Diagnostic Snapshot

Guess What Is in My Brain

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Author's disclosure of conflict of interest is found at the end of this article.

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Abstract

Magnetic resonance imaging (MRI) of the brain is an important diagnostic tool used by neurologists. This article explores the workup and management for a patient with a brain lesion and highlights the importance of neuroimaging. Similarities and differences in MRI findings for meningioma, central nervous system lymphoma, and glioblastomas are discussed, along with common MRI sequences and their utility.

ONCOLOGY HISTORY

Ms. S is a 52-year-old woman with refractory stage IIB classical Hodgkin lymphoma first diagnosed in 2015. A month before diagnosis, she sought treatment from her primary care physician for swelling on the right side of her neck, drenching night sweats, and episodes of unexplained fever that had lasted for 2 weeks. She underwent ultrasonography of the thyroid, which revealed complex masses. A CT study of the neck revealed multiple enlarged bilateral level 4 and 5 lymph nodes on the right side and 1 on the left side. Excisional biopsy of the right neck masses revealed nodular sclerosing grade 2 classic Hodgkin lymphoma. She was then referred to our institution for treatment.

Beginning a month after diagnosis, she was treated with four cycles of ABVD (doxorubicin hydrochloride, bleomycin sulfate, vinblastine sulfate, and dacarbazine) chemotherapy. Bleomycin was discontinued because of pulmonary toxicity, and she subsequently received two cycles of AVD (doxorubicin hydrochloride, vinblastine sulfate, and dacarbazine).

Five months after diagnosis, she underwent a biopsy of a fluorodeoxyglucose (FDG)-avid supraclavicular lymph node that showed persistent Hodgkin lymphoma. She subsequently received three rounds of salvage chemotherapy with the ICE (ifosfamide, carboplatin, and etoposide) regimen and then received an autologous stem cell transplant with the standard-of-care BCNU (carmustine), etoposide, cytarabine, and melphalan (BEAM) regimen and had no major complications. She then received brentuximab for 4 months, at which point disease progression was noted. She was then started on nivolumab (Opdivo), but treatment was discontinued after 4 months due to pneumonitis. She was then treated with radiation therapy. PET/CT then showed FDG-avid lymph nodes in the right neck. Ms. S underwent salvage radiotherapy to her bilateral neck and mediastinum, and her disease was in complete remission for 5 years.

HISTORY OF PRESENT ILLNESS

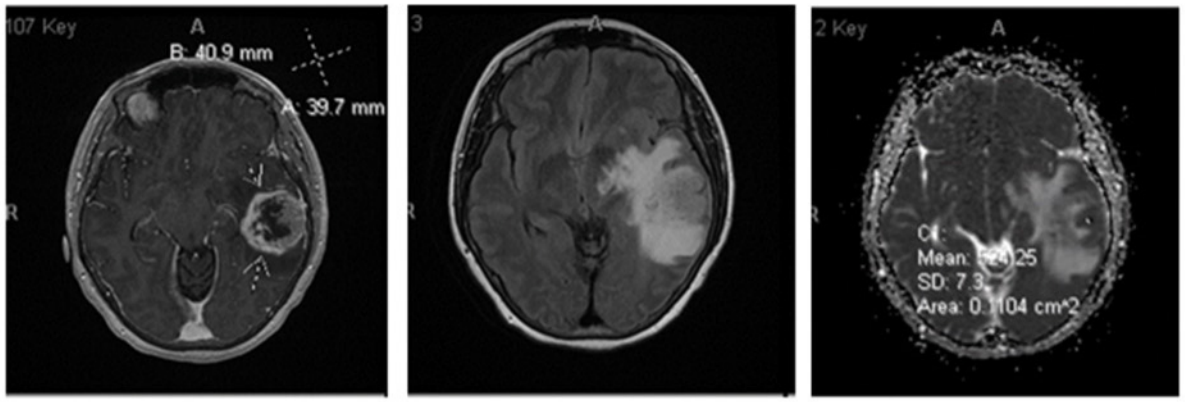
Five years after remission of her lymphoma, Ms. S started experiencing left frontotemporal

pounding headaches, which she managed symptomatically. Three weeks after the onset of the headaches, she started having word-finding difficulties that became progressively worse. She contacted her oncologist, who advised her to go to the emergency department.

PHYSICAL EXAM

Ms. S's preliminary workup included a thorough history and physical examination and a complete neurological examination. Her neurological exam revealed difficulty with finding words, inability to repeat words, and difficulty describing a picture. She was otherwise neurologically intact. She did not have any signs of infection, and the results of blood cultures and urinalysis were within reference ranges.

She underwent systemic imaging with intravenous-contrast CT scans of her chest, abdomen, and pelvis. These scans showed no new or progressive lymphadenopathy suggestive of recurrent lymphoma. Ms. S also underwent MRI of the brain with and without contrast, which revealed a centrally necrotic mass in the left temporal lobe, measuring 4.0 × 4.1 × 4.2 cm (anteroposterior × transverse × craniocaudal), with a thick rind of soft tissue enhancement. On a fluid-attenuated inversion recovery (FLAIR) sequence, there was surrounding hyperintensity involving the temporal lobe and extending into the insula, basal ganglia, and thalamus. There was a regional mass effect with partial effacement of the left lateral ventricle, an 8-mm midline shift, and uncal protrusion. The lesion demonstrated increased vascularity. There was anterior displacement of the middle cerebral artery branches and diffuse effacement of the sulci within the left hemisphere. The lesion abuts the temporal horn of the left lateral ventricle. Areas of diffusion restriction were identified within the enhancement with susceptibility within the lesion (Figure 1).



Post contrast | FLAIR sequence | ADC sequence

Figure 1. Ms. S's workup imaging. FLAIR = fluid-attenuated inversion recovery; ADC = apparent diffusion coefficient.

DIFFERENTIAL DIAGNOSIS

THE MOST LIKELY DIAGNOSIS BASED UPON IMAGING IS:

- A ☐ Primary central nervous system lymphoma
- B ☐ Glioblastoma multiforme
- C ☐ Meningioma

SEE BACK FOR ANSWER ▶

THE MOST LIKELY DIAGNOSIS BASED UPON IMAGING IS:

A Primary central nervous system lymphoma

B Glioblastoma multiforme (correct answer)

C Meningioma

DISCUSSION

A Primary central nervous system lymphoma. Primary central nervous system lymphoma (PCNSL) is a rare form of extranodal non-Hodgkin lymphoma. It is usually confined to the brain, eyes, and cerebrospinal fluid and does not spread systemically (Grommes & DeAngelis, 2017). It can develop in immunocompetent or immunosuppressed patients (e.g., patients with HIV/AIDS, organ transplant recipients, and those being treated with immunosuppressive agents; Grommes & DeAngelis, 2017). The neurologic signs of PCNSL—focal neurologic deficits, mental status changes, behavioral changes, symptoms indicating high intracranial pressure, and seizures—depend on the site of CNS involvement and typically develop over weeks (Grommes & DeAngelis, 2017). On T1 MRI with gadolinium contrast, the imaging pattern characteristic of PCNSL is a single, frontal, homogenously enhancing brain lesion. A FLAIR sequence shows a relatively small area of edema surrounding the main lesion, while restricted diffusion in the tumor is apparent on diffusion-weighted imaging (DWI)/apparent diffusion coefficient (ADC; Hochberg et al., 2007).

In the case of Ms. S, we can see in the image from the T1-weighted sequence with contrast that the tumor is not homogeneously enhanced but has a hypointense area of necrosis in its center. Primary central nervous system lymphoma cannot be ruled out, but based on the imaging results, it is not a likely diagnosis. Per the standard of care, a tissue sample is needed to confirm the diagnosis.

B Glioblastoma multiforme (correct answer). Glioblastoma multiforme (GBM) is a highly malignant type of glioma, a set of CNS tumors arising from glial cells or their precursors. Gliomas are divided into four grades; grade 4, or GBM, is the most aggressive (Holland, 2000). On contrast-enhanced MRI, GBM appearances vary, but it classically appears as a rim-enhancing mass with central necrosis (Nelson & Cha, 2003). The standard treatment of GBM is surgical resection of as much of the tumor as is safe, followed by radiation therapy and chemotherapy (usually with DNA damaging or DNA replication–inhibiting agents). Even under the best of circumstances, in which all the enhancing tumors seen on MRI scans have been surgically removed and the patients have been fully treated with radiation and chemotherapy, this disease has a poor prognosis with an average survival duration of 15 to 18 months (Table 1; Kotecha et al., 2023).

C Meningioma. Meningioma usually originates from meningothelial arachnoid cap cells. Most meningiomas are sporadic, benign, and slowly growing. The clinical manifestations of meningioma depend on the location and the size of the tumor (Alruwaili & De Jesus, 2022). Whereas some patients have no symptoms, others develop neurological deficits. Although most meningiomas are sporadic, some risk factors have been identified, including obesity, alcohol use disorder, exposure to ionizing radiation or radiotherapy, exposure to exogenous hormones, use of hormone replacement therapy or oral contraceptives, and breast cancer (Alruwaili & De Jesus, 2022). Contrast-enhanced MRI of the brain is the most useful tool for diagnosing meningioma because it can distinguish extra-axial from intra-axial lesions, as meningiomas are homogenously enhanced and have a distinctive feature called the dural tail (Alruwaili & De Jesus, 2022).

On Ms. S's postcontrast image, the lesion is not homogeneously enhancing, nor is a dural tail present (Figure 2 and Table 2).

TREATMENT PLAN

Ms. S underwent a left temporal craniotomy with gross total resection of the tumor. A pathologic examination revealed grade 4 GBM with no MGMT promoter methylation. The standard of care for newly diagnosed GBM includes resection or biopsy followed by radiotherapy to the

Table 1. MRI Sequences Commonly Used for Brain Imaging

MRI sequence	Description	Appearance	Use
T1-weighted	T1-weighted sequence (the anatomical sequence) tends to have a short TE and TR.	White matter appears white, gray matter appears gray, fat is bright, and fluid is dark.	Evaluation of normal anatomy.
T2-weighted	T2-weighted sequence (the reverse anatomical sequence) tends to have a long TE and TR.	White matter is gray, gray matter is white, fat is bright, and fluid (such as CSF) is bright.	Evaluation of pathological conditions.
T1-weighted with contrast	T1-weighted sequence performed while infusing gad. Gad changes signal intensities by shortening T1.	Pathologies with hypervascularization appear bright.	Examination of vascular structures and breakdowns in the blood-brain barrier (using gad-enhanced images).
FLAIR	Similar to T2-weighted sequences, except that the TE and TR are very long.	Abnormalities appear bright, and normal CSF fluid is attenuated and dark.	Evaluation of pathological conditions. Detects subtle changes on the periphery of the brain hemispheres and in the periventricular region close to the CSF.
DWI	DWI is based on measuring the Brownian motion of water molecules. It is a series of T2 weighted images.	Similar to FLAIR. CSF fluid is dark, and the cortex of the brain is bright. Signal intensity is reduced in highly cellular tumors, tumors with regions of increased cellularity, cytotoxic edema, and postoperative injuries.	Detection of acute ischemic stroke and characterization and differentiation of brain tumors and intracranial infections.
ADC mapping	ADC mapping measures the amount of water molecule diffusion within tissue and is calculated using DWI data.	Similar to inverted DWI. Bright CSF and dark brain parenchyma.	Detection of stroke and calculating stroke timing. Characterization and differentiation of brain tumors. Differentiation between cytotoxic and vasogenic edema.

Note. ADC = apparent diffusion coefficient; CSF = cerebrospinal fluid; DWI = diffusion-weighted imaging; FLAIR = fluid-attenuated inversion recovery; gad = gadolinium; MRI = magnetic resonance imaging; TE = time to echo; TR = time to repetition. Information from Drake-Pérez et al. (2018); Haouimi & Jones (2009); Villanueva-Meyer et al. (2017); Baba & Niknejad (2013); Dmytriw et al. (2017).

Table 2. Differences and Similarities of MRI Findings in Primary CNS Lymphoma, Glioblastoma, and Meningioma

Primary CNS lymphoma	Glioblastoma	Meningioma
• Intense homogeneous enhancement can be seen in high-grade tumors, enhancement is absent to moderate in low-grade tumors. • Peripheral rings are seen in 10%–15% of cases of PCNSL. • Restricted diffusion with ADC mapping is lower in primary CNS lymphomas than in high-grade gliomas and metastases.	• T1-weighted imaging with gad can reveal variable enhancement of the tumor and central necrosis. FLAIR reveals vasogenic edema. • DWI enhances the signals of solid tumors. ADC produces signals similar to those for white matter. • More than 90% of non-enhancing necrotic/cystic tumor areas have facilitated diffusion.	• A dural tail is seen in 60%–72% of cases. • Intense and homogeneous enhancements are seen on T1-weighted images with gad contrast. • Increased diffusion restrictions are seen in grade 2 and 3 tumors.

Note. ADC = apparent diffusion coefficient; CNS = central nervous system; DWI = diffusion-weighted imaging; FLAIR = fluid-attenuated inversion recovery; gad = gadolinium; MRI = magnetic resonance imaging; PCNSL = primary central nervous system lymphoma. Information from Gaillard (2008a, 2008b, 2008c).

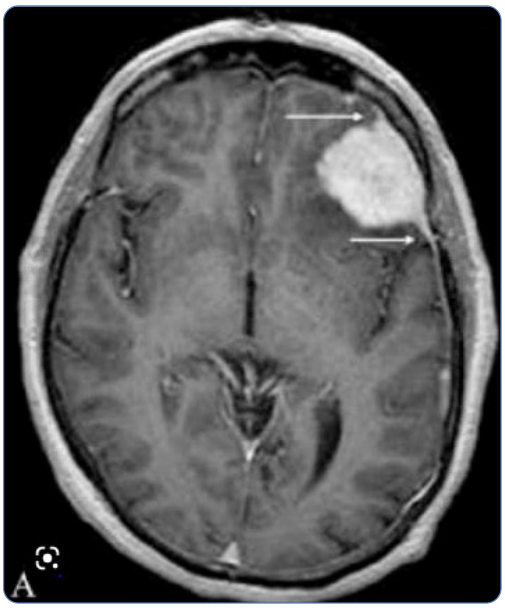


Figure 2. Contrast-enhanced axial MRI showing dural tail sign in meningioma (arrows). Image from Chavhan & Shroff (2009).

tumor-involved field and concurrent or adjuvant chemotherapy with the DNA-damaging alkylating agent temozolomide. Ms. S was discharged with plans for a follow-up in 3 to 4 weeks to discuss choosing between standard therapies and available clinical trials.

Disclosure

The author has no conflicts of interest to disclose.

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