Adrenal masses in infancy and childhood: A clinical and radiological overview

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Introduction

- Neoplastic adrenal masses usually originate from medulla or cortex.
- The medulla derives embryologically from neural crest and the cortex from fetal mesoderm.
- Neoplasms arising from medulla include:
  - Neuroblastic tumor: neuroblastomas, ganglioneuroblastomas, ganglioneuromas
  - Pheochromocytomas
Introduction

- Other locations of neurogenic tumors are along sympathetic nerve chain from the neck to the pelvis.
- Carcinomas and adenomas are cortex tumors causing mostly endocrine abnormalities.
Adrenal masses

- Neuroblastic tumor
- Pheochromocytoma
- Adenomas and carcinomas
- Adrenocortical hyperplasia
- Adrenal hemorrhage
- Lymphangioma (rarely)
- Teratoma (rarely)
- Ectopic adrenal tissue in testis
- Others
Neuroblastoma

- Neuroblastoma is the most common extracranial solid neoplasm.
- Presentation age is mostly between 0 – 5 years.
- Favourable prognosis in infants and newborn (congenital type of neuroblastoma).
- In older children the prognosis depends on site and stage of disease.
Neck 1-5%

Posterior mediastinum 20%

Retroperitoneum 30-35%

Adrenal 35%

Pelvis 2-3%

1% metastasis of unknown origin
Biological behaviour of neuroblastoma

- Hallmarks of neuroblastomas are their propensity to secrete catecholamine (90 – 95 %) depending on immaturity.
- The secreted catecholamines are vanillylmandel acid (VMA) and homovanillic acid (HVA).
- The secretion of vasoactive peptide results in intractable diarrhea in some cases.
- Poor prognosis is expected in patients with N-myc oncogene amplification ( > 10 copies).
Clinical presentation of neuroblastoma

- Pain caused by either local effects from the primary tumor or metastatic disease
- Abdominal distention
- Malaise
- Irritability
- Weight loss
- Shortness of breath
- Horner syndrome (ptosis pupillary constriction).
- Opsoclonus-myoclonus.
- Chronic secretory diarrhea because of secretion of vasointestinal peptide.
## International neuroblastoma staging system

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>Localized tumor confined to the area of origin. Complete excision.</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>Tumor with incomplete excision.</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>Tumor with complete or incomplete excision with ipsilateral lymphnodes.</td>
</tr>
<tr>
<td>Stage III</td>
<td>Tumor infiltrating acrossing the midline with or without lymphnodes.</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Dissimination of tumor with lymphnodes, bone, bonemarrow, liver and other organs.</td>
</tr>
<tr>
<td>Stage IV S</td>
<td>Localized tumor as stage I or II. Dissiminated limited only to liver, skin and bonemarrow.</td>
</tr>
</tbody>
</table>
Clinical data in 32 cases with neuroblastic adrenal tumor

<table>
<thead>
<tr>
<th>Pathologic features</th>
<th>Neuroblastomas n=29 (91 %)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ganglioneuroblastoma n=2 (6 %)</td>
</tr>
<tr>
<td></td>
<td>Ganglioneurinoma n=1 (3 %)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male: n=24 (75 %)</td>
</tr>
<tr>
<td></td>
<td>Female: n=8 (25 %)</td>
</tr>
<tr>
<td>Age</td>
<td>Neonates and infants: n=10 (31 %)</td>
</tr>
<tr>
<td></td>
<td>Older children (&gt;1yr): n=22 (69 %)</td>
</tr>
<tr>
<td>Tumor location</td>
<td>Right-sided n=15 (49 %)</td>
</tr>
<tr>
<td></td>
<td>Left-sided n=16 (50 %)</td>
</tr>
<tr>
<td></td>
<td>Double-sided n=1 (1 %)</td>
</tr>
<tr>
<td>Catecholamine excretion (VMA)</td>
<td>Positive: n=27 (85 %)</td>
</tr>
<tr>
<td></td>
<td>Negative: n=3 (9 %)</td>
</tr>
<tr>
<td></td>
<td>Not performed: n=2 (6 %)</td>
</tr>
</tbody>
</table>
## Diagnostic procedures of neuroblastic adrenal tumor

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Number (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated urinary catecholamines and their metabolites</td>
<td>n=27</td>
</tr>
<tr>
<td>MIBG (Metaiodobenzylguanidine) scintigraphy (sensitivity 88%, specificity 99%)</td>
<td>n=24</td>
</tr>
<tr>
<td>Sonography</td>
<td>n=26</td>
</tr>
<tr>
<td>CT (Computed Tomography)</td>
<td>n=9</td>
</tr>
<tr>
<td>MRI (Magnetic Resonance Imaging). Indicated in cases with paraganglionic neuroblastoma with possible intraspinal involvement</td>
<td>n=2</td>
</tr>
<tr>
<td>PET (Positron Emission Tomography) scan</td>
<td>n=0</td>
</tr>
</tbody>
</table>
Site of metastases in 32 cases of neuroblastic adrenal tumor

<table>
<thead>
<tr>
<th>Metastasis Type</th>
<th>Own cases</th>
<th>Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone infiltration</td>
<td>n=18 (56%)</td>
<td>83%</td>
</tr>
<tr>
<td>Bone metastases</td>
<td>n=11 (34%)</td>
<td>70%</td>
</tr>
<tr>
<td>Liver metastases</td>
<td>n=6 (20%)</td>
<td>29%</td>
</tr>
<tr>
<td>Pleura metastases</td>
<td>n=3 (10%)</td>
<td>5%</td>
</tr>
<tr>
<td>CNS metastases</td>
<td>n=1 (3%)</td>
<td>7%</td>
</tr>
<tr>
<td>Skin</td>
<td>n=1 (3%)</td>
<td>4%</td>
</tr>
</tbody>
</table>
Staging in 32 cases of neuroblastic adrenal tumor

- Stage I  n=4
- Stage II n=0
- Stage III n=0
- Stage IV  n=21
- Stage IV S n=7
An infant with histologically benign ganglioneurinoma.

Another infant with histologically double-sided adrenal neuroblastoma.
Right-sided histologically ganglioneuroblastoma stage IV.

Left-sided histologically adrenal neuroblastoma stage IV.
9 month old boy with left-sided adrenal neuroblastoma stage IV. Note the fronto-orbital metastasis.
Double-sided adrenal neuroblastoma stage IVs with liver metastasis.
Left-sided adrenal neuroblastoma stage I.

Note the normal right-sided adrenal.
Metastasis of left femur by neuroblastoma.

Huge lymphoma in a case of stage IV neuroblastoma.

Pleural metastasis with effusion by neuroblastoma.

Liver metastasis by neuroblastoma stage IVs.
Pheochromocytoma

- Pheochromocytoma arises from neuroectodermal chromaphin tissue.
- Uncommon in pediatric population (only 10% in childhood).
- Pheochromocytomas are sporadic, however observed familiar by multiple endocrine neoplasia (MEN) 2A and 2B, Von Hippel-Lindau syndrome and neurofibromatosis type I.
- The most frequent presentation age is 6-14 years.
- 30% of pheochromocytomas are multiple.
- 15 – 20% are located extra adrenal.
Pheochromocytoma

Clinical signs and symptoms:
- Tachycardia
- Hypertension (20 % normotensive)
- Nausea
- Vomiting
- Weight loss
- Palpitation
- Sweating
- Episodic headache
Diagnostic procedures in pheochromocytoma

- Measurement of urinary catecholamine and its metabolites norepinephrine and epinephrine
- MIBG scan (Meta-Iodobenzylguanidine)
- Abdominal sonography
- Abdominal CT
- MRI
- PET scan (positron emission tomography)
Clinical data of 6 cases of pheochromocytoma

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td>n=3</td>
<td>n=3</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>3-18 yrs (average 12 yrs)</td>
<td></td>
</tr>
<tr>
<td><strong>Inheritance</strong></td>
<td>Sporadic n=3</td>
<td>Hereditary n=3</td>
</tr>
<tr>
<td><strong>Urinary catecholamine metabolites</strong></td>
<td>Positive in all cases (noradrenaline)</td>
<td></td>
</tr>
</tbody>
</table>
Location and imaging approaches in 6 cases of pheochromocytoma

<table>
<thead>
<tr>
<th>Location</th>
<th>Imaging approach</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>One-sided adrenal</td>
<td>MIBG</td>
<td>n=4</td>
</tr>
<tr>
<td>Double-sided adrenal</td>
<td>US</td>
<td>n=1</td>
</tr>
<tr>
<td>Multifocal extra adrenal</td>
<td>CT</td>
<td>n=1</td>
</tr>
<tr>
<td></td>
<td>MRI</td>
<td>n=4</td>
</tr>
</tbody>
</table>

n=4 indicates 4 cases, n=1 indicates 1 case.
2 boys aged 7 (A) and 12 year (B) with a left-sided adrenal pheochromocytoma.
Adrenocortical neoplasms

- Uncommon in childhood, frequency total population: 1 : 500,000/year
- Mostly occur in children older than 3 years.
- Girls are affected three times more than boys.
- Carcinomas are three times more common than adenomas.
- The majority are functioning tumors with endocrine abnormalities.
  - Boys with pseudo-precocious puberty.
  - Girls with virilization.
Adrenocortical neoplasms

- Sonography is the initial modality, CT and MRI are both modality of choice.
- Adenomas are small with homogeneous structure.
- Carcinomas are often large masses and inhomogeneous.
2 year old girl with adrenocortical adenoma with clinical sign of virilisation (A).

11 year old girl with a left-sided adrenal carcinoma with virilisation and precocious puberty. Note the lung metastasis (B).
4 year old boy with an adrenocortical adenoma with sign of precocious puberty. Note the large testis with calcification.
Adrenal hyperplasia

- Adrenocortical hyperplasia can be primary or secondary.
- Primary hyperplasia usually results in Cushing syndrome and is uncommon in childhood.
- Adrenal gland is normally rarely visible on US in older children.
- An adrenal hyperplasia should be expected in case of enlargement and visibility.
- CT and MRI are the modalities of choice in diagnosis of adrenocortical hyperplasia.
An infant with McCune Albright syndrome. Note the adrenal hyperplasia on CT, renal calcification, skeletal fibrous dysplasia and café-au-lait spots.
Adrenal hemorrhage

- Commonly occurs in perinatal period.
- Hypoxia, stress and traumatic delivery are possible pathogenesis.
- Neonates with adrenal hemorrhage may present with prolonged jaundice and anemia depending on severity of bleeding.
- Sonography is the first modality of choice in recognition of adrenal hemorrhage.
- Short term follow up by sonography is needed to differentiate adrenal hemorrhage from a congenital neuroblastoma.
A neonate with right-sided adrenal hemorrhage in the postnatal age (A) and a few weeks later with sign of regression and calcification (B).
A neonate with suprarenal mixed type lymphangiom
13 year old girl with an adrenal teratoma.

Note the fluid level with fat layer above the sedimented material.
Extra-adrenal tissue in testis
14 year old boy with adrenogenital syndrome with ectopic adrenal tissue left testis.
Adrenogenital syndrome with adrenal tissue both testes in a 13 year old boy.
Differential diagnosis of suprarenal masses.

- Extra adrenal neuroblastoma
- Wilms tumor
- Hepatoblastoma
- Rhabdomyosarcoma
- Infections
- Cystic nephroma
- Neurofibroma
2 year old boy with an extra-adrenal neuroblastoma on the left side.

10 year old girl with a extra-adrenal located ganglioneuroblastoma left-sided.
7 year old girl with a Wilms tumor localised in the upper pole of the right kidney.

3 year old boy with a nephroblastoma of the right kidney.
1.5 year old girl with a hepatoblastoma.

9.5 year old boy with hepatoblastoma.
16 year old girl with a diaphragmatic right-sided rhabdomyosarcoma.
1 year old boy with a dysplastic hydronephrotic upper pole system.

One month old girl with dysplastic upper pole with an ectopic ureter.
3 month old girl with an extra-renal retroperitoneal mature teratoma.
Conclusion

- Adrenal medulla is the most common site of neuroblastic tumors (35%).
- Boys are affected more frequent (3:1) by adrenal neuroblastoma.
- Neonatal hemorrhage should be differentiated from congenital neuroblastoma by MIBG and early regression signs of hemorrhage.
- Hereditary and multifocal pheochromocytomas have a propensity to malignancy.
Conclusion

- CT and MRI together with MIBG are adequate procedures for staging neuroblastoma.
- MRI is the modality of choice to exclude intraspinal infiltration in cases with extrarenal neuroblastoma.
- Malignancy can not be differentiated from adrenocortical adenomas by various imaging modalities.