

## Differential diagnosis and minimally invasive surgery of an antenatal adrenal mass

### Diagnóstico diferencial y cirugía mínimamente invasiva de un tumor suprarrenal de hallazgo antenatal

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#### Abstract

**Introduction:** Adrenal masses are uncommon in newborns. The differential diagnosis includes benign masses (adrenal hemorrhage, extralobar pulmonary sequestration) and malignant ones (neuroblastoma) that may be a finding during an obstetric ultrasound. The use of complementary imaging methods allows a better diagnosis approach during the postnatal period, with implications for the management of these patients. **Objective:** To report the case of a female newborn with diagnosis of an adrenal mass, and to discuss differential diagnoses and management alternatives of adrenal lesions in newborns. **Case report:** Two-month-old female infant, referred for adrenal tumor study diagnosed at 22 weeks gestational age. Postnatal ultrasound showed a tumor compatible with neuroblastoma. The patient was asymptomatic, and the laboratory studies showed no relevant findings. The lesion was excised by laparoscopy. A histological study confirmed pulmonary sequestration. **Conclusions:** Extralobar pulmonary sequestration should be considered in the differential diagnosis of an adrenal mass in the newborn. Minimally invasive surgery should be the preferred surgical technique choice in these cases, given the technical feasibility and benefits in the recovery and cosmetic issues of the patient.

#### Keywords:

neuroblastoma;  
adrenal tumor;  
extralobar pulmonary  
sequestration;  
children

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## Introduction

The antenatal diagnosis of adrenal tumors diagnosis is increasing due to the widespread use of obstetric ultrasound<sup>1,2</sup>. Adrenal masses have an incidence of 1.9:1,000 newborns<sup>3</sup>. The most important differential diagnosis is with neuroblastoma (NB), a malignant neoplasm with originated from the adrenal gland in 90% of the cases<sup>3,4</sup>. Table 1 details other differential diagnoses<sup>3-5</sup>. After birth, abdominal ultrasound should be performed. Additional information can be obtained with CT scan or MRI if malignancy is suspected<sup>3-5</sup>. Thus, it is possible to discriminate the lesion origin in 81-85% of cases<sup>3</sup>. Conservative management, with ultrasound monitoring and the use of serum markers, is a reasonable therapeutic approach, although this is still matter of debate<sup>6-9</sup>.

The objective of this article is to report the case of a newborn with antenatal diagnosis of adrenal mass, who was successfully treated with minimally invasive surgery. The histopathology study reported an extralobar pulmonary sequestration (EPS). Differential diagnoses and possible management alternatives are discussed.

## Clinical case

2-month-old female with adrenal mass detected by obstetric ultrasound at 22 weeks of pregnancy. A hy-

poechoic left adrenal mass of 22 x 16 mm was identified (Figure 1a). Mother with no morbid history, two previous births, well-controlled physiological pregnancy. Ultrasound follow-up at 35 weeks of gestational age confirmed the presence of a hypoechoic infradiaphragmatic mass of approximately 20 x 20 mm, apparently separated from the left adrenal gland (Figure 1b). Vaginal delivery at 38 weeks, adequate weight for gestational age, no perinatal morbidity. Normal physical examination, no palpable abdominal masses, female genitals without signs of virilization or hyperpigmentation.

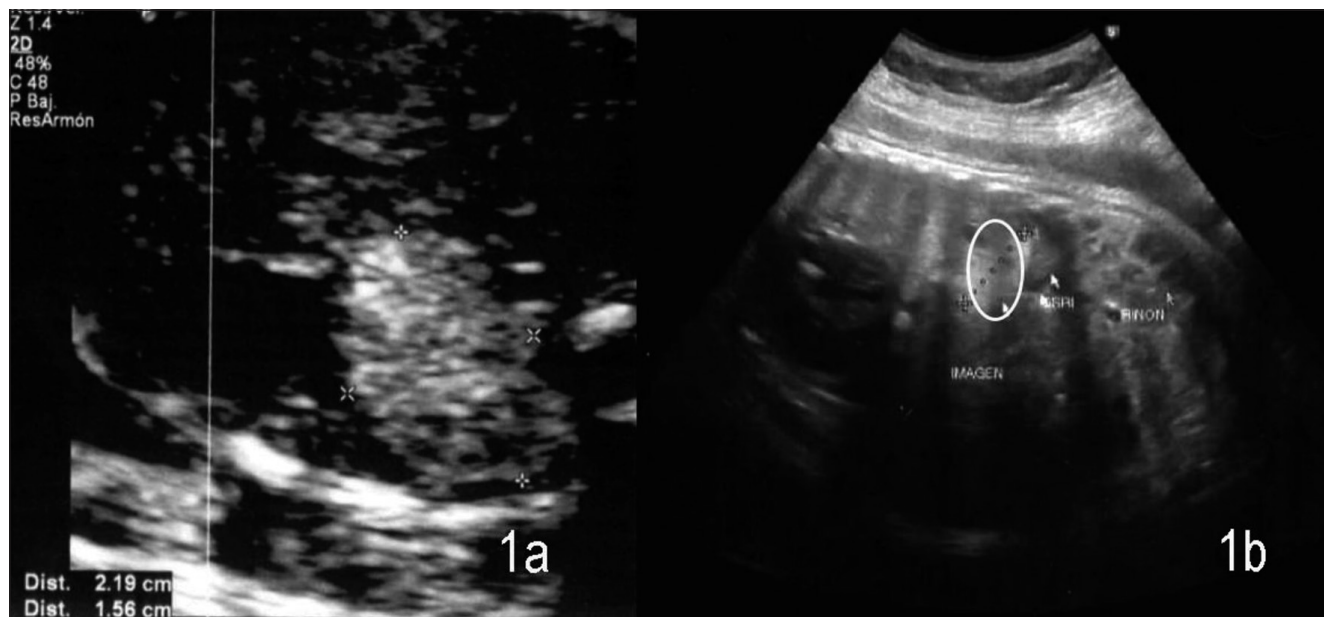
At seven weeks, urinary catecholamines were measured, which were in the high normal range for age (metanephrine 206 µg/g creatinine, and normetanephrine 1,250 µg/g creatinine), and referral was decided for study and management.

The functional study of the tumor was completed with plasma levels of metanephrines, testosterone, aldosterone, renin, cortisol, androstenedione, epinephrine, norepinephrine, and dopamine, all within normal limits.

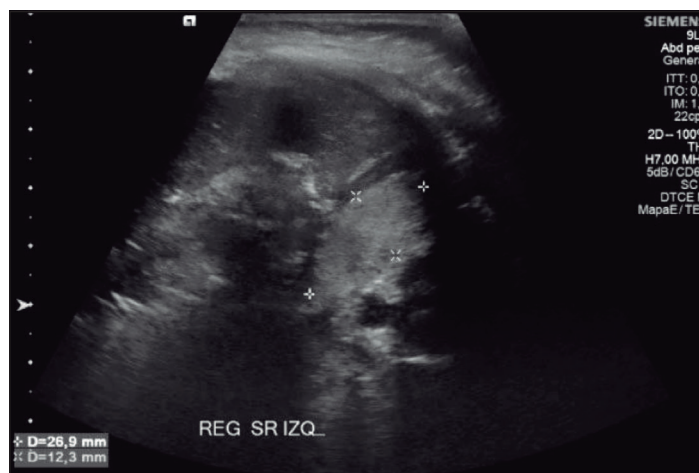
The preoperative study was completed with abdominal ultrasound that showed a solid, uniform lesion, echoic with respect to adjacent tissue, with partially defined edges, without evident calcifications, measuring approximately 2.7 x 1.2 x 1.7 cm. No abnormal blood flow was observed in the Doppler ultrasound. Adjacent to the lesion there was a tissue resembling adrenal gland (Figure 2). The MRI complemented the

**Table 1. Differential diagnoses of adrenal mass**

	Benign	Malignant
Fetal	Congenital adrenal hyperplasia	Neuroblastoma
	Extralobar pulmonary sequestration	Congenital mesoblastic nephroma
	Upper pole hydronephrosis	Wilms Tumor
	Partial obstructive cystic dysplasia of the kidneys - Urinoma	
	Gastric duplication cysts	
	Splenic cyst	
Childhood	Adrenal adenoma	Neuroblastoma
	Ganglioneuroma	Ganglioneuroblastoma
	Congenital adrenal hyperplasia	Paraganglioma
	Extralobar pulmonary sequestration	Pheochromocytoma
	Adrenal hemorrhage	Adrenal carcinoma
	Intestinal duplication	Teratoma
	Splenic cyst	
	Partial obstructive cystic dysplasia of the kidneys	
	Urinoma	
	Adrenal myelolipoma	
Adrenal cyst		



**Figure 1.** Antenatal ultrasound where the lesion is identified at different gestational ages. **1a.** Ultrasound at 23 weeks of gestational age, shows a hypoechoic mass of 22 x 16 mm. **1b.** Ultrasound at 35 weeks, infradiaphragmatic hypoechoic mass is identified in relation to the 20 x 20 mm kidney (white ellipse).



**Figure 2.** Abdominal ultrasound at 7 weeks confirms an infradiaphragmatic echogenic well-defined mass. There is no image of vessels with Doppler US.

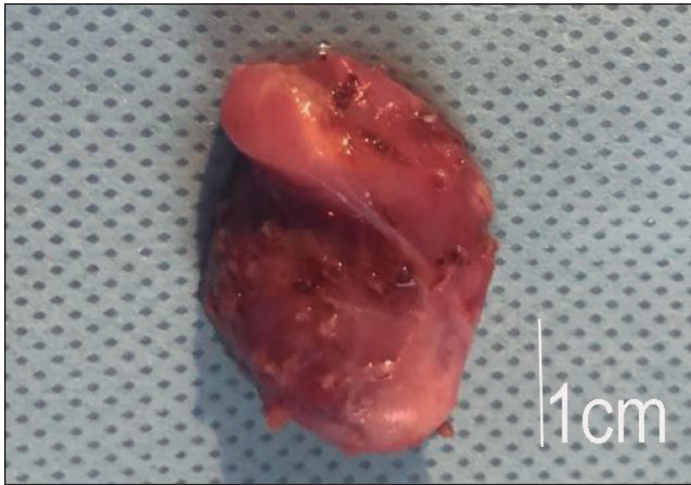


**Figure 3.** Pre-operative MRI. Adrenal mass is marked with (\*).

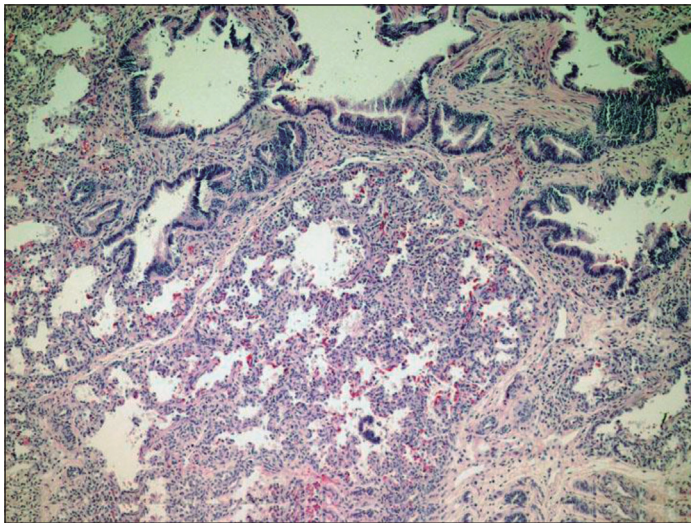
study and showed a solid mass of 21 mm in the left adrenal region (Figure 3). There were no blood flow alterations.

Tumor resection was performed laparoscopically without incident. Under general anesthesia and with the patient in a 45° left lateral position, a laparoscopic exploration with 5mm umbilical trocar inserted with open technique, an auxiliary trocar of 5mm in RIF, and two working instruments of 3mm inserted percutaneously. The colon was detached, releasing the splenic angle and accessing the transcavity. A well-defined adrenal mass adjacent to the gland was identified, of rubber-like consistency, with discreetly increased irrigation. Dissection and comple-

te resection of the lesion was performed which was extracted through the umbilical port (Figure 4). The patient was monitored for 24 hours, restarted breastfeeding immediately after surgery, and was discharged in good condition at 48 hours. During follow-up at 2 and 6 weeks, she was in good condition, with no evidence of tumor recurrence on ultrasound or any other local complications.



**Figure 4.** Operative specimen. A well defined, lobulated mass, completely excised.



**Figure 5.** Microphotograph showing areas of alveolar and of bronchiolar differentiation with Microphotograph showing areas of alveolar and of bronchiolar differentiation with thickening of alveolar septa and fibrosis around the abnormal airways. HE, 80x.

The histopathological study showed a lung tissue lesion with canalicular stage structure, in which immature bronchiolar structures with respiratory epithelium, some alveolar conduits with macrophages, and no alveoli identification are recognized. Stromal fibroblast and smooth muscle fascicles. Some larger spaces with respiratory epithelium and immature hyaline cartilage. No evidence of malignancy was observed. These findings are compatible with pulmonary sequestration (Figure 5).

## Discussion

The incidence of adrenal masses follows a bimodal distribution, and is more frequent in children under

5 years, and then from the fourth and fifth decade of life<sup>10</sup>. In newborns, it is important to establish the differential diagnosis between NB, adrenal hemorrhage (0.2% of newborns), and other lesions such as EPS, which are infrequent<sup>4</sup>. Pheochromocytoma and ganglioneuroma are tumors of school-age children, while adrenal adenoma, although rare in children, occurs before age 5 or after age 10<sup>11</sup>.

Most adrenal tumors occur as incidental finding before birth or during childhood. They can also present as a palpable mass, abdominal pain, secondary arterial hypertension, kidney failure, precocious puberty, and fever or shock, depending on their origin<sup>12</sup>.

The imaging study of choice for evaluating adrenal masses in pediatric age is abdominal ultrasound<sup>3,4,5,11</sup>. This allows to define the characteristics of the mass: size, structure, location, blood flow, and relationship with adjacent structures. Lesions suspected of malignancy should be studied with CT scan or MRI<sup>3</sup>. Other imaging methods, such as Iodine-123 (<sup>123</sup>I) metaiodobenzylguanidine (MIBG) scintigraphy, may be used as a complementary study, especially for staging in NB<sup>11,13</sup>.

There are several reports in the scientific literature published of EPS simulating NB. Curtis et al. describe that in 1997 for each EPS, 2.5 NB<sup>5</sup> were diagnosed. In addition, Kalenahalli et al. reported an atypical EPS case, given the absence of other associated malformations, which would be present in up to 65% of EPS cases<sup>14</sup>. Some elements of EPS in ultrasound are: location in the left adrenal space, visualization of an aberrant artery (usually from the aorta) on the Doppler ultrasound, displaced adrenal gland, visible as a separate entity, and diagnosis during the second trimester of pregnancy. In the NB, the most frequent situation is to observe a complex cystic image (50% of the cases), without unique nutrient artery image; the diagnosis generally occurs from the third trimester of the pregnancy. It is unusual to visualize the ipsilateral adrenal gland<sup>4</sup>. Additionally, the absence of catecholamine metabolites in urine (vanillylmandelic acid [VMA] and homovanillic acid [HVA]) supports the diagnosis of EPS<sup>3</sup>. The negative MIBG scintigraphy supports the benign character of the lesion, given that more than 90% of NBs are avid for the marked isotope<sup>13</sup>. In the presented case, the diagnosis was the NB given the suspicious imaging study and urinary catecholamines in the limit of the normal range.

The good prognosis of NB in early stages has led to questions about the need for immediate resection in patients with prenatally detected adrenal masses<sup>6-8</sup>. In the follow up of lesions that remain stable over time in terms of their appearance, size, and markers in blood or urine, partial or complete regression of the lesions has been observed<sup>2</sup>, which would allow to avoid or de-

fer surgery<sup>6,7,15</sup>. Although the management of EPS has traditionally been surgical, Yoon et al. describe significant rates of spontaneous regression at four years, associated with certain imaging elements, suggesting that surgical treatment could be considered in patients who meet this time period, have not presented regression or have presented complications<sup>9</sup>. In another report, Obeidat et al. describe a case similar to the one presented, which was followed-up through ultrasound until spontaneous resolution at 2 years of age<sup>16</sup>. Since the 1990s, the information regarding the possibility of observing selected patients with an NB diagnosis began to increase, since a significant percentage (up to 60%) return over time<sup>6-8</sup>. The first observation protocols included patients with a diagnosis of NB detected by universal screening at 6 months of age, patients under one year of age at the time of follow-up, in stages I-II, with a solid lesion less than 5 cm in size or cystic lesion less than 3.1 cm, without vascular compromise and with negative serum markers<sup>6</sup>. An important series suggests that up to 81% of patients younger than 6 months could be observed without surgical treatment and that the remaining percentage have benign behavior, with a 3-year survival of 100%<sup>6-8</sup>. Other smaller series suggest that even 60% of children under one year of age may be included in this category.

Nuchtern et al. published in 2012 the results of a prospective follow-up protocol in patients younger than 6 months with a diagnosis of NB stage INSS I of the Children's Oncology Group Study, followed-up between 2001 and 2010<sup>15</sup>. 83 patients were monitored by ultrasound and urine VMA/HVA for 90 weeks, at weeks 3-6-12-24-66 and 90, and CT scan/MRI three times. The criteria for defining the need for surgical resection was growth greater than 50% of the initial volume or increase in urinary metabolites higher than 50% of the basal value. 56 patients (67.4%) completed the observation period, 71% of them had residual mass < 1 ml at the end of follow-up. 16 patients underwent surgical resection before completing the observation time, 10 of them had NB, and 2 had disease progression. Two patients had EPS. Event-free survival was 100 and 96% for patients with cystic and solid masses respectively. Resection-free survival was 79.8% at 3 years. Surgery was avoided in 81% of the patients<sup>15</sup>. In this case, early resection was chosen, considering an important degree of parental anxiety and expectations for the establishment of a definitive diagnosis, associated with the technical feasibility of performing minimally invasive surgery expeditiously.

Pulmonary sequestration is a congenital malformation of the lower airway. It consists of a lung mass not communicated with the tracheobronchial tree, irrigated by an artery derived from systemic circulation<sup>17</sup>. Congenital malformations of the pulmonary airway

have an incidence of 1: 10,000 - 1:35,000 live births, where the most frequent is congenital pulmonary airway malformation (CPAM), formerly called congenital cystic adenomatoid malformation (CCAM), with an incidence of 1 in 7200 live births (18). Pulmonary sequestration, which is a rare malformation, represents 0.15-6.4% of the group<sup>1</sup>. According to its relationship with the parenchyma, they are divided into intralobar (they do not have visceral pleura) and extralobar (they have visceral pleura). This last group accounts for 25% of the cases and can be found both inside and outside the chest (5-10%). Most EPS are left and are located between the lower lobe of the lung and the diaphragm. It is accepted that 50% of them are associated with other congenital anomalies<sup>11,14</sup>. Antenatal diagnosis with ultrasound is increasingly common<sup>3</sup>. EPS is usually diagnosed early in life, while intralobar pulmonary sequestration is usually diagnosed later, manifesting itself mainly as repeated infections in the same anatomical area. This is rare in the EPS<sup>17</sup>. In Chile, there are few publications on this subject and there is no national data of pulmonary malformations that would allow us to know its real incidence<sup>19</sup>. A series of 17 CPAM cases was recently published, which retrospectively analyses the cases that occurred between 2005 and 2016 in two reference hospitals in Spain, and reports an incidence of 1.7/10,000 births<sup>20</sup>.

The typical image of the EPS in the ultrasound is that of a uniform mass, usually pyramidal. Identifying a nutrient artery from the aorta or another systemic vessel may help to establish the diagnosis<sup>11</sup>. Despite this, establishing a preoperative diagnosis is extremely difficult and is usually done with histopathological analysis. If the diagnosis is prenatal, the imaging study should be supplemented after birth, preferably with a CT scan<sup>4</sup>.

The management of pulmonary sequestration has traditionally been surgical and should be urgent in children with respiratory distress at birth, but may be deferred in asymptomatic children or those with recurrent infections. In completely asymptomatic children, the decision between surgery and observation is controversial, where the main reason for conservative management is the low complication rate of EPS. Arguments in favor of early surgery are the need for diagnostic confirmation (as opposed to other alternatives such as NB), the risk decrease of subsequent complications, and the best prognosis when surgery is performed before it develops<sup>1,2</sup>. Surgical resection can be done by video-assisted thoracoscopy or laparoscopy<sup>2</sup>. Partial lobectomy is the treatment of choice in intralobar sequestration, while in EPS the mass is resected with blood vessels ligation<sup>1</sup>. The complication rate is low<sup>1,2</sup>.

The first report of laparoscopic approach in pul-

monary sequestration dates from the year 2000, in a 4-month-old patient, born prematurely at 31 weeks of gestational age, with antenatal diagnosis of pulmonary sequestration<sup>21</sup>. New studies have supported these results, thus laparoscopy is the technique of choice<sup>12,22-24</sup>.

## Conclusions

Adrenal tumors in newborns are rare, and the differential diagnosis includes benign and malignant lesions, the most important of them is NB. Pulmonary sequestration is a rare pulmonary congenital malformation and surgery is the treatment of choice.

Considering the evidence available in scientific literature, it has been questioned whether all congenital adrenal masses should be resected, especially those that are asymptomatic. However, given the low morbidity of minimally invasive surgery and the relevance of establishing a diagnosis, we believe it is reasonable to consider early resection of this type of lesion as opposed to expectant management. Parents of patients should know the management alternatives, their risks, and benefits, and participate in the therapeutic decision that is advised in each case by the treatment team.

## Ethical Responsibilities

**Human Beings and animals protection:** Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

**Data confidentiality:** The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

**Rights to privacy and informed consent:** The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

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## Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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