RESIDENT & FELLOW SECTION

Section Editor
John J. Millichap, MD

Clinical Reasoning: Corpus callosum lesion with multiple strokes

Zubeda Sheikh, MD
Nidhiben Anadani, MBBS
Bhrugav Raval, MBBS
Leroy Sharer, MD
Machteld Hillen, MD

Correspondence to Dr. Sheikh: Zubeda.karim@gmail.com

SECTION 1

A 71-year-old woman with hypertension, diabetes, and recent stroke presented with acute left hemiparesis, which started 3.5 hours earlier but improved by the time of emergency department evaluation. Examination showed mild left-sided pronator drift and sensory extinction. Her history was significant for resection of a right frontoparietal meningioma for which she had received adjuvant radiation therapy 3 years previously.

Question for consideration:

1. How would you evaluate this patient?

GO TO SECTION 2

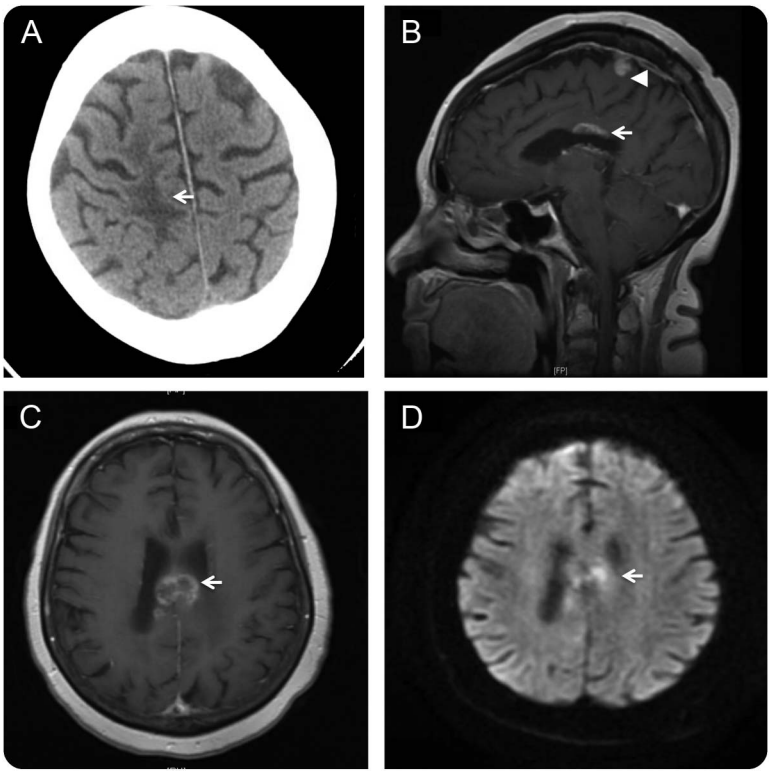
From the Departments of Neurology (Z.S., N.A., B.R., M.H.) and Pathology (L.S.), Rutgers New Jersey Medical School, Newark, NJ.
Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

SECTION 2

Given the patient's vascular risk factors and recent stroke, acute ischemic stroke was considered high in the initial differential diagnosis. The patient was rapidly evaluated with a noncontrast head CT, which showed postoperative changes from a right frontoparietal craniotomy and an area of encephalomalacia in the right frontoparietal region (figure 1A) but no acute ischemic changes. CT angiogram of head and neck demonstrated 20% stenosis of the right carotid bulb.

Thrombolytics were not administered as the patient's motor deficits had rapidly improved and her sensory extinction could be explained by the right frontoparietal encephalomalacia. She fit criteria for TIA and was admitted for further evaluation. Her HBA1C was 7.7, total cholesterol 187, low-density lipoprotein 95, high-density lipoprotein 80, and triglycerides 60. Transesophageal echocardiography showed a small, mobile, linear echodensity on the ventral aspect of aortic valve consistent with a Lambl excrescence. Brain MRI showed fluid-attenuated inversion recovery hyperintensity in the body of corpus callosum, extending to both hemispheres, with patchy diffusion-weighted imaging (DWI) and apparent diffusion coefficient positivity and gadolinium enhancement. A smaller lesion was present posterior to the main lesion on the right (figure 1, B–D). In addition, an enhancing lesion was seen abutting the superior sagittal sinus, consistent with residual meningioma (figure 1B). Previous health records were obtained to clarify the pathology of the previously resected lesion and the dose of radiation. The patient had undergone gross total resection of a dural-based parafalcine WHO grade I meningioma. A portion of the tumor that was attached to the superior sagittal sinus was not removed, due to concern for injury to the sinus. The resected specimen contained an area of metastatic neuroendocrine carcinoma with highly atypical, synaptophysin-positive, nonmeningothelial cells. After a staging workup did not reveal a primary, this second tumor was thought to be malignant transformation of the meningioma. The woman was treated with 6,000 cGy of partial brain radiation in 30 fractions, after which she developed mild cognitive dysfunction.

Figure 1 Initial MRI brain



(A) Noncontrast head CT shows encephalomalacia (arrow) in the right frontoparietal region. (B) Sagittal T1 postcontrast MRI shows a contrast-enhancing lesion in the body of corpus callosum (arrow) and a residual meningioma (arrowhead) in the frontal parasagittal region. (C) Axial postcontrast sequence shows heterogeneously enhancing lesion in body of corpus callosum (arrow). (D) Diffusion-weighted imaging sequence exhibits patchy increased signal in the corpus callosum (arrow).

Question for consideration:

1. What is the differential diagnosis of the corpus callosum lesion seen in this patient?

GO TO SECTION 3

SECTION 3

Corpus callosum lesions have a broad differential diagnosis, with the greatest concern for a neoplasm in an elderly patient. The most common tumors affecting the corpus callosum are glioblastoma multiforme (GBM) and lymphoma.

GBM spreads by direct extension along white matter tracts, and may grow through the corpus callosum into both hemispheres, resulting in a butterfly appearance. GBM was considered as the lesion was heterogeneously enhancing and located in corpus callosum, which are characteristic features of GBM. Central necrosis, another classic feature of GBM, was not present in our patient.[1] Lymphoma was considered because of the location of the lesion in the corpus callosum, the presence of multiple lesions, and restricted diffusion within the lesion. Lymphoma typically shows homogeneous enhancement and affects the periventricular white matter, deep gray matter, and corpus callosum. It classically has low T2 signal due to high cellularity.[1] Although rare, metastases were considered in this particular patient as a portion of her previously resected meningioma had shown pathology consistent with neuroendocrine carcinoma.

Although the corpus callosum can be involved in cerebral infarcts, these most commonly occur in the splenium. Isolated infarction of the corpus callosum is rare because of its rich blood supply.[2] This patient's lesion showed restricted diffusion in combination with contrast enhancement, which can be seen in subacute infarctions. We considered this in the differential diagnosis because of a history of previous stroke and presence of multiple vascular risk factors.

Radiation necrosis develops at the site of maximum radiation delivery, enhances with contrast, grows over time, and has surrounding edema with mass effect.[3] Since the lesion was located in the field of radiation of the patient's prior parasagittal tumor, we considered radiation necrosis in our differential diagnosis.

Demyelinating lesions such as multiple sclerosis (MS) commonly affect the corpus callosum but we thought this to be unlikely because of the age of our patient and MS lesions are typically small and oval, radiating from the ventricular surface to inferior aspect of corpus callosum as well as in the periventricular, juxtacortical, and infratentorial white matter.

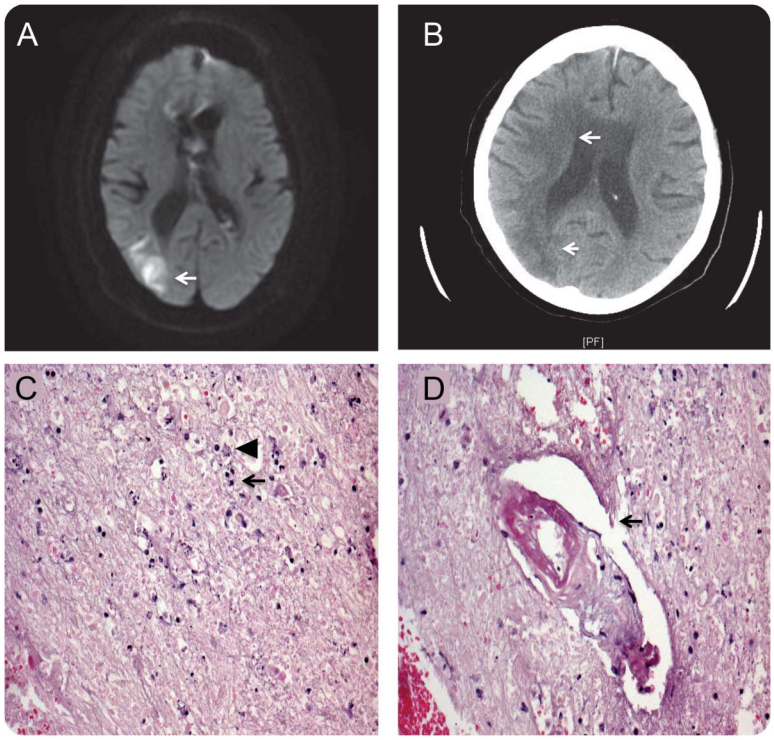
Toxic insults such as Marchiafava-Bignami disease (MBD) rarely involve the corpus callosum. MBD causes necrosis of corpus callosum, eventually resulting in atrophy and cavitation.[4] Our patient did not have risk factors for MBD such as alcoholism or malnutrition.

Question for consideration:

1. What is Lambl excrescence and what is its significance?

GO TO SECTION 4

Figure 2 Repeat imaging and pathology of resected lesion



(A) Repeat MRI of brain shows a new infarct involving the right parietal lobe (arrow). (B) Subsequent head CT shows infarcts in right frontal and parietal lobes (arrows). (C) Biopsy (hematoxylin & eosin [H&E] ×25) exhibits necrosis along with degenerating polymorphs (arrow) and lipid-laden macrophages (arrowhead). (D) Biopsy (H&E ×25) shows blood vessel (arrow) with fibrinoid necrosis without any evidence of inflammation in the vessel wall.

SECTION 4

Lambl excrescence is a filiform lesion found along the line of closure of the aortic valve leaflets and thought to be the result of wear and tear. It has been reported as a potential cause of ischemic stroke and is treated with dual antiplatelet agents or anticoagulants.[5]

On hospital day 3, the patient became less responsive and was noted to have a subtle left facial weakness. Over the next 2 days, she developed a left hemiparesis, and repeat MRI showed acute infarction in the right parietal lobe (figure 2A). It was unclear if the lesion in the corpus callosum and the new stroke were part of the same pathology. The patient had multiple vascular risk factors and Lambl excrescence, which could be the cause of the ischemic stroke independent of the corpus callosum lesion. It has been hypothesized that a GBM can lead to ischemia by causing a procoagulant state or by compression of cerebral arteries by tumor.[6] Intravascular lymphoma can cause multiple and recurrent ischemic strokes, while radiation-induced vasculopathy can cause ischemic strokes as well as tumor-like lesions.

Question for consideration:

1. What would be the definitive test to diagnose this patient's condition?

GO TO SECTION 5

SECTION 5

The patient underwent a gross total resection of the corpus callosum lesion on day 5 of hospitalization. On day 10, her mental status further worsened and head CT showed infarction in the right frontal, right parietal, and left parasagittal frontal lobes (figure 2B). Mild stenosis of the distal M1 segment of right middle cerebral artery was noted on repeat CT angiography. Her mental status improved over next few days, but she remained minimally verbal with left hemiplegia and failure to swallow.

The tissue resected at surgery revealed extensive necrosis, with inflammatory cells including mononuclear cells, degenerating polymorphs, and lipid-laden macrophages (figure 2C). Large blood vessels showed fibrinoid necrosis and hyaline change without vasculitic change or thrombosis (figure 2D). There were no neoplastic cells, ischemic changes, or evidence of viral infection. These findings were consistent with radiation necrosis with evidence of radiation vasculopathy. Biopsy is the gold standard for a definitive diagnosis of radiation necrosis.[7] Though different imaging modalities like DWI/diffusion tensor imaging, magnetic resonance spectroscopy, PET, and SPECT have been used, no single imaging modality reliably differentiates between radiation necrosis and tumor recurrence.

DISCUSSION Radiation injury to the CNS can be acute (few days to weeks), early delayed (1–6 months), or late delayed (6 months to several years after radiation therapy). Acute injury presents as fatigue, worsening of prior neurologic deficits, and symptoms of increased intracranial pressure. It is thought to be dose-related due to disruption of the blood–brain barrier. MRI may be normal or may show diffuse brain edema.[7] The disease is usually self-limited and nonprogressive. Early delayed injury is characterized by pronounced somnolence, lethargy, and anorexia, often occurring in the setting of concomitant chemotherapy. Transient demyelination is the suspected mechanism. Acute and early delayed reactions can present as an expanding mass with contrast enhancement mimicking tumor progression (pseudoprogression) and is reversible.[8]

Late delayed injury is irreversible and progressive with changes in the white matter, radiation necrosis, and vascular lesions including lacunar infarctions, large vessel occlusions, and telangiectasias. Radiation necrosis can occur within a few weeks to as late as 19 years after therapy, with 80% of cases occurring within 3 years.[7] It is associated with high-dose local radiation and is rare with whole brain radiation.[9] Pathologically it is thought to be due to glial and endothelial injury. Histopathologic features include parenchymal coagulative necrosis and fibrinoid necrosis of blood vessel walls. Radiologic diagnosis of radiation necrosis can be difficult, as it is indistinguishable from tumor recurrence. The gold standard diagnostic test is surgical resection and histopathologic examination. Management of radiation necrosis includes a trial of dexamethasone and surgical debulking when this fails. A recent placebo-controlled trial demonstrated the efficacy of bevacizumab in improving neurologic symptoms and reducing the volume of radiation necrosis,[10] although the lesion may recur after therapy.

Tumors and demyelination are the most common etiologies of a corpus callosum lesion. Radiologically, radiation necrosis is indistinguishable from a highly malignant tumor and should be in the differential in any patient presenting with a mass after radiation treatment, especially when there is evidence of a vasculopathy. Although she had Lambl excrescence, our patient's infarctions were thought to be due to radiation vasculopathy.

AUTHOR CONTRIBUTIONS

Dr. Sheikh conceptualized and designed the manuscript, drafted the case presentation and discussion, and contributed to the images. Dr. Anadani drafted the discussion of radiation-induced changes in brain. Dr. Raval created the neuroimages and edited the manuscript. Dr. Sharer made the pathologic diagnosis, created pathology images, and edited the manuscript. Dr. Hillen revised and edited the manuscript and approved all final changes.

STUDY FUNDING

No targeted funding reported.

DISCLOSURE

Z. Sheikh, N. Anadani, B. Raval, and L. Sharer report no disclosures relevant to the manuscript. M. Hillen has received research support from Roche, Biogen Idec, Novartis, NIH/National Institute of Neurological Disorders and Stroke, and CHDI Foundation. Go to Neurology.org for full disclosures.

REFERENCES

1. Uchino A, Takase Y, Nomiyama K, Egashira R, Kudo S. Acquired lesions of corpus callosum. Eur Radiol 2006;16:905–914.
2. Chrysikopoulos H, Andreou J, Roussakis A, Pappas J. Infarction of the corpus callosum: computed tomography and magnetic resonance imaging. Eur J Radiol 1997;25:2–8.
3. Kumar AJ, Leeds NE, Fuller GN, et al. Malignant gliomas: MR imaging spectrum of radiation therapy- and chemotherapy-induced necrosis of the brain after treatment. Radiology 2000;217:377–384.
4. Hillbom M, Saloheimo P, Fujioka S, Wszolek ZK, Juvela S, Leone MA. Diagnosis and management of Marchiafava-Bignami disease: a review of CT/MRI confirmed cases. J Neurol Neurosurg Psychiatry 2014;85:168–173.
5. Chu A, Aung TT, Sahalon H, Choksi V, Feiz H. Lambl's excrescence associated with cryptogenic stroke: a case report and literature review. Am J Case Rep 2015;16:876–881.
6. Rojas-Marcos I, Martin-Duverneuil N, Laigle-Donadey F, Taillibert S, Delattre JY. Ischemic stroke in patients with glioblastoma multiforme. J Neurol 2005;252:488–489.

7. Walker AJ, Ruzevick J, Malayeri AA, et al. Postradiation imaging changes in the CNS: how can we differentiate between treatment effect and disease progression? Future Oncol 2014;10:1277–1297.
8. Parvez K, Parvez A, Zadeh G. The diagnosis and treatment of pseudoprogression, radiation necrosis and brain tumor recurrence. Int J Mol Sci 2014;15: 11832–11846.
9. Cerghet M, Redman B, Junck L, Forman J, Rogers LR. Prolonged survival after multifocal brain radiation necrosis associated with whole brain radiation for brain metastases: case report. J Neurooncol 2008;90:85–88.
10. Levin VA, Bidaut L, Hou P, et al. Randomized double-blind placebo-controlled trial of bevacizumab therapy for radiation necrosis of the central nervous system. Int J Radiat Oncol Biol Phys 2011;79:1487–1495.

Clinical Reasoning: Corpus callosum lesion with multiple strokes

Zubeda Sheikh, Nidhiben Anadani, Bhrugav Raval, et al.

Neurology 2017;88;e137-e142
DOI 10.1212/WNL.0000000000003797