Adrenal masses in the neonate: the value of sequential ultrasound.

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Learning objectives

The aim of this exhibit is to review the most frequent adrenal masses in the neonate, their imaging features and to emphasize the value of ultrasound to monitor this pathology.
Background

In children, the initial diagnosis of an adrenal mass is usually made by ultrasound. Furthermore, this technique is useful to demonstrate regression in the case of adrenal hemorrhage. CT or MRI are performed to evaluate tumor extension and its relation with adjacent organs. The role in diagnostic imaging is to differentiate between renal and adrenal masses and characterize adrenal tumors and their extension. In the neonate and children we could find more frequently some types of adrenal masses such as neuroblastoma, ganglioneuroma, pheochromocytoma, adrenocortical tumors and hemorrhage.

1. NEUROBLASTOMA

The neurogenic tumors [neuroblastoma (NB), ganglioneuroblastoma (GNB), and ganglioneuroma (GN)] are a spectrum of sympathetic tissue tumors ranging from the immature and malignant neuroblastoma to the mature and benign ganglioneuroma. Fig. 1 on page 10

Although ganglioneuroma tends to be a more homogeneous tumor than neuroblastoma or ganglioneuroblastoma, at imaging evaluation is not possible to differentiate among these three tumors.

In terms of malignancy, ganglioneuroblastoma is an intermediate form between ganglioneuroma and a neuroblastoma. It is most common in children between 2 and 4 years old, and unusual in children above 10 years of age. It appears as an encapsulated, solid or mixed solid-cystic lesion often containing calcifications.

Neuroblastoma is the third most common malignancy in childhood after leukemia and primary brain neoplasm, and the most frequent extracranial malignant solid tumor.

It mostly appears in children under 4 years with a peak age of 2-3 years.

The majority are adrenal but they also originate from other organs derived from neural crest cells, such as sympathetic lymph nodes of lower abdomen, Zuckerkandl gland, presacral region, chest and nasopharynx.

Clinical manifestations vary with age, stage, location and metabolic alterations due to catecholamines production.
It usually manifests as a palpable mass. Two thirds of patients have disseminated disease at the time of presentation with metastatic involvement of bone, liver, lymph nodes and less commonly chest, gonads, brain and skin.

In 90% of the cases catecholamines in urine are elevated.

Paraneoplastic syndromes are a rare presentation, including myoclonic encephalopathy (with better prognosis than those case of NB without it), watery diarrhea with hypokalemia due to VIP (vasoactive intestinal peptide) or hypertension. Other uncommon presentations include “racoon eyes” and Virchow adenopathy due to adrenal mass with metastasis in chest and neck.

Some groups of patients could have better prognosis, as in disseminated neuroblastoma without bone metastasis (IV S) or in multifocal neuroblastoma (there isn’t disseminate disease).

In a fetus or newborn the neuroblastoma could manifest more often as hepatomegaly due to metastasis than as a primary tumor. The mass can have massive intratumoral hemorrhage and can mimic adrenal hemorrhage.

Neuroblastoma can transform into ganglioneuroma, a more benign tumor, or even dissapear.

The diagnosis of neuroblastoma is established by tumor tissue sampling demonstrating unequivocal neuroblastoma cells or a combination of positive bone marrow aspirate and increased urinary catecholamine metabolites (vanillylmandelic acid and homovanillic acid).

STAGING

The staging is based in cross-sectional imaging and MIBG scan to asses metastasic disease Fig. 2 on page 10 Fig. 3 on page 11

The International Neuroblastoma Risk Group Staging System (INRGSS)

The INRGSS was designed for the International Neuroblastoma Risk Group (INRG) pre-treatment classification system. The INRGSS uses the results of imaging tests taken before surgery and does not include surgical results or spread to lymph nodes to determine the stage.
**Stage L1:** The tumor is located only in the area where it started; no risk factors found on imaging scans, such as CT or MRI.

**Stage L2:** The tumor has not spread beyond the area where it started and the nearby tissue; risk factors are found on imaging scans, such as CT or MRI.

**Stage M:** The tumor has spread to other parts of the body (except stage MS).

**Stage MS:** The tumor only has spread to the skin, liver, and/or bone marrow.

**IMAGING FINDINGS**

**Radiography:**
- Approximately 40-60% of neuroblastomas contain calcifications. Fig. 4 on page 12. Fig. 5 on page 13. Fig. 6 on page 14.
- Metastatic osseous lesions are often lytic and permeative located in metaphyses more frequently.

**Ultrasound:**
- This exam can show a hyperechoic heterogeneous suprarenal mass with internal hypoechoic areas due to necrosis and hyperechoic foci that are caused by hemorrhage, thrombosis or calcifications. Fig. 7 on page 15. Fig. 8 on page 16. Fig. 9 on page 17.
- It could be seen hypoechoic metastatic involvement of the liver.

**Magnetic resonance imaging:**
- Neuroblastoma can be seen as an aggressive, often large, solid, inhomogeneous tumor that enhances after contrast administration and may have internal necrotic areas Fig. 10 on page 18. Fig. 11 on page 19 but this feature is less common than in Wilms tumor. This tumor doesn’t have a definable capsule.
- The mass can cross the midline and encase blood vessels Fig. 12 on page 20, infiltrate adjacent organs and extend into the extradural space via spinal foramina, Fig. 13 on page 21 more frequently in paraspinal sympathetic chain neuroblastoma. The tumor can extend to chest showing paraspinal soft tissue thickening.
- MRI can demonstrate vessel’s encasement and metastatic bone marrow involvement with more resolution than CT or US.
- Liver metastasis are often multiple and hypervascular. After chemotherapy the liver show a "pseudocirrhotic" appearance or can develop focal nodular hyperplasia.

- Radiotherapy can lead to vessels stenosis years after successful treatment.

### 2. GANGLIONEUROMA

It is the most mature benign tumor originated from neural crest tissue and it’s less common than neuroblastoma.

More benign forms of neuroblastoma can turn into ganglioneuroma, as well as neuroblastoma and its metastases after successful chemotherapy.

Most often it manifests as an asymptomatic mass incidentally discovered. Sometimes it can cause local mass effect with cough, abdominal pain or dyspnea or infrequently symptoms due to increased secretion of catecholamines.

GN and NB may present similar radiologic features and the final diagnosis is made histologically by the degree of cellular maturation and differentiation although, some features can help us to guide the diagnosis. The GN appears in older children, with a peak age of 6 years of age and two thirds of cases don’t have elevated catecholamines in urine. MIBG scans are negative in 50% of GN and this tumor has a slower growth rate and show increased diffusion in MRI while NB shows restricted diffusion.

### 3. PHEOCHROMOCYTOMA

This is a rare tumor in childhood and is often associated with MEN syndromes or phakomatoses.

Two thirds arise in the adrenal medulla and if they occur outside the suprarrenal gland are termed paragangliomas.

Most of pheochromocytomas in children are benign and manifest with signs of sympathetic overstimulation like flushing, headache, tachycardia, hypertension or hypertensive crisis. **Fig. 14** on page 22

Levels of urinary or serum catecholamines or their metabolites are elevated.

They are not large at the time of diagnosis and ultrasound may not detect them.
MRI and CT are useful to localize the tumor, and assess multiplicity (it can be single or multiple, with more tendency to be bilateral Fig. 15 on page 23 in children but not necessarily synchronous). MIBG scan is useful in multifocal tumors, metastatic or recurrent disease or suspected thoracic location.

Smaller tumors have soft tissue attenuation, they are homogeneous and present smooth margins.

Larger masses are more heterogeneous, ill-defined and can have internal necrotic areas. Fig. 16 on page 24

Pheochromocytomas can have punctate calcifications and moderate to intense enhancement.

We can find local invasion, lymphadenopathy, and distant metastases.

After iodinated contrast administration catecholamines plasma levels can be increased but it doesn´t always result in a symptomatic hypertensive episode.

4. ADRENOCORTICAL TUMORS

Adrenocortical tumors (ACT) in childhood constitute about 0,2% of all pediatric malignancies.

The imaging features of all ACT neoplasms are quite similar to other adrenal masses, so the diagnosis will be made with both clinical and imaging findings.

Usually there is increased secretion of adrenocortical hormones, such as the 17-ketosteroids or plasma dehydroepiandrosterone sulfate (DHEA-S), abnormal urinary DHEA concentrations are less sensitive.

These tumors often present in young children with precocious puberty, Cushing's syndrome, Conn's syndrome, feminization in boys, virilization in girls and accelerated skeletal maduration. Fig. 17 on page 24

It can be difficult to differentiate between adenoma and carcinoma. There are some radiologic findings suggestive of malignancy: size greater than 6 cm, heterogeneous mass with areas of low attenuation due to necrosis and hemorrhage, irregular outline, calcifications, lymphadenopathy, metastases (more frequent in lung and liver) and vascular invasion. Fig. 18 on page 25 Fig. 19 on page 26 Fig. 20 on page 27 Fig. 21 on page 28
5. ADRENAL HEMORRHAGE

Adrenal hemorrhage is the most common adrenal mass in neonates and it’s more frequent than in older children. It often occurs in the right side due to compression between the liver and the kidney, and it is bilateral in 10% of cases.

It can be caused by birth trauma, anoxia, stress, dehydration or renal vein thrombosis (more frequently in left side due to common venous drainage of adrenal and left kidney).

Adrenal hemorrhage is often asymptomatic and can be an incidental finding. In some patients it can manifest as a unilateral flank mass, anemia, jaundice, hypovolemic shock or scrotal hematoma as a unusual clinical manifestation.

IMAGING FINDINGS

The diagnosis is based on sequential ultrasound in order to evaluate involution. MRI will be performed if the mass shows a solid appearance or agressive features.

On ultrasound (US), initially it’s observed as a complex solid-appearing echogenic and mildly inhomogeneous mass Fig. 22 on page 29 that usually maintains the adreniform shape. It is relatively hypovascular on Doppler imaging. Doppler can be helpful to detect renal vein thrombosis. Subsequently, it is followed by liquefaction showing a cystic appearance, and decreased size. Old hemorrhage is seen as hyperechoic area in adrenal gland.

Adrenal hemorrhage usually resolves completely, Fig. 23 on page 30 Fig. 24 on page 31 but it can have rimlike calcification that turns into a triangular shape when the mass decreases. Fig. 25 on page 32

On computed tomography (CT) without contrast administration acute adrenal hemorrhage cause a hyperdense (50-75 Hounsfield units) distortion of suprarrenal’s shape. Thickening of the adjacent diafragmatic crura and streakiness of periadrenal fat could be observed. Adrenal pseudocyst due to organized chronic hematoma appears as a mass with hypoattenuating center with or without calcifications.

MRI

Acute phase (< 1 week):
- Adrenal hemorrhage shows an iso-slightly low signal on T1-weighted images and markedly low signal on T2-weighted images.

- It doesn’t show significant enhancement after contrast administration.

**Subacute phase (1-8 weeks):**

- It has high signal on T1 and T2 weighted images and in large hemorrhages fluid-fluid levels could be observed.

- On T1 weighted images there could be a rim hyperintense signal.

**Chronic phase (> 8 weeks):**

- Hemosiderin results in low signal on T1 and T2 weighted images with a hypointense rim in both sequences as the result of deposition of hemosiderin and fibrosis.

- Clots in the renal vein have high signal on T1 and T2 weighted images.

- Later, we can find adrenal atrophy or hemorrhagic adrenal pseudocyst visualized as a nonenhancing thin-rimmed cystic lesion.

The main features that will help us to differentiate it from neuroblastoma is size involution on follow-up exams, the hypovascularity or non significant enhancement, greater tendency to liquefaction and that hemorrhage causes less often vein thrombosis. Moreover, in adrenal hemorrhage there is absence of increased vanillyl mandelic acid blood levels.
Fig. 1: Anatomic distribution of sympathetic ganglia, extending from the neck to the pelvis, including the adrenal medulla (sympathetic tissue shown in blue).

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
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<tbody>
<tr>
<td>1</td>
<td>Limited to organ of origin</td>
</tr>
<tr>
<td>2</td>
<td>Regional spread, not crossing the midline (= vertebral body)</td>
</tr>
<tr>
<td>3</td>
<td>Extension across the midline (= contralateral margin of vertebral body)</td>
</tr>
<tr>
<td>4</td>
<td>Metastatic disease to distant lymph nodes, liver, bone, brain, lung</td>
</tr>
<tr>
<td>4S</td>
<td>Stage 1 and 2 with metastatic disease confined to liver, skin, bone marrow; no radiological evidence of bone metastases/osteolysis</td>
</tr>
</tbody>
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**Fig. 2:** Staging of neuroblastoma.

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Fig. 3: Case 1: Neuroblastoma. Coronal MIBG anterior (A) and posterior (B) views demonstrate focal MIBG uptake in right adrenal region (arrows).

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Fig. 4: Case 1: Neuroblastoma. A)PA and lateral B) chest radiographs in a 3 y/o children with 3 day history of cough. Coarse calcifications are seen in the right suprarenal region (arrows).

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Fig. 5: Case 1: Neuroblastoma. Abdominal CT with i.v. contrast administration demonstrate a partially calcified right adrenal mass (arrow) with internal hypodense areas which can represent necrosis or hemorrhage.

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Fig. 6: Case 1: Neuroblastoma. Coronal (A) and Sagittal (B) abdominal CT with i.v. contrast administration demonstrate a partially calcified right adrenal mass (arrow) with internal hypodense areas which can represent necrosis or hemorrhage.

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**Fig. 7:** Case 3: Neuroblastoma. Abdominal ultrasound shows a well-defined large (9.7 x 5.6 cm) heterogeneous adrenal mass (arrows). (*) Right kidney.

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Fig. 8: Case 2: Neuroblastoma. Abdominal ultrasound shows an approximately 6 cm heterogeneous solid well-defined left adrenal mass.

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Fig. 9: Case 1: Neuroblastoma. Ultrasound (longitudinal view) performed after visualization of adrenal calcifications in a radiography. We can observe a hyperechoic adrenal mass with dirty posterior shadowing related to calcification (arrow).

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**Fig. 10:** Case 2: Neuroblastoma. Coronal T1 weighted sequence after Gadolinium administration that shows a well-defined enhancing left adrenal mass (long arrow) with internal hypointense area (short arrow) possibly related to hemorrhage or necrosis.

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Fig. 11: Case 3: Neuroblastoma. Abdominal CT with i.v. contrast administration, shows a large heterogeneous right adrenal mass with hypodense areas related to necrosis (arrow). Mild enhancement was seen.

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Fig. 12: Axial T2-weighted image showing vessel’s encasement (arrow) in a retroperitoneal neuroblastoma that crosses the midline.

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Fig. 13: Axial T2-weighted image showing invasion of spinal canal via left foramina (arrow).

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**Fig. 14:** Case 5: Pheochromocytoma. 15 y/o boy with fists to his face and muscle pain. Family History of Pheochromocytoma. PA chest radiography (A) and chest CT with i.v. contrast administration (B) show multiple diffused bilateral alveolar opacities consistent with ARDS.

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![Figure 14: Pheochromocytoma.](image)

**Fig. 15:** Case 5: Pheochromocytoma. 15 y/o boy with fists to his face and muscle pain. Family history of pheochromocytoma. Abdominal ultrasound that exhibit bilateral adrenal masses. They are hypoechoic and relatively homogeneous with some internal foci with cystic appearance.
Fig. 16: Case 5: Pheochromocytoma. Axial (A) and coronal (B) abdominal CT with i.v. contrast administration shows well defined, heterogeneous bilateral adrenal masses (arrows) with hypodense central areas that could represent necrosis.

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Fig. 17: Case 6: Adrenal carcinoma. AP radiography of left hand and wrist shows signs of accelerated bone maduration. According to the female standards compiled by Greulich and Pyle, the estimated bone age is approximately between 10 and 11 years. For the patient's chronologic age of 3 years and 7 months, the standard deviation is 7.5 months.

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Fig. 18: Case 6: Adrenal carcinoma in a 3 years old female with significant masculinization. Abdominal ultrasound, transversal view, showing a large and heterogeneous right adrenal mass with internal hyper and hypoechoic areas that could represent calcification or necrosis respectively.

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Fig. 19: Case 6: Adrenal carcinoma in a 3 years old female with significant masculinization. Abdominal CT with i.v. contrast administration showing a large right adrenal mass with heterogeneous appearance, with hypodense central areas (white arrow) probably due to necrosis. There are internal hyperdense areas consistent with calcifications (black arrow).

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Fig. 20: Case 6: Adrenal carcinoma in a 3 years old female with significant masculinization. Coronal (A) and sagittal (B) abdominal CT with i.v. contrast administration showing a right round-shaped and well-defined large adrenal mass that has a heterogeneous appearance, with hypodense central areas probably due to necrosis. There are internal hyperdense images consistent with calcifications.

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Fig. 21: Case 6: Adrenal carcinoma in a 3 years old female with significant masculinization. Sixty minutes following the intravenous administration of 4 mCi of FDG PET scan shows avid uptake in the right adrenal gland.

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**Fig. 22:** Case 7: Adrenal hemorrhage. A) Abdominal ultrasound, longitudinal view of right flank, shows a heterogeneous adrenal mass (arrow) with some internal hypoechoic areas. (*) Kidney. B) Doppler ultrasound doesn’t exhibit significant hypervascularity.

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Fig. 23: Case 7: Adrenal hemorrhage. Follow-up abdominal ultrasound, longitudinal view of the right kidney. The adrenal mass has completely resolved.

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**Fig. 24:** Case 7: Adrenal hemorrhage. A) Abdominal ultrasound, transversal view, shows a heterogeneous adrenal mass with internal anechoic areas. B) Follow-up abdominal ultrasound. Longitudinal view of the right kidney. The adrenal mass has completely resolved.

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**Fig. 25:** Abdominal radiography. Residual calcifications following right adrenal hemorrhage (arrow).

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Findings and procedure details

We have made a bibliographical research of the main types of adrenal masses in neonate and children and a review of their demographics, radiologic findings and management.

A 1.5 Tesla MRI was used to perform the exams.

Protocol included the following sequences: axial and coronal T1 and T2-weighted sequences, coronal STIR sequence, axial T2 weighted sequence with fat saturation, axial T1 weighted sequences with fat saturation and following contrast administration.

Ultrasound were performed with a convex and a multi-frequency high resolution linear transducer.
Conclusion

The major findings of this exhibit are:

1. The most frequent radiological appearance of neuroblastoma is a solid mass with or without calcifications.

2. Hemorrhage is often visualized as a heterogeneous cystic mass.

3. Ultrasound is a valuable exam for an initial diagnosis of adrenal masses, and also, will allow the radiologist to confirm the total involution of hemorrhage.

4. CT/ MRI will be necessary to assess neuroblastoma staging.
References


