary tumors to deal with.

→ Regarding the histotype, meningiomas are the most common subsequent brain tumors among aging adult survivors of childhood cancer who were exposed to cranial radiation.

→ Higher doses of irradiation are associated with an increased risk of developing atypical/anaplastic or multiple meningiomas and a shorter latency period.



A typical meningioma in a 40-year-old man who underwent whole-brain RT for acute lymphoblastic leukemia during childhood. Coronal T2 and contrast-enhanced T1 weighted images (a and d) and axial FLAIR, T1 and contrast-enhanced T1 weighted images (b, c and e) show a hyperenhancing extra-axial dural based tumor (typical meningioma) on the right frontoparietal convexity. The lesion displaces and compresses the adjacent brain parenchyma, which demonstrates hypersignal on T2 and FLAIR compatible with vasogenic edema (a and b).

IMAGING

Conclusion

The structures surrounding the target lesion are inevitably exposed to radiation, and a wide variety of radiation induced changes may be observed at posttreatment imaging.

Knowledge of the radiation treatment plan, amount of normal structures included, location of the target lesion, and amount of time elapsed since RT is markedly important at follow-up imaging.

The reporting radiologist should be familiar with the timeline and expected imaging appearances after RT to avoid pitfalls in image interpretation.

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