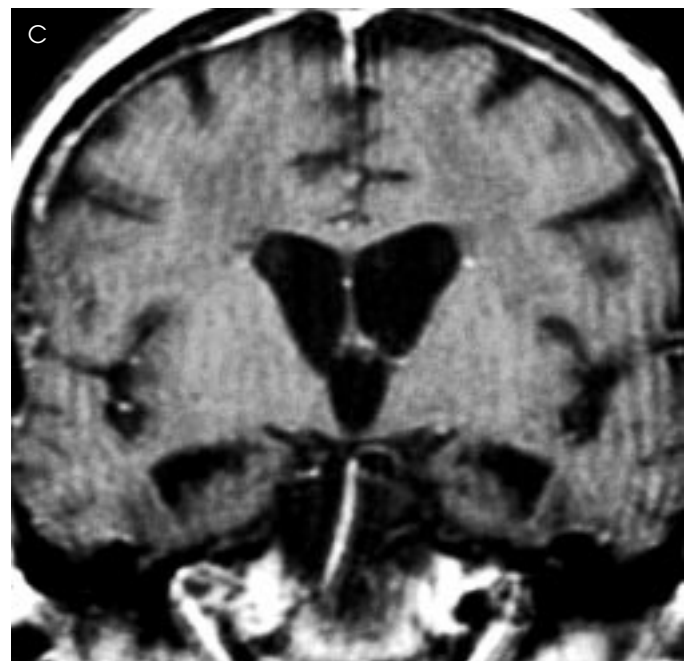
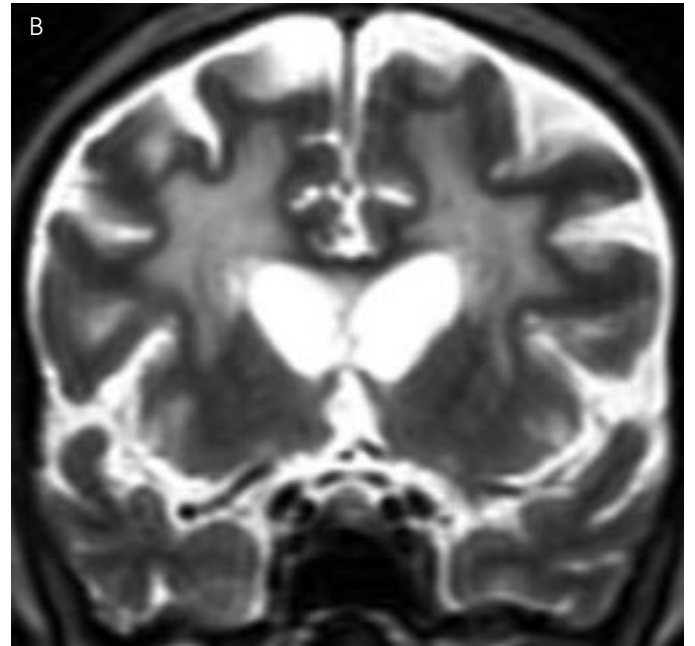


Case W10

Clinical Presentation

A 54-year-old woman is noted to have progressive cognitive decline. Her history is notable for prior whole brain radiation for metastatic disease.



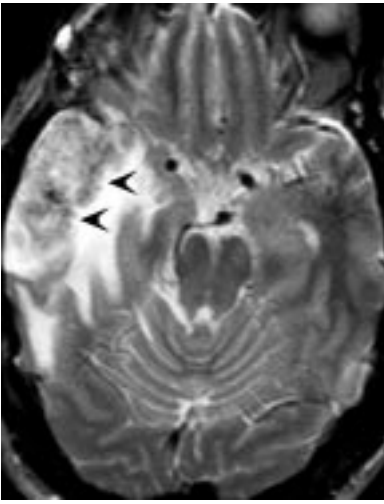


Fig. D. A patient with a history of prior surgery and radiation therapy for a basal cell carcinoma invading the frontal bone presents following a seizure. An axial T2-WI demonstrates a heterogeneous mass in the right temporal lobe (*arrowheads*), with surrounding vasogenic edema.

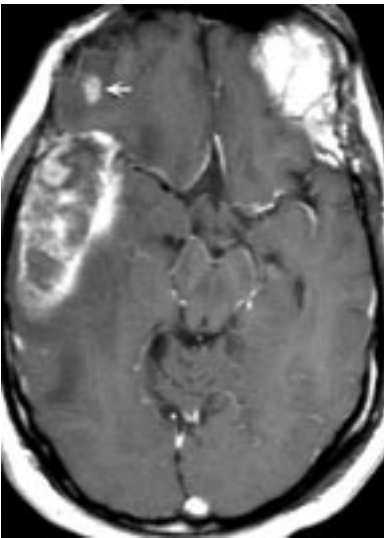


Fig. E. An axial post-gadolinium T1-WI (same patient as Fig. D) demonstrates irregular enhancement of the right temporal lobe mass, as well as focal enhancement in the right frontal lobe (*arrow*). At surgery, only necrotic tissue consistent with radiation necrosis was found.

Radiologic Findings

A non-contrast CT scan (Fig. A) demonstrates mild prominence of the ventricles and sulci, as well as symmetric low density in the periventricular white matter. A coronal fast spin-echo T2-WI through the frontal lobe (Fig. B) demonstrates confluent symmetric T2 prolongation in the deep and subcortical white matter. There is no associated mass effect. A coronal post-gadolinium T1-WI (Fig. C) shows abnormal hypointensity in the white matter, but no evidence for enhancement.

Diagnosis

White matter injury secondary to radiation therapy (radiation leukoencephalopathy)

Differential Diagnosis

- Chemotherapy-induced white matter changes (often indistinguishable, need clinical history)
- White matter toxins such as toluene or carbon monoxide (typically accompanied by lesions involving the deep gray nuclei, need appropriate clinical history)
- White matter changes of aging (often patchy but may be confluent)
- Multiple sclerosis (usually discrete plaques, although may be diffuse)
- Acute disseminated encephalomyelitis (may be diffuse but is usually asymmetric, more common in children)

Discussion

Background

Radiation therapy has significant effects on the CNS. These effects may be classified by their time of occurrence after injury.

- *Acute:* 1 to 6 weeks after therapy, transient worsening of symptoms, usually a self-limited course
- *Early delayed:* weeks to months after therapy, usually asymptomatic and resolves without therapy. In patients who have received hyperfractionated therapy, focal necrosis with enhancement and worsening symptoms may occur.
- *Late delayed:* months to years after therapy. Changes include diffuse white matter injury, focal necrosis, global atrophy, mineralizing microangiopathy, vascular telangiectasia, optic neuropathy, and large vessel vasculopathy. These changes are generally irreversible and often progressive.

Diffuse white matter injury occurs in 40 to 50% of patients who receive whole brain radiation therapy. The prevalence of severe radiation effects increases with age, volume of irradiated brain, radiation dose, and the interval between treatment and imaging. Abnormalities on imaging studies are generally seen with doses above 50 Gy, although neurocognitive effects may be observed at lower doses, especially in children.

Pearls

- The severity of imaging findings correlates poorly with the clinical presentation.
- Cerebral and cerebellar atrophy often accompany diffuse white matter damage.

Pitfalls

- Focal radiation necrosis may be indistinguishable from tumor progression.
- Newer modalities such as positron emission tomography and proton MR spectroscopy may be helpful in distinguishing focal radiation necrosis from tumor progression. Serial imaging is also helpful in making this distinction (Figs. F and G), but may allow tumor to progress as a patient is followed over time.

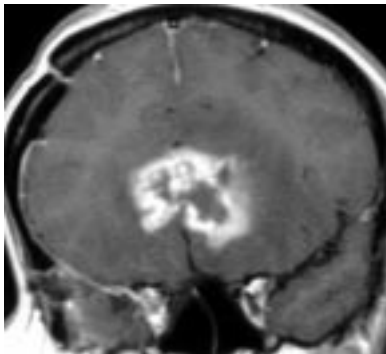


Fig. F. A coronal post-gadolinium T1-WI in a 35-year-old woman previously radiated for astrocytoma shows a centrally necrotic mass with surrounding vasogenic edema involving the genu of the corpus callosum. At this time, the patient refused further therapy for a presumed tumor recurrence.

Etiology

Radiation effects on the CNS are a consequence of injury to small vessels (leading to ischemia) and direct damage to glial cells (leading to demyelination). Neurons themselves are relatively radioresistant.

Clinical Findings

Diffuse white matter injury is often subclinical and is discovered only on routine imaging studies. Some patients may develop personality change, cognitive decline, memory loss, and frank dementia.

Complications

When chemotherapy (particularly intrathecal methotrexate) is given in conjunction with whole brain radiation, a necrotizing leukoencephalopathy may develop, which may lead to rapid clinical deterioration and death. Other forms of radiation injury such as focal radionecrosis may also occur in conjunction with diffuse white matter changes. Patients with focal radiation necrosis have symptoms related to a space-occupying lesion and may require surgical debulking if edema and mass effect cannot be controlled with high-dose steroids (Figs. D and E).

Pathology

Gross

- Global parenchymal volume loss and diffuse myelin pallor

Microscopic

- Vessel walls demonstrate arteriolar hyalinization, fibrinoid necrosis, and spontaneous thrombosis
- Parenchyma shows areas of demyelination and astrogliosis, and may show large atypical globular cells

Imaging Findings

CT

- Symmetric white matter hypodensity

MR

- Symmetric T2 prolongation in the periventricular and deep white matter, which varies from small foci at the angles of the ventricles to an intense band of high signal extending from the ventricle to the gray-white junction
- Signal changes may involve the corpus callosum and the subcortical U fibers
- Mass effect and enhancement do not occur unless there is superimposed focal radiation necrosis
- A sharply demarcated border paralleling therapy ports may be observed

Treatment

No therapy is available for diffuse white matter injury

Prognosis

Variable, from asymptomatic to progressive cognitive decline and dementia

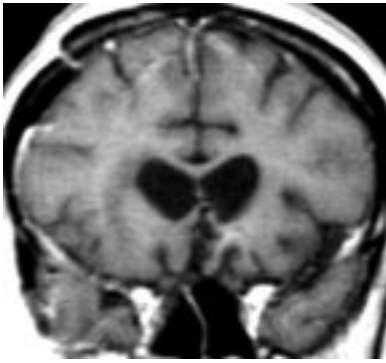


Fig. G. A coronal post-gadolinium T1-WI in the same patient as Figure F 12 months later demonstrates complete regression of the mass. This represents presumed focal radiation necrosis.

Suggested Readings

Rabin BM, Meyer JR, Berlin JW, et al. Radiation-induced changes in the central nervous system and head and neck. *Radiographics* 16:1055–1072, 1996.

Schultheiss TE, Kun LE, Ang KK, Stephens LC. Radiation response of the central nervous system. *Int J Rad Oncol Biol Phys* 31:1093–1112, 1995.

Valk PE, Dillon WP. Radiation injury of the brain. *AJNR* 12:45–62, 1991.