Overview

• Melanoma
  – Background
  – Brain metastases: Epidemiology, Symptoms, Treatment

• Menu of imaging modalities in brain melanoma

• Case presentation
  – Patient AC clinical history and imaging by MRI
  – Variety of appearances of brain melanoma on MRI

• Utility of alternative imaging modalities (CT, FDG-PET)
Let’s discuss why we want to learn about diagnostic imaging of metastatic melanoma in the brain
Melanoma

- Tumor of melanocytes
- 4% of all dermatologic cancers, but 80% of all skin cancer deaths
- 619% ↑ in annual diagnoses, 165% ↑ in annual mortality (1950-2000)
- Metastasizes to virtually any organ unlike other skin cancers
- Stage IV median survival < 1 yr

(Source for Fig. 1A and B: Tsao et al., 2004)

# Melanoma: Metastasis

<table>
<thead>
<tr>
<th>SITE</th>
<th>CLINICALLY</th>
<th>AUTOPSY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>18-36%</td>
<td>70-87%</td>
</tr>
<tr>
<td>Liver</td>
<td>14-20%</td>
<td>54-77%</td>
</tr>
<tr>
<td><strong>Brain</strong></td>
<td><strong>12-20%</strong></td>
<td><strong>36-54%</strong></td>
</tr>
<tr>
<td>Bone</td>
<td>11-17%</td>
<td>23-49%</td>
</tr>
<tr>
<td>GI tract</td>
<td>1-7%</td>
<td>26-58%</td>
</tr>
</tbody>
</table>

Other sites: Heart, Pancreas, Adrenals, Kidney, Thyroid

Donohoe (2010) UpToDate
Melanoma: Metastasis

• 3rd most common cause of brain metastases

• Highest propensity to metastasize to the brain of all primary tumors in adults

• Clinical features:
  – Headaches & symptoms from increased pressure
  – Focal neurologic deficits
  – Seizures; cognitive impairment

“Given the recognized neurotropism of melanoma, neurological symptoms in a melanoma patient should prompt diagnostic imaging studies.” (Sloan et al., 2009)
Let’s preview the menu of tests and their use in brain melanoma imaging
Imaging of Brain Metastases

• **Indications**
  – Neurologic symptoms in patients with known melanoma
  – Accurate prognosis and optimal palliative treatment
  – Re-staging
  – R/O brain metastases before initiating new chemotherapy

1. **MRI with contrast**: *Study of choice to assess melanoma in CNS!*
   – *More sensitive than CT for detecting brain mets*
   – Detect spinal cord and leptomeningeal involvement
   – Detect associated hemorrhage or melanin
   – Contraindications: non MRI-compatible objects in/on the patient

2. **CT**: Patients with MRI contraindications; emergency setting; staging

3. **¹⁸FDG-PET/CT**: Less sensitive for brain mets, but can be useful

Before we proceed, let’s get our eyes used to the normal brain anatomy on a few MRI images
We have:

1) Learned why diagnostic imaging of metastatic melanoma in the brain is important

2) Reviewed the menu of tests relevant for our discussion

3) Familiarized ourselves with a bit of normal brain anatomy

We are now ready to apply and expand our knowledge…
Case Presentation
Patient AC and Her Intractable Melanoma Brain Mets
Patient AC

42 yo female with history of metastatic melanoma, presented to ED in 3/07 with headache

2/07: Diagnosed with the first brain mets from melanoma after experiencing severe headaches; underwent whole brain radiation; dexamethasone wean to begin TMZ

1d prior to admission: Onset of “slight” bifrontal headaches

Day of admission: Worse headaches, pain 5-6/10

Neurologic ROS unremarkable
As the patient presented to the ED with acute headache, CT was first ordered to r/o bleed
Patient AC: CT 3/07

Multiple brain lesions, the largest mass in the right frontal lobe measuring 2.3 cm, iso- to hyper-attenuating (isodense to hyperdense), with extensive edema.

Axial CT w/o contrast, 3/07

(Source for Fig. 2: PACS, BIDMC)
Patient AC

MRI was recommended for further evaluation of intracranial masses
Patient AC: MRI 3/07

Nodular area in the right frontal lobe of heterogeneous hyper- and iso-intensity, surrounded by extensive area of vasogenic edema

Sagittal T1-weighted MR w/o contrast, 3/07
Axial T1-weighted MR w/o contrast, 3/07
Nodular area in the right frontal lobe measuring ~ 2.1 cm in diameter with diffuse heterogeneous enhancement after administration of Gadolinium-DTAP; surrounding edema non-enhancing.
Patient AC: MRI 3/07

Nodular area in the right frontal lobe of heterogeneous hypo- and iso-intensity extensive area of vasogenic edema

Predominant: \( T1 \uparrow \), \( T2 \leftrightarrow \) or \( \downarrow \), enhancing

Axial \( T2 \)-weighted MR w/o contrast, 3/07

(Source for Fig. 5: PACS, BIDMC)
What do we make of these findings?

Let’s study how melanoma brain mets should appear on MRI
MRI of Brain Melanoma

Variable MR pattern dependent on melanin & hemorrhage!

1] Melanin (free radicals = paramagnetic)

<table>
<thead>
<tr>
<th></th>
<th>T1 signal</th>
<th>T2 signal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanotic pattern</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Amelanotic pattern</td>
<td>↓ / ↔</td>
<td>↑</td>
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Key: 
↑ = hyperintensity 
↓ = hypointensity 
↔ = isointensity

2] Evolution of blood products if hemorrhagic metastasis

<table>
<thead>
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<th>T2 signal</th>
<th>Time</th>
<th>Hgb</th>
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<tbody>
<tr>
<td>Hyperacute</td>
<td>↔ / ↓</td>
<td>↑</td>
<td>&lt; 24h</td>
<td>Oxy-Hgb, intracellular</td>
</tr>
<tr>
<td>Acute</td>
<td>↔ / ↓</td>
<td>↓</td>
<td>1-3d</td>
<td>Deoxy-Hgb, intracellular</td>
</tr>
<tr>
<td>Early subacute</td>
<td>↑</td>
<td>↓</td>
<td>&gt; 3d</td>
<td>Met-Hgb, intracellular</td>
</tr>
<tr>
<td>Late subacute</td>
<td>↑</td>
<td>↑</td>
<td>&gt; 7d</td>
<td>Met-Hgb, extracellular</td>
</tr>
<tr>
<td>Chronic</td>
<td>↓</td>
<td>↓</td>
<td>&gt; 14d</td>
<td>Ferritin and hemosiderin, extracellular</td>
</tr>
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MRI of Brain Melanoma: Companion Patient 1, Classic "Melanotic Melanoma"

Axial T1-weighted MR w/o contrast
Hyperintense on T1, Hypointense on T2

Axial T2-weighted MR w/o contrast

(Source for Fig. 6: Escott (2001) RadioGraphics)
MRI of Brain Melanoma: Companion Patient 2, Classic “Amelanotic Melanoma”

Axial T1-weighted MR w/o contrast

Axial T2-weighted MR w/o contrast

Hypointense (or isointense) on T1, Hyper- or iso-intense on T2

(Source for Fig. 7: Escott (2001) RadioGraphics)
Armed with this knowledge, we can now go back to our Patient AC…
Patient AC: MRI 3/07

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- **Predominant: T1 ↑, T2 ↓ or ↔, enhancing**
- Suggest melanoma metastasis, predominantly with
  - melanin OR
  - blood products (likely early subacute)
  - surrounded by edema
DDx of Intracranial Lesions with Increased Signal on T1

- **Hemorrhagic lesions**
  - Infarcts
  - Infections
  - Intraparenchymal hematoma
  - Cortical contusions
  - Diffuse axonal injuries
  - Subarachnoid hemorrhage
  - Vascular malformations and aneurysms associated with hemorrhage and/or thrombosis
  - Hemorrhagic primary tumors
    - **Hemorrhagic metastases**
      - Melanoma
      - Renal cell carcinoma
      - Choriocarcinoma
      - Bronchogenic carcinoma
      - Thyroid carcinoma
  - Protein-containing lesions
    - Colloid cyst of third ventricle
    - Craniopharyngioma
    - Rathke’s cleft cyst
    - Atypical epidermoid

- **Fatty lesions**
  - Lipoma
  - Dermoid
  - Lipomatous meningioma

- **Calcified/ossified lesions**
  - Endocrine-metabolic disorders
  - Calcified neoplasms
  - Infections
  - Dural osteomas

- **Lesions with other mineral accumulation**
  - Acquired hepatocerebral degeneration
  - Wilson’s disease

- **Melanin-containing lesions**
  - Melanoma metastases
  - Leptomeningeal melanosis

- **Miscellaneous**
  - Ectopic neurohypophysis
  - Multiple sclerosis (chronic stage)
  - Neurofibromatosis type I

4/07 – 4/10: Progressing brain mets; multiple radiosurgeries, radiotherapy, and chemotherapy

4/10
- 45 yo, presents with severe bilateral “sharp” headaches
- Similar to headaches from prior metastatic disease
- Associated nausea
Patient AC: MRI 4/10

Enhancing nodule in the right temporal lobe, hyper-intense on T1 pre-GAD

(Source for Fig. 8: PACS, BIDMC)
Patient AC: MRI 4/10

Plan for patient AC: Compassionate use of ipilimumab for systemic therapy

9A Axial T1 w/ contrast, 4/10

9B Axial T1 w/o contrast, 4/10

Small, punctate enhancing lesion in the right posterior parietal lobe, iso-intense on T1 pre-GAD

(Source for Fig. 9: PACS, BIDMC)
As we have learned from the multiple MR images, beware of atypical and various appearances of melanoma mets!

1) They can adhere to OR deviate from the typical “melanotic and amelanotic” patterns.

2) They can be subtle and small OR easily discernible.

3) They may or may not hemorrhage.

4) They can be stable OR rapidly growing!
What about imaging modalities other than MRI?

Let’s briefly discuss our patients PG and MO…
Companion Patient 3, PG: CT without Contrast

69 yo man with known malignant melanoma presents to the ED following syncope, brief shaking movements in 4/10

CT w/o contrast, 4/10

Multiple hyperattenuating (hyperdense) lesions, ex. In the left frontal lobe and right occipital lobe → metastatic melanoma?

(Source for Fig. 10: PACS, BIDMC)
Expected CT of Brain Melanoma

- Variety of appearances on CT!
  - Single or multiple
  - Small, large, or both
  - Hyper-dense, iso-dense, hypo-dense, or mixed pre-contrast

Table I. Characteristics of intra-axial metastases (N = 89)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>32</td>
<td>36</td>
</tr>
<tr>
<td>Multiple</td>
<td>57</td>
<td>64</td>
</tr>
<tr>
<td>Size</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small</td>
<td>53</td>
<td>59.6</td>
</tr>
<tr>
<td>Large</td>
<td>23</td>
<td>25.8</td>
</tr>
<tr>
<td>Both</td>
<td>13</td>
<td>14.6</td>
</tr>
<tr>
<td>Attenuation in relation to brain before contrast medium</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>76</td>
<td>85.4</td>
</tr>
<tr>
<td>Low</td>
<td>1</td>
<td>1.1</td>
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<tr>
<td>Isodense</td>
<td>5</td>
<td>5.6</td>
</tr>
<tr>
<td>Mixed</td>
<td>7</td>
<td>7.9</td>
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<tr>
<td>Contour</td>
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<td></td>
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<tr>
<td>Nodular</td>
<td>80</td>
<td>89.9</td>
</tr>
<tr>
<td>Irregular</td>
<td>9</td>
<td>10.1</td>
</tr>
</tbody>
</table>

(Source for Table: McGann et al. (1991) Brit J Radiol.)
DDx of Hyperdense Intracranial Lesions without Contrast

- Meningioma
- Lymphoma
- GBM
- Ependymoma
- Colloid cyst
- Craniopharyngioma
- Germinoma
- Hemorrhage
- **Metastatic tumors**
  - Melanoma
  - Renal cell carcinoma
  - Choriocarcinoma
  - Thyroid carcinoma

Companion Patient 3, PG: CT without Contrast

- Patient PG has a pacemaker + renal insufficiency → no f/u on MRI or CT C+
- Patient PG was scheduled for whole brain cranial irradiation
- Remember, CT w/o contrast offers only limited evaluation for melanoma brain mets
Companion Patient 4, MO: FDG-PET/CT

58 yo woman with history of metastatic melanoma (pulmonary and liver lesions) re-staged on FDG-PET 12/04

Avid uptake in the left medial occipital lobe, hyperdense on CT C-
Companion Patient 4, MO: DDx for Increased Signal on PET

- Infection
- Inflammation
- **Neoplasm**
- Beware of physiologic uptake (brain, myocardium, exercising muscle, thymus in children and post-chemo patients, thyroid in patients with thyroid disease, etc)

Companion Patient 4, MO: FDG-PET/CT

Given the PET finding, MRI w/ contrast indicated

Round, well-circumscribed mass in the left occipital lobe, hyperintense and homogeneously enhancing; confirms PET/CT → stereotactic radiosurgery

(Source for Fig. 12: PACS.BIDMC)
FDG-PET for Brain Melanoma Mets

- Less sensitive for detection of mets in the brain due to high background FDG accumulation in the cortex

- CAN detect new metabolically active lesions: f/u using conventional imaging methods

- CAN be useful to w/u lesions identified in MRI: Recurrence (avid) versus radiation necrosis effects (non-avid)

Summary

1. Radiologic imaging of melanoma metastases to the brain is clinically important

2. MRI with contrast enhancement is the imaging modality of choice for brain metastases of melanoma, and we saw multiple examples in our patient AC

3. Metastatic melanoma lesions in the brain have a variety of appearances due to hemorrhage and melanin: Beware!

4. While MRI is the preferred test, CT and FDG-PET/CT have their uses in melanoma imaging in the brain: Remember when and why these imaging modalities can be useful
Acknowledgements

- Gillian Lieberman, MD
- Kevin Donohoe, MD
- Neel Madan, MD
- Johannes Roedl, MD
- Maria Levantakis
References


