Primary CNS Lymphoma in Immunocompetent and Immunocompromised Patients

Ruth Foreman, PhD, HMSIII
Gillian Lieberman, MD

December 2009
Objectives

- Learn the differential diagnosis of brain masses
- Understand the common imaging features of primary CNS lymphoma on both CT and MRI
- Learn the differences in imaging features of primary CNS lymphoma between immunocompetent and immunocompromised patients
- Understand the role of imaging in primary CNS lymphoma

*We will be doing all of this with the aid of patient cases*
Our patient, AG

- 81 year old female who presented to BIDMC ED with a one-month history of word-finding difficulty and a one-week history of seizure activity
Neuroradiographic Imaging

Used for detection of lesions, localization, determining extent of disease and characterization

- CT
- MRI

- Contrast enhancement increases the sensitivity of both modalities for the detection of brain tumors
Neuro CT

- Utilized for evaluating acute brain hemorrhage
  - speed
  - high sensitivity in detection
  - wide-spread availability
- Better than MRI at detecting calcifications - evaluating for cerebrovascular disease
- Indications:
  - sudden-onset neurologic symptoms
  - if patient has contraindications for MRI (ferromagnetic implants, unstable)
  - often performed if patient presents to ED
Neuro MRI

- Most sensitive for neurologic lesion detection
  - Superior tissue resolution
- Multiplanar capability - determination of tumor site of origin
AG: Non-contrast Head CT
AG: Non-contrast Head CT with highlighted findings

- L frontal lobe mass lesion
- Iso- to hyperdense compared to surrounding gray matter
- Surrounding vasogenic edema
- No evidence of hemorrhage (would show high attenuation)
Differential diagnosis for intracranial mass

- Primary brain tumor
  - Glioma, lymphoma, meningioma
- Metastatic brain tumor
- Infection
  - Abscess, toxoplasmosis
- Inflammatory
  - Multiple sclerosis, post-infectious encephalomyelitis
- Vascular
  - Hemorrhage
  - Infarction
How can we further characterize this lesion and narrow our differential?

- MRI
AG: Head MRI, image 1

T2 axial MRI sequence  PACS BIDMC
AG: Head MRI, image 1 with highlighted findings

- Homogeneous, hypointense mass
- Surrounding vasogenic edema

T2 axial MRI sequence

PACS BIDMC
AG: Head MRI, image 2
AG: Head MRI, image 2 with highlighted findings

- Homogeneous, hypointense mass
- Surrounding vasogenic edema
AG: Head MRI findings from T2 sequences

- Homogeneous, hypointense mass involving left cerebral hemisphere (frontal lobe)
- Surrounding vasogenic edema
AG: contrast-enhanced MRI, image 1
AG: contrast-enhanced MRI, image 1, findings highlighted

- Homogeneously enhancing mass
AG: contrast-enhanced MRI, image 2
AG: contrast-enhanced MRI, image 2, highlighted findings

Homogeneously enhancing mass
AG: contrast-enhanced MRI, image 3
AG: contrast-enhanced MRI, image 3, findings highlighted

- Enhancement of the corpus callosum
AG: Summary of findings from contrast enhanced MR images

- Homogeneously enhancing mass with involvement of the corpus callosum
AG: diffusion weighted imaging, image 1
AG: diffusion weighted imaging, image 1, highlighted findings

- Restricted diffusion of lesion as seen by increased signal intensity

DWI, axial PACS BIDMC
AG: diffusion weighted imaging, image 2
AG: diffusion weighted imaging, image 2, highlighted findings

- Restricted diffusion of lesion showing corpus callosum involvement
Summary of AG’s radiographic findings

- CT: isodense to hyperdense mass lesion
- MRI:
  - T2: homogeneous, hypointense signal with vasogenic edema
  - Contrast enhanced: homogeneously enhancing lesion with involvement of corpus callosum
  - DWI: restricted diffusion of lesion with corpus callosum involvement

Does this now help us narrow our original differential?
Refined Differential Diagnosis for AG’s brain mass

- Lymphoma
  - AG’s radiographic findings are classic for CNS lymphoma
- Lymphoma
- Lymphoma
- Lymphoma
- Lymphoma
- Glioblastoma multiforme
  - Considered due to corpus callosum involvement, but usually shows T2 hyperintensity with heterogeneous enhancement
- Acute disseminated encephalomyelitis (ADEM)
  - Usually shows hyperintense T2 signal
Primary CNS Lymphoma

- Represents 3-5% of all primary brain tumors and 1% of all lymphomas
  - Increased incidence (since 1990s) in immunocompromised AND immunocompetent patients
- Immunocompromise is the only known risk factor
- Non-Hodgkin type, usually of B-cell origin
- Display high nucleus-to-cytoplasm ratio, which gives it its characteristic imaging findings:
  - CT: isodense to hyperdense mass lesion
  - MRI:
    - T2: homogeneous, hypointense signal
    - Contrast-enhanced: homogeneously enhancing lesion
    - DWI: restricted diffusion of lesion
- Although it has characteristic imaging findings, histopathologic tissue diagnosis needed for definitive diagnosis
Primary CNS Lymphoma, continued

- Often involves cerebral hemispheres, periventricular white matter, corpus callosum, subependymal region, deep gray matter, and often the meninges
- Highly aggressive
- Treated with methotrexate-based chemotherapy with or without whole-brain radiation
  - Surgery does not improve survival
- Prognosis based on a number of factors and ranges from a 2-year overall survival of 80% to 15%
  - Negative prognostic factors include age >60, elevated serum LDH, elevated CSF protein and tumor location in deep brain structures
- Survival is 1.5 months without treatment, but is increased to 44 months with chemotherapy
Role of imaging in further diagnosis of CNS lymphoma

- Stereotactic needle biopsy
  - Overlay MRI with intra-operative CT using software to determine the coordinates for precise needle biopsy
  - This is done because it is frequently difficult accurately image the extent of lesion on CT

http://www.elekta.com/assets/stereotactic_neurosurgery/images/Biopsy_application+_Arc_with_counter_scale_HIGH_RES.jpg
Back to AG: tissue diagnosis

- Primary CNS lymphoma was confirmed from tissue analysis taken by stereotactic biopsy
- She was referred to a neuro-oncologist for further care management
CNS Lymphoma in Immunocompetent vs. Immunocompromised patients

<table>
<thead>
<tr>
<th></th>
<th>Competent</th>
<th>Compromised</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (yr)</td>
<td>60</td>
<td>30</td>
</tr>
<tr>
<td>Multiple lesions</td>
<td>30-50%</td>
<td>63-81%</td>
</tr>
<tr>
<td>Necrosis</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>CT density</td>
<td>Hyperdense</td>
<td>Hyperdense</td>
</tr>
<tr>
<td>CT enhance</td>
<td>Homogeneous</td>
<td>Heterogeneous</td>
</tr>
<tr>
<td>MR T1 signal</td>
<td>Iso- to hypo-</td>
<td>Iso- to hypo-</td>
</tr>
<tr>
<td>MR T2 signal</td>
<td>Iso- to hypo-</td>
<td>Iso- to hypo-</td>
</tr>
<tr>
<td>MR enhance</td>
<td>Homogeneous</td>
<td>Heterogeneous</td>
</tr>
</tbody>
</table>

Haque et al., 2008.
CNS Lymphoma in Immunocompromised patients

- In immunocompromised patients, there can be atypical disease location (brainstem, cranial nerves, cavernous sinuses)

- In immunocompromised patients, lymphoma can resemble abscess and toxoplasmosis
  - If considering lymphoma vs. toxoplasmosis
    - Favor lymphoma if unifocal and toxo if multifocal
    - May have to perform PET imaging
      - Increased glucose uptake in lymphoma, decreased uptake in toxo
  - If lymphoma vs. abscess (heterogeneous peripherally enhancing mass on T2-weighted images)
    - Abscess may have thin, hypointense rim due to free radicals on T2-weighted images

Haque et al., 2008.
Let’s review the common findings of primary CNS lymphoma again, using a companion patient, LM.
Companion patient: LM, contrast enhanced MRI

Enhancement in subependymal distribution with extension into the corpus callosum
LM: leptomeningeal involvement

Enhancement of leptomeninges

T1-gadolinium, axial  PACS BIDMC
LM: Head MRI, image 1

- Hypointense periventricular signal
LM: Head MRI, image 2

- Hypointense periventricular signal
LM: Head MRI, image 3

- Hypointense signal in subependymal spaces and corpus callosum
LM: Head MRI, image 4

- Hypointense signal in corpus callosum
Restricted diffusion in periventricular distribution
LM: more diffusion weighted images

- Restricted diffusion in subependymal distribution with extension into the corpus callosum
Summary of LM’s radiographic findings

- Periventricular and subependymal involvement with extension into the corpus callosum
- T1 contrast-enhanced: uniform enhancement
- T2 weighted: hypointense signal
- DWI: restricted diffusion
Review of the radiologic features of primary CNS lymphoma

- CT: isodense to hyperdense lesion
- MRI:
  - T2 weighted: homogeneous, hypointense signal
    - Can be heterogeneous if patient is immunocompromised
  - Contrast enhanced T1: homogeneously enhancing lesion
  - DWI: restricted diffusion of lesion
- Typically involves cerebral hemispheres, corpus callosum, periventricular white matter, subependymal region
  - Atypical locations in immunocompromised patients
Summary

- Discussed the differential diagnosis of brain masses
- Familiarized with the common imaging features of primary CNS lymphoma on both CT and MRI
- Discussed differences in imaging features of primary CNS lymphoma between immunocompetent and immunocompromised patients
- Gained an understanding for the role of imaging in primary CNS lymphoma
Many Thanks!

- Dr. Gillian Lieberman
- Dr. Gul Moonis
- Dr. Iva Petkovska
- Maria Levantakis
References


