Radiological Evaluation of Melanoma

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Adapted from http://cienciaaldia.files.wordpress.com/2009/03/reveal_melanoma.jpg
Overview

• Patient presentation
• Overview of metastatic melanoma
• Radiological staging of melanoma
  – Lymphoscintigraphy (LS)
  – Positron-Emission Tomography with 2-Fluoro-2-Deoxyglucose (FDG-PET)
  – Ultrasound (U/S)
  – Computed Tomography (CT)
  – Magnetic Resonance Imaging (MRI)
• Gallery of images from companion patients
• Summary
Our Patient JK: Presentation

• 66 yo M tobacco farmer

• 01/2007: ulcerated melanoma with evidence of lymphovascular invasion removed from posterior neck. 5.6 mm thick 10 mitoses per square millimeter and was Clark's level IV, extending broadly to the base.

• 05/14/2007:
  1) left cheek lesion: melanoma in situ followed by wide local excision
  2) melanoma in his left shoulder: invasive to 3.5 mm, completely excised
Brief Review of Melanoma
Melanoma: Staging Systems

1) Key Features:
   Depth of Primary Lesion, Spread to lymph nodes or distant site

2) Additional Features on some systems:
   Ulceration, Mitotic Index, sentinel lymph node findings, LDH levels

Balch CM et al. CA Cancer J Clin., 2004
Melanoma: Importance of Staging

1) consistent terms and definitions based on prognosis
2) compartmentalization of patients into definable risk groups criteria for stratification and reporting results of clinical trials
3) comparisons of treatment results among different centers
4) tool for clinical decision making

Balch CM et al. CA Cancer J Clin., 2004
Melanoma: Metastasis

Most common organs (percentages on autopsy from patients with advanced melanoma):
- lymph nodes (73.6%)
- lungs (71.3%)
- liver (58.3%)
- brain (49.1%)
- bone (48.6%)
- heart (47.2%)
- adrenal glands (46.8%)
- gastrointestinal tract (43.5%) [most common metastasis to small bowel]
(multiple organ metastases in 95% of these patients on autopsy)

Modes of metastasis:
- Hematogenesis
- Lymphatic
- Direct invasion

Common causes of fatality include: Respiratory Failure, increased ICP and hemorrhage from brain metastases, bowel obstruction

## Metastasis: Overview of genetics

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>Genes/Genes Products</th>
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<tbody>
<tr>
<td><strong>Tumor initiation</strong></td>
<td>Unlimited growth potential, survival, genomic instability</td>
<td>KRAS, BRAF, EGFR, HER2, PTEN, BRCA1, VHL1</td>
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<td><strong>Metastasis initiation</strong></td>
<td>Invasion, marrow mobilization, angiogenesis, epithelial-to-mesenchymal transition</td>
<td>RHOC, LOX, VEGF, CSF-1, ID1, TWIST1, MET, FGFR, MMP-9, NEDD9</td>
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<tr>
<td><strong>Metastasis progression</strong></td>
<td>Vascular remodeling, immune evasion, extravasation</td>
<td>EREG, COX-2, MMP-9, CCL5, ANGPTL4</td>
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<tr>
<td><strong>Metastasis virulence</strong></td>
<td>Organ-specific functions</td>
<td>CXCR4, RANKL, CTGF, interleukin-11, endothelin-1</td>
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Metastasis: Seed and Soil

"What is it that decides what organs shall suffer a case of disseminated cancer?"

"When a plant goes to seed, its seeds are carried in all directions, but they can only live and grow if they fall on congenial soil."

Stephen Paget

Paget, S. *Lancet*, 1889
Metastasis: Melanocyte differentiation program predisposes to metastasis

1) Transformed melanocytes metastasize widely (unlike other cells of origin)

2) Dependent on Slug, a transcription factor that is important for neural crest migration during development

Back to our patient
Our Patient JK:
Review of presentation

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Our Patient JK: Lymphoscintigraphy

Sentinel node localization with demonstrating two foci of tracer (Tc-99m in sulfur colloid) localization in the left neck:

Pathology on sentinel node biopsy was negative for metastasis

For intermediate thickness melanoma:
SN biopsy reduces 5-year disease free survival (78.3±1.6% in biopsy group and 73.1±2.1% with observation), does not affect 5-year melanoma-specific survival

Morton et al. NEJM, 2006
Development of a new neck mass in our patient’s left posterior neck
Our Patient JK: new neck nodule

• 10/2007: Pt. noted a palpable nodule in the left posterior neck

• Physical exam: NAD. No other palpable lymphadenopathy, anicteric, CTAB, no masses, A+O x 3, cranial nerves II-XII in tact, strength 5/5 throughout, normal gait
Our Patient JK: CT scan for mass

CT +C neck 10/2007

21 x 20 mm mass
Our Patient JK: Ultrasound (U/S)-guided biopsy of mass

Echogenic needle is visualized in hypoechoic mass (lymph node)

U/S-guided Fine Needle Aspiration (FNA)

Pathology revealed metastatic melanoma in 1 lymph node with extracapsular extension
Assessment for metastatic disease in our patient
Our Patient JK: CXR to assess for metastasis

- No evidence of metastasis on CXR
- Important as a baseline study
Some suspicious findings observed on CT:

1. Right middle lobe ground-glass opacity.
2. 1.3-cm lesion within segment VI of the liver suspicious for metastasis.
3. Two hyperdense enhancing lesions arising off the lower pole of the left kidney, concerning for metastases.
4. Soft tissue nodule within the mesentery, superior to the pancreas, measuring 2.2 x 1.7 cm, concerning for metastasis.
Our Patient JK: Positron Emission Tomography (PET)

No evidence of FDG-avid disease

(Post-surgical inflammatory changes with mildly increased FDG uptake in the left cervical region)

Meta-analysis: 83% sensitivity, 85% specificity for PET. PET-CT offers increased morphological information.
- strengths: deep soft-tissue, lymph nodes, visceral metastases
- weaknesses: Small lesions, especially in brain, can be missed

Krug et al., Radiology, 2008; Strobel et al., Radiology, 2007
Our Patient JK: New lung lesion

- Patient followed with CT every 6 months
- New left lower lobe lung nodule (1cm) noted on 7/08 (left; top)
- by 11/08 nodule grown to at least 3cm by CT and CXR
- Markedly FDG-avid 3cm lesion confirmed on PET-CT 11/20/08 (not shown)
- Excision in 12/08: pathology confirmed metastatic melanoma
Disease progression found on continued surveillance studies
Our Patient JK: Progression on PET scan

Interval development of FDG-avid liver metastases

(suspicious hypodensities had been noted on interim CTs: not previously found to be FDG-avid)

PET 12/07

PET 5/09

Courtesy of Dr. Callahan and nuclear medicine, BIDMC
Our Patient JK: Brain mass found on PET-CT

Large, predominantly photopenic lesion in the right frontal lobe with mass-effect; a small high-attenuation focus (CT) is FDG-avid on PET

Courtesy of Dr. Callahan and nuclear medicine, BIDMC
Our Patient JK: Brain mass on follow-up MRI

T1 bright Mass at Grey-white junction

T1 signal: Intrinsic signal from paramagnetic effect of melanin or Hemorrhage

This slightly higher slice shows extinction on GRE Consistent with hemorrhage

Large right frontal hemorrhage; suspicious for metastasis

PACS, BIDMC, 2009
# Hemorrhage: Appearance on MRI

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<thead>
<tr>
<th>Age</th>
<th>T1 Weighted</th>
<th>T2 Weighted</th>
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<tbody>
<tr>
<td>Hyperacute</td>
<td>Hours old, mainly oxyhemoglobin with surrounding edema</td>
<td>Hypointense</td>
</tr>
<tr>
<td>Acute</td>
<td>Days old, mainly deoxyhemoglobin with surrounding edema</td>
<td>Hypointense</td>
</tr>
<tr>
<td>Subacute</td>
<td>Weeks old, mainly methemoglobin</td>
<td>Hyperintense</td>
</tr>
<tr>
<td>Chronic</td>
<td>Years old, hemosiderin slit or hemosiderin margin surrounding fluid cavity</td>
<td>Hypointense</td>
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Our Patient JK: 2nd Lesion on Brain MRI

Ring enhancing lesion in cerebral peduncle consistent with metastasis.
Hematocrit level suggests hemorrhage.
Our Patient JK: Cerebral peduncle on PET-CT

Midbrain lesion not easily visualized on PET CT

Courtesy of nuclear medicine and Dr. Callahan, BIDMC
Neurosurgery for decompression, evacuation of frontal lobe hematoma and resection of underlying lesion

Revealed large hemorrhagic cyst lined by metastatic melanoma, confirmed by pathology (right)

Tx:
- Whole brain radiation
- Dexamethasone
- anti-convulsant

Our Patient JK: Brain Pathology

H+E staining of neurosurgical specimen reveals melanin consistent with metastatic melanoma

Courtesy of Dr. Matthew Anderson (Pathology), BIDMC
Selected findings of metastatic melanoma in companion patients
Companion Patient #1: Melanoma to the heart on CT

41 yo M who presented in 2004 with a pathological rib fracture. Discovered to be metastatic melanoma, now extensive metastases.
Companion Patient #2: Another cardiac metastasis on PET-CT

Patient is a man in his 40s who presents with atypical chest pain

Subtle lesion at heart base

Marked FDG-avidity

Turned out to be metastatic melanoma
(Primary lesion subsequently found on foot)

Chest CT

PET

Fusion

Courtesy of Dr. Faisal Khosa, BIDMC
Companion Patient #3: Multiple metastases on PET

89 yo man with known melanoma; re-staging

1) Extensive FDG-avid lymphadenopathy within the neck, subpectoral regions, axillae, pericardial distribution, mesentery, and retroperitoneum.

2) FDG-avid nodules within the right upper and right middle lobes, consistent with lung metastases.
Companion Patient #3: Abdominal findings on PET-CT

CT

PET-CT fusion

Courtesy of Dr. Kevin Donohoe, BIDMC
Companion Patient #3: Abdominal findings on PET-CT
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PET-CT fusion
Companion Patient #3: Abdominal findings on PET-CT

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PET-CT fusion
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Companion Patient #3: Abdominal findings on PET-CT
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Abdominal findings on PET-CT
Summary
Summary: Radiology in the management of melanoma

Lymphoscintigraphy: sentinel lymph node biopsy
U/S or CT: image guided biopsies
CXR, CT, PET, Brain MRI, (others: e.g. Bone Scan): stage disease/monitor progression

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References


