

Case Report

Suprarenal Neuroblastoma with Liver Metastasis: A Case Report

Luiza Manfroi Lattmann, Sthefany Mais* and Sandra Lucia Schuler

Department of Medicine, Universidade Positivo, Brazil

*Corresponding author

Sthefany Mais, School of Health Sciences, Department of Medicine, Universidade Positivo, Curitiba, PR, Brazil, Tel: +55 41 3995 9660; Email: sthefanymais@outlook.com

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Abstract

Neuroblastoma, an embryonic tumor arising from primitive cells of the sympathetic autonomic nervous system, is the most common extracranial solid neoplasm in childhood. The clinical presentation is heterogeneous as it depends on the tumor size and primary location. For diagnosis, one must perform histological analysis or find tumor cells in the bone marrow associated with increased metabolites of catecholamines, but correlation with immunological methods and laboratory tests are highly recommended for confirmation. This type of cancer usually has a good regression rate, in addition to being usually susceptible to surgical resection, but chemotherapy and radiotherapy can be applied. This report tells the story of a patient with less than 3 months of age diagnosed with adrenal neuroblastoma with secondary hepatic impairment, in this case, there was a good response to applied therapies, resulting in tumor regression.

Keywords

- Adrenal gland neoplasm
- Abdominal neoplasm
- Hepatomegaly
- Clinical oncology

ABBREVIATIONS

NSE: Neuron-specific enolase; CGA: Synaptophysin, and Chromogranin A; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; LDH: Lactate Dehydrogenase; pO_2 : Partial pressure of oxygen; pCO_2 : Partial Pressure of Carbon Dioxide; FISH: Fluorescence *in situ* hybridization; SIOP: International Society of Pediatric Oncology.

INTRODUCTION

Neuroblastoma is a type of embryonic tumor that arises from primitive cells of the sympathetic autonomic nervous system, occurring mainly in the medulla of the adrenal glands, but it can affect the paraspinal ganglia as well [1]. This is the most common extracranial solid neoplasm in childhood, with a middle-age incidence of 17 months of life [1-3]. The survival rate changes according to each case, associating both with high rates of morbidity mortality and a good proportion of complete regression, being the age at the diagnosis the greatest predictor of prognosis [1-5]. Tumors classified as low and intermediate-risk have a better prognosis, with the vast majority having complete regression with little intervention. In contrast, only 40% of patients with high-risk tumors survive despite multimodal therapies [3,4].

The clinical presentation of this pathology is quite heterogeneous, depending mainly on its size and primary location [1,2,6]. Masses in the neck or upper chest can cause ptosis, miosis, and anhidrosis - the so-called Horner syndrome [1]. Tumor in the abdomen can generate pain due to abdominal distension, whereas those in the spine can compress the spinal cord and result in paralysis [1,6]. Another common sign of the disease is a failure in weight gain or even weight loss, leading to wasting

syndrome [6]. As for metastasis, the two most common sites are regional lymph node chains and bone marrow, but cortical bone and liver can also be reached [1,6].

The diagnosis of neuroblastoma requires unequivocal histological analysis of the tumor tissue by pathology methods, or by the presence of tumor cells in the bone marrow associated with increased metabolites or catecholamines in urine or blood [7]. However, the correlation with immunological methods, such as the use of antibodies against neuron-specific enolase (NSE), synaptophysin, and chromogranin A (CGA), are highly recommended to confirm the diagnosis [8]. In addition, serum or urine dopamine dosage is also indicated to document the adrenergic nature of the tumor [8]. To assess the extent of the disease and further staging of cancer, the recommended complementary tests are chest x-ray, computed tomography (CT) or magnetic resonance imaging (MRI) scan, and bone marrow aspirate [7-9].

These tumors are commonly encapsulated and therefore subject to surgical resection, but more advanced stages can infiltrate adjacent structures and make removal impossible [1]. As for cases in which total resection is not possible, conventional chemotherapy, myeloablative regimens, immunotherapy, and autologous stem cell transplantation can be applied as therapy [10-12]. As previously mentioned, although this type of cancer has a good regression rate, this does not apply to patients who need more intensive therapies, in which the disease may progress and lead to death, despite the multimodal therapies applied [12].

CASE PRESENTATION

Female patient, 2 months and 18 days-old, born at 39 weeks and 2 days, weighing 3405g, via cesarean delivery by maternal

choice, with uneventful pregnancy and labor. She was presented to the emergency department with a history of distension, abdominal induration, vomiting, and greater irritability from the first month of life. The patient also had a previous diagnosis of hepatomegaly and liver nodules, in addition to a solid mass in the right kidney, visualized by imaging (**Figure 1**). On physical examination, she presented globose and distended abdomen, extensive varicose veins in the abdominal wall, and hepatomegaly up to the umbilical scar, without signs of peritoneal irritation.

In addition to MRI suggestive of right adrenal neuroblastoma with secondary hepatic involvement, the patient had abnormal laboratory tests. Lactate dehydrogenase (LDH) of 349 U/L, venous blood gases with the reduced partial pressure of oxygen (pO₂), increased partial pressure of carbon dioxide (pCO₂), and oxygen saturation of 37%. The laboratory tests performed are detailed in **Table 1** with the respective laboratory reference values.

A contrast-enhanced chest CT showed no changes, concluding that there was no pulmonary involvement. The bone marrow biopsy sample confirmed the presence of poorly differentiated and infiltrating neoplasm in liver tissue. The investigation of the amplification of the N-MYC gene by fluorescence in situ hybridization (FISH), was negative. Immunophenotyping of hematologic neoplasms did not show non-hematopoietic cells in the evaluated sample. Finally, the segmental genomic profile evaluating the deletion in the long arm of chromosome 11 and the deletion of the 1p36 region of chromosome 1 showed no abnormalities.

The patient was classified as a stage 4S neuroblastoma with intermediate risk according to the International Society of Pediatric Oncology (SIOP) protocol, meaning chemotherapy as the first therapy. The drugs used in the first treatment cycle were 18 mg/kg carboplatin on the first day and 4 mg/kg etoposide from the first to the third day. On the second day, she developed eyelid edema and weight gain due to fluid retention, being treated with hydration reduction associated with a loop diuretic. The patient is being followed up with monthly chemotherapy cycles in the hospital and is in good evolution, and the disease is in remission.

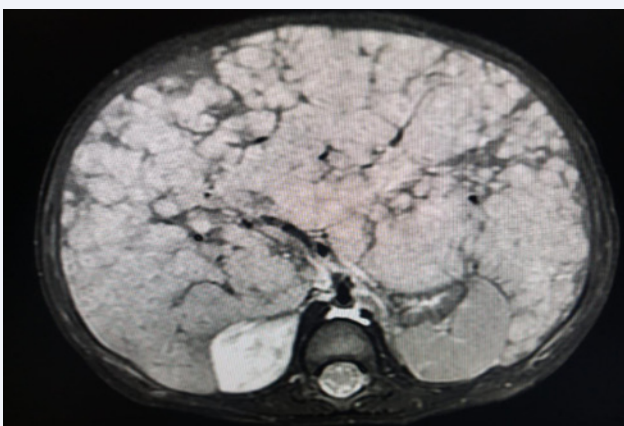


Figure 1 Magnetic resonance imaging reveals a solid mass in the right adrenal pocket and massive hepatomegaly due to several nodular formations.

Table 1: Results of complementary exams performed and laboratory reference values.

	Values found	Reference values
Lactate dehydrogenase (LDH)	349 U/L	120.0 a 246.0 U/L
Venous blood gas		
pH	7,36	7,32 a 7,43
pO ₂	23 mmHg	38 a 50 mmHg
HCO ₃	27,1 mmol/L	22 a 29 mmol/L
pCO ₂	48 mmHg	35 a 45 mmHg
O ₂ saturation	37%	60 a 75%
Alpha-fetoprotein	1.987,0 ng/mL	33,8 a >3.000 ng/mL
Amplification of the N-MYC gene	No hybridization pattern compatible with the amplification of the N-MYC gene in 200 analyzed nuclei were identified. Result ISCN nuc ish(MYCNx1~7)[144/200].	
Immunophenotyping of hematologic neoplasms	Immunophenotypic analysis of bone marrow (right side) shows 2.4% of myeloid lineage precursor cells. No non-hematopoietic cells were seen in this sample with the flow cytometry technique.	
11q23+ segment deletion search	No deletion was detected in the long arm of chromosome 11 up to the 11q23 region in 200 analyzed nuclei.	
1p deletion search*	The deletion of the 1p36 region of chromosome 1 was not detected.	
<i>pO₂ = partial pressure of oxygen; HCO₃ = bicarbonate; pCO₂ = partial pressure of carbon dioxide; O₂ = oxygen; * in neuroblastoma sample; * by fluorescence in situ hybridization (FISH) technique.</i>		

DISCUSSION

Neuroblastoma accounts for 8 to 10% of childhood tumors and approximately 14% of deaths in children due to cancer. Therefore, the study and analysis of cases of this pathology are of paramount importance so that its diagnosis is made correctly and as soon as possible [3]. The mean age for diagnosis of the disease occurs at 23 months of life, and there is a direct relationship between a worse prognosis and diagnosis after the first or second year of life [3]. This finding further supports the importance of knowledge about neuroblastoma for the diagnosis is not delayed and shows that the case reported is interesting from the start. Our patient was diagnosed before the third month of life, a considerably younger age group than the average, showing that this diagnosis should be considered even in very young children. In addition, this information is not in complete disagreement with the literature as 40% of patients who present some symptoms at the time of diagnosis are less than one year old [3].

The clinical presentation can be varied, depending on the anatomical position of the tumor. As most tumors occur in the abdominal region, abdominal masses are the main characteristic, manifesting constipation and distension [13]. Our patient had abnormal blood gases that can be explained by the significant increase in the abdominal mass, making lung expansion difficult and, consequently, worsening the breathing pattern, without major complications such as acidosis. Respiratory dysfunctions are important symptoms, especially in cases where there is significant hepatomegaly [3].

For better prognostic detail, genetic studies are widely used. The N-MYC gene, for example, is one of the characteristics for classification into high-risk neuroblastoma, in which there is a reduction in the survival rate and response to treatments [14]. Immunophenotyping of hematologic neoplasms is performed to identify the presence of metastatic cells in the bone marrow, consequently correlating with a worse prognosis [15]. Finally, the search for changes in the genomic profile during the research is interesting because they are more common in more advanced stages of the disease, associated with a higher risk of recurrence in patients with neuroblastoma and a reduction in event-free survival [16]. Our patient, therefore, has a chance of a favorable prognosis and outcome, as these three tests were negative.

Neuroblastoma can be subdivided into stages: L1 for localized tumors without the involvement of vital structures; L2 for locoregional tumors that affect one or more vital structures; M for distant metastasis; MS for metastatic disease in children with less than 18 months old and with metastasis restricted to the skin, liver, and/or bone marrow [13,17]. The 4S stage of the patient in this study has a better prognosis when we analyze the literature, with the vast majority having spontaneous regression or needing low doses of chemotherapy or radiotherapy, especially in cases where there is clinical dysfunction related to the size of the tumor [3,17]. In addition, there is a classification according to the risks according to the SIOP protocol, which is low, intermediate, and high risk. Being less than 18 months old and with an absence of N-MYC amplification, our patient is defined as an intermediary risk [18].

The main purpose of chemotherapy treatment for intermediate-risk neuroblastoma is to reduce the mass for surgical resections, but it can also be indicated as monotherapy in selected cases or those tumors with spinal cord compression or pulmonary involvement due to hepatic involvement [13]. In the case of a 4S tumor, chemotherapy or low doses of radiotherapy are reserved for patients with large masses or hepatomegaly that trigger mechanical obstruction, respiratory failure, or liver dysfunction [3]. Surgical resection and moderate doses of drugs such as cisplatin, doxorubicin, etoposide, and cyclophosphamide, increase the survival of more than 95% in patients with tumors with favorable characteristics, such as the patients in this case [3]. Thus, the approach we used was adequate in the light of the currently available literature.

Given the above, the approach of a patient who had symptoms, physical examination, and laboratory changes resulting from an extensive tumor mass, was correct according to the literature, as well as the follow-up and the established treatment plan. In addition, this report highlights that the diagnosis of adrenal neuroblastoma can be made from the first months of life, as well as reinforce the good prognosis of cases with early treatment.

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