Radiologic Evaluation of Neuroblastoma

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Presentation Goals

• Understand what neuroblastoma is, where it occurs and how it presents clinically

• Be aware of the many imaging modalities used for diagnosis, staging and follow-up of neuroblastoma

• Recognize the classic characteristics of neuroblastoma on imaging
What is Neuroblastoma?

- Most common extracranial solid tumor in children
- 90% are diagnosed in kids under the age of 5 years
- Derived from neural crest cells
- 85-95% of neuroblastoma patients excrete excess catecholamine metabolites (VMA, HVA, NE and DA) in their urine
Where does it occur?

- Neuroblastoma can occur anywhere along the sympathetic chain or in the adrenal gland.
- 65% are found in the retroperitoneum (majority of these arise from the adrenal medulla).
- Other primary sites: posterior mediastinum, pelvis, neck.

Clinical Presentation

- Patients may present with a wide range of symptoms that result from excess hormone production or mass effects of primary tumor or metastases
- May have palpable mass, abdominal pain or hypertension from compression of renal arteries
- Frequently appear ill with nonspecific systemic symptoms (weight loss, malaise, bruising, irritability, anemia, anorexia, fever)
- 2/3 patients have metastatic disease at time of diagnosis
Our Patient: Patient 1

- K.F. is a 5 y.o. girl who presents to ED
- CC: diffuse abdominal pain for 2 days
- Also reports constipation, vomiting and BRBPR x1
- s/p biopsy of left orbital mass 1 week earlier (pathology not yet available)
- Abdomen is soft with tenderness in both upper quadrants on exam
- Found to be anemic in ED
Our Patient:
Abdominal Plain Film

Patient 1

Plain film reveals large upper left quadrant mass
Ddx for Left Upper Quadrant Abdominal Mass in 5 y.o.

- Neuroblastoma (or other neural tumor)
- Wilms Tumor (or other renal tumor)
- Lymphoma
- Sarcoma
- Teratoma
- Abscess
- Splenomegaly
# Neuroblastoma vs. Wilms Tumor

<table>
<thead>
<tr>
<th></th>
<th>Neuroblastoma</th>
<th>Wilms</th>
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<tbody>
<tr>
<td><strong>Average Age at Dx:</strong></td>
<td>2 years</td>
<td>3 years</td>
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<tr>
<td><strong>Relation to Kidney:</strong></td>
<td>Displaces Kidney</td>
<td>Arises from Kidney</td>
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<tr>
<td><strong>Growth Pattern:</strong></td>
<td>Engulfs Vessels</td>
<td>Displaces Vessels</td>
</tr>
<tr>
<td><strong>Vascular Invasion:</strong></td>
<td>Does not occur</td>
<td>Invades Renal Vein and IVC</td>
</tr>
<tr>
<td><strong>Calcification:</strong></td>
<td>Common (&gt;90%)</td>
<td>Uncommon (~15%)</td>
</tr>
<tr>
<td><strong>Common Sites of Metastasis:</strong></td>
<td>Cortical Bone, Marrow, Liver, Orbit</td>
<td>Lungs</td>
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Adapted from Sepulveda K. [http://www.uth.tmc.edu/radiology/ICF/0028.pps#267,8,Slide 8](http://www.uth.tmc.edu/radiology/ICF/0028.pps#267,8,Slide 8)
Neuroblastoma vs. Wilms Tumor

Lonergan GJ, Schwab CM, Suarez ES, Carlson CL. From the Archives of AFIP. Radiographics 2002; 22: 911-34

Patient 2

Patient 3

Neuroblastoma

Wilms Tumor

Courtesy of Dr. George A. Taylor
Diagnostic Imaging: Ultrasound

- Excellent screening modality
- Neuroblastoma appears as a solid, echogenic, usually heterogeneous mass
- Anechoic areas represent hemorrhage or cystic change
- Calcifications show increased echogenicity, with or without shadowing
- Doppler may show flow in vessels compressed by tumor

Lonergan GJ, Schwab CM, Suarez ES, Carlson CL. From the Archives of AFIP. Radiographics 2002; 22: 911-34
Diagnostic Imaging: CT

- Excellent for evaluating primary lesion and extent of disease
- Neuroblastoma appears as soft tissue density with areas of low attenuation due to hemorrhage and necrosis
- Mass often has an irregular shape and lacks a well-defined capsule
- More than 90% of neuroblastomas have visible calcifications on CT
- Often inadequate for evaluation of intraspinal extension
Our Patient: Coronal CT

Patient 1

• CT reveals a 10 x 12 x 13 cm left suprarenal mass
• Mass is heterogeneous with peripheral enhancement and low attenuation centrally (suggesting necrosis)
• Mass extends medially to involve lymph nodes
• Left kidney is displaced inferiorly
• Renal vessels are encased by surrounding mass
Our Patient: Axial CT

Patient 1

- Image reveals lymphadenopathy and anterior displacement of the aorta
Our Patient: Axial CT

Patient 1

• Bone window image demonstrates a small area of calcification anteriorly within the mass
Diagnostic Imaging: MRI

- Often considered modality of choice for evaluation of abdominal neuroblastoma
- Excellent for examining relationship of mass to surrounding organs and vessels
- Good for evaluating marrow metastases by imaging the pelvis and lower extremities in young children or the vertebrae in older children
- Neuroblastoma appears as heterogeneous low signal on T1-weighted images and high signal on T2-weighted images (bright signal on T1 represents hemorrhage)
- Calcification may be harder to detect than on CT
Images demonstrate lower right quadrant neuroblastoma beginning to invade the right first sacral foramen.

Lonergan GJ, Schwab CM, Suarez ES, Carlson CL. From the Archives of AFIP. Radiographics 2002; 22: 911-34
Diagnostic Imaging: MRI

Patient 6

- MRI is the imaging modality of choice for evaluation of thoracic neuroblastoma

- Coronal, contrast enhanced T1-weighted image demonstrates heterogeneous enhancement of a mass in the posterior mediastinum and retroperitoneum

Lonergan GJ, Schwab CM, Suarez ES, Carlson CL. From the Archives of AFIP. Radiographics 2002; 22: 911-34
Our Patient: Coronal MRI of Orbital Lesion

- Contrast enhanced T1-weighted image shows a homogeneous, hyperintense lesion in the left anterior cranial fossa, orbital roof and superior orbit.
Diagnosed…Now what?

- Radiologic evaluation of our patient’s abdominal mass demonstrated many classic findings of neuroblastoma arising from the left adrenal medulla
- Pathology reports from the biopsy of the patient’s orbital mass confirmed that this lesion was also neuroblastoma
- Now that we know what our patient has, what do we do next?
- Additional staging studies must be performed to assess extent of disease and develop treatment plan
Additional Imaging for Staging and Follow-up: Bone Scan

- Uses technetium 99m methylene diphosphonate which is taken up by cells active in metabolism of bone
- More sensitive for cortical bone metastases than skeletal survey (conventional radiography)
- Very useful for follow-up (new areas of uptake highly suspicious for recurrent disease)
- Lesions must be distinguished from areas of physiologic increased uptake (metaphyses)
- Low specificity (trauma may cause false positives)
Our Patient: Bone Scan

Bone scan reveals several areas of abnormal uptake (visible in multiple ribs, right clavicle, lumbar spine, left hip, left superior orbital region, right parieto-occipital region, lumbar spine and left hip).
Additional Imaging for Staging and Follow-up: MIBG Scan

- MIBG is an analogue of a catecholamine precursor and is taken up by catecholamine-producing cells
- High sensitivity and specificity for neuroendocrine tumors
- Best study to show extent of extraskeletal involvement
- Useful to look for primary tumor of unknown location
- Very useful for follow-up studies (new areas of uptake highly suspicious for recurrent disease)
- Cortical bone uptake cannot be distinguished from marrow involvement
- Up to 30% of primary tumors do not take up MIBG
MIBG scan reveals several areas of increased uptake (especially remarkable at the site of the primary tumor in the upper left quadrant of the abdomen)
International Neuroblastoma Staging System

- **Stage I**: Localized tumor confined to the area of origin; complete gross resection with or without microscopic residual disease: identifiable ipsilateral and contralateral lymph nodes negative macroscopically.

- **Stage II A**: Localized tumor with incomplete gross excision: identifiable ipsilateral and contralateral lymph nodes negative microscopically.

- **Stage II B**: Unilateral tumor with complete or incomplete gross resection with positive ipsilateral regional lymph nodes: contralateral lymph nodes negative microscopically.

- **Stage III**: Tumor infiltrating across the midline with or without regional lymph node involvement; unilateral tumor with contralateral regional lymph node involvement; or midline tumor with bilateral regional lymph node involvement.

- **Stage IV**: Dissemination of tumor to distant lymph nodes, bone, bone marrow, liver, or other organs (except as defined in stage 4S)

- **Stage IV S**: Localized primary tumor (as defined for stage 1 or 2A or 2B) with dissemination limited to skin, liver, or bone marrow (<10% tumor cells, and MIBG scan negative in the marrow). Limited to infants <1 year of age.

Standard Treatment

Treatment regimens vary by disease severity (estimated based on stage, patient age, histology and biological markers):

- Low Risk Disease: surgery +/- chemo, radiation if tumor is unresectable or unresponsive
- Intermediate Risk Disease: chemo + surgery, radiation if tumor is unresectable or unresponsive
- High Risk Disease: chemo + surgery + radiation
# Prognosis

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<tr>
<th>Age</th>
<th>Survival %</th>
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<tbody>
<tr>
<td>&lt;1 year</td>
<td>74</td>
</tr>
<tr>
<td>1-2 years</td>
<td>43</td>
</tr>
<tr>
<td>2-3 years</td>
<td>18</td>
</tr>
<tr>
<td>&gt;3 years</td>
<td>14</td>
</tr>
<tr>
<td>Overall</td>
<td>36</td>
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<table>
<thead>
<tr>
<th>Stage</th>
<th>Survival %</th>
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</thead>
<tbody>
<tr>
<td>I</td>
<td>95-100</td>
</tr>
<tr>
<td>II</td>
<td>82-83</td>
</tr>
<tr>
<td>III</td>
<td>42-81</td>
</tr>
<tr>
<td>IV</td>
<td>10-30</td>
</tr>
<tr>
<td>IV S</td>
<td>60-90</td>
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- Age at diagnosis and stage are the most important prognostic factors in neuroblastoma.
- Also important is site of primary tumor (mediastinal tumors have a better prognosis than do retroperitoneal tumors).
Our Patient: Follow-up Coronal CT

Patient 1

K.F. at time of diagnosis

K.F. after 4 cycles of chemo (notice ↓ tumor size)
Summary

- Neuroblastoma is a common childhood malignancy, arising from neural crest cells.
- Although it can occur anywhere along the sympathetic chain, neuroblastoma is most often found in the retroperitoneum.
- Most patients have substantial metastatic disease at the time of diagnosis.
- Symptoms at presentation vary widely but may include vague systemic symptoms.
- Diagnosing neuroblastoma and evaluating extent of disease requires a multitude of imaging studies (plain film, ultrasound, CT, MRI, bone scan, MIBG scan).
- Neuroblastoma has a characteristic appearance on imaging (heterogeneous mass, lacking a clear capsule, displacing kidney inferiorly, encasing vessels, often calcifying).
- Many imaging modalities are also useful in performing follow-up studies.
References

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- Sepulveda K. http://www.uth.tmc.edu/radiology/ICF/0028.pps#267,8,Slide 8
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