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Case report

CONGENITAL NEUROBLASTOMA: A RARE CASE OF PLURIVISCERAL METASTATIC DISSEMINATION

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ABSTRACT

Neuroblastoma is one of the most common neonatal tumors. It involves children in early infancy and originates from neural crest cells of the adrenal gland medulla or sympathetic glia. We report an unusual case of congenital poorly differentiated neuroblastoma with multiple metastases in the brain and cerebellum. The biophysical profile showed a prominent polyhydramnios at 25.3 weeks of gestation; meantime, the mother was diagnosed with gestational diabetes. The mass was detected during the third ultrasonographic examination at 31.4 weeks of gestation. The fetus lived only one day after birth and the postmortem examinations were performed subsequently. An autopsy was performed both to understand the causes of death and to identify any profiles of professional responsibility. The histological examination confirmed the diagnosis: a neoplasm arising from the lower right limb and pelvis.

1. Introduction

Neuroblastoma is a tumor that originates from the neural crest cells and can arise anywhere along the sympathetic nervous system, and is included in the family of Peripheral neuroblastic tumors (PNTs). It is the most common childhood cancer and the most common solid extracranial tumor in children diagnosed during the first two years of life [1]. The occurrence of neuroblastoma is unusual in adolescents and adults [2]. Lots of these tumors have been diagnosed during the third trimester using ultrasound and mostly, about 90%, originate from adrenal glands. Although neuroblastoma can metastasize in utero, congenital neuroblastomas with multiple metastases are rare [3].

2. Case presentation

We report a case of a male-infant born at 31.4 weeks of the pregnancy by emergency caesarian section because the last ultrasonography showed oligohydramnios and an undefined formation in the sacral region.

At birth, clinical data was critical and a large mass was observed on the right leg where the doctors performed an ultrasonography, which showed a retroperitoneal solid mass. The newborn was brought into the operating room with a suspected diagnosis of teratoma extended to the lower limb. After the mass reduction surgery, the clinical condition worsened and the baby died.

In Italy, legal authorities provide that if someone dies in the hospital, an autopsy must be performed both to understand the causes of death and to verify that the doctors followed the guidelines, identifying a potential professional responsibility. Even in this case, prosecutors requested an autopsy [4].

We chose a multidisciplinary approach by performing the autopsy in the presence a forensic pathologist, a gynecologist, and also an anatomopathologist.

The autopsy was performed four days after the baby's death. The external examination showed a hydropic male infant with normal volumetric data for age-growth. Anthropometric data were: weight 2159 gr, cranial circumference 29 cm, chest circumference 30 cm, abdominal circumference 29 cm, right foot length 6 cm.

The macroscopic examination of the brain only showed edema.

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The left and right pleural cavities and pericardial sac were free from spilling. Except for the heart, the other organs were normal for age-growth. In the right inguinal region, we observed a surgical wound of 11 cm while the limb measured 13.5 cm [Figure 1].

After autopsy section, the major data was revealed using histopathology [Figure 2], specifically, in the brain, cerebellum, adrenal glands and in the retroperitoneal tissues there were findings of a neuroblastoma mass.

A further study was done using some tumoral markers. Our case showed strong positivity for antibodies against neuron-specific enolase (NSE) [Figure 3] and intermediate filaments [Figure 4].

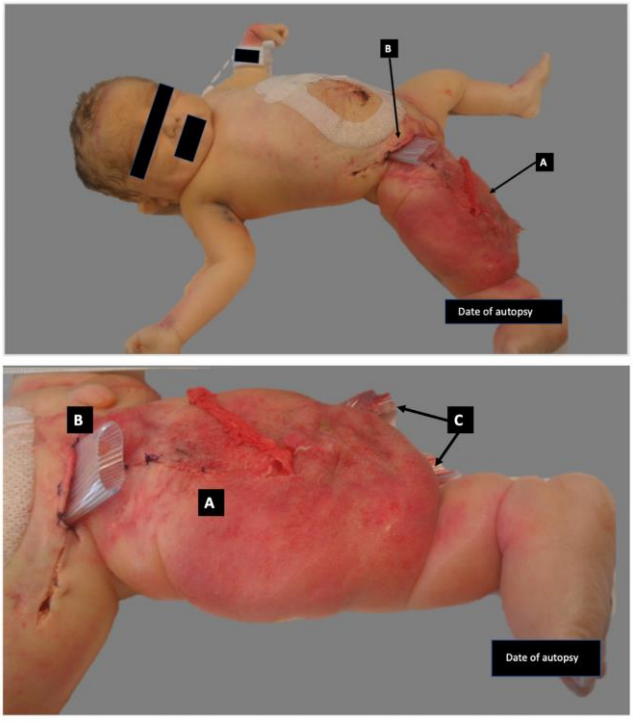

Figure 1. Panoramic photo and detail of the surgery site. A: surgical incision. B: anterior drainage site in right iliac pit. C: posterior drains.

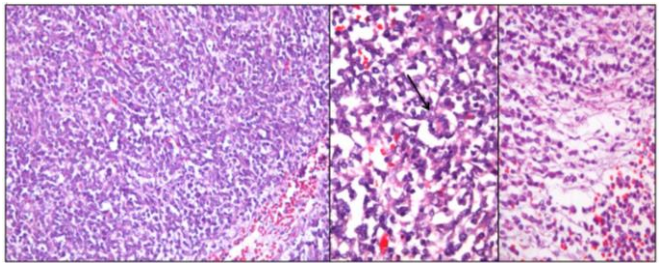

Figure 2. Atypical lobulated neoplasia characterized by small, round to oval, monomorphic cells with hyperchromic nucleus and high nuclear/cytoplasmic ratio (s.c. blue cells); at the periphery, the lobules showed congested capillaries and a thin reticular pattern (a). Homer-Wright rosettes (b) and neurofilament protein(c) was found in the tumor. (H & E stain; a 10x a 10x, b-c 40x)

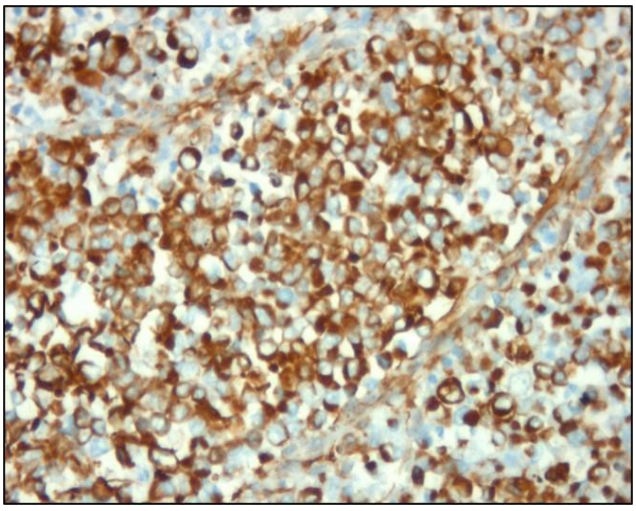

Figure 3. Immunohistochemical stain against NSE. 40x

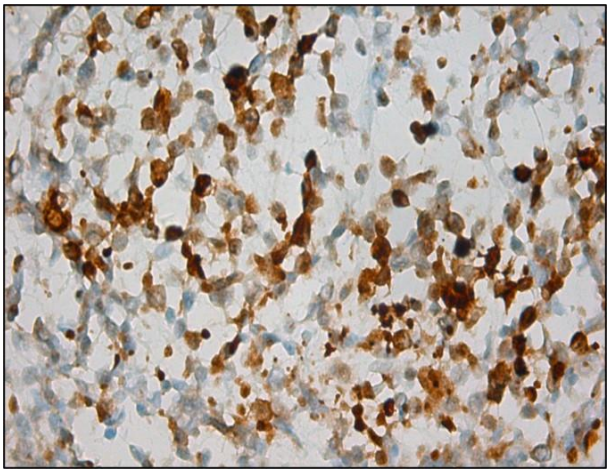

Figure 4. Immunohistochemical stain against intermediate filaments. 100x.

3. Discussion

Although congenital tumors are very rare, neuroblastoma is the most common tumor in early childhood. In 1864, neuroblastoma was described for the first time by Virchow. He described a child with an abdominal mass, which he identified as "glioma" [5]. In 1983, Fenart et al. reported a rare case of a retroperitoneal neuroblastoma observed throughout the routine monitoring of gestation [6]. The most common primary site is the adrenal gland, followed by abdominal, thoracic, cervical and pelvic sympathetic ganglia. In about 1% of cases, the primary site is not found. Disease dissemination occurs through hematogenous and lymphatic routes. It usually metastasizes into bone, bone marrow and liver [7] and less frequently to pulmonary [8] and intracranial sites, as our case. Other cases can appear with multiple metastases [9,10,11].

The majority of neuroblastomas are sporadic and are not related with any specific chromosomal abnormality, inherited predisposition, or associated congenital anomalies.

However, there are some exceptions. *LMO1* was observed in approximately 12 percent of patients with neuroblastoma, which plays a causal role in tumorigenesis. Another study reported germline mutations in the succinate dehydrogenase complex, subunit B (*SDHB)*, adenomatous polyposis coli (*APC*), anaplastic lymphoma kinase (*ALK)*, and breast cancer susceptibility gene 2 (*BRCA2*) in 1 out of 100 patients with neuroblastoma. Furthermore, in a small percentage of cases, about 2%, there is a family history. In these cases, there is an autosomal dominant transmission with incomplete penetrance and a broad spectrum of clinical behavior. Inherited cases usually present at an earlier age than sporadic cases (mean age 9 versus 17 months), and a large proportion have bilateral adrenal or multifocal disease.

Neuroblastoma is normally diagnosed during the third trimester at an average of 33 weeks of gestation, although in the literature there are reported cases with a diagnosis at 23 weeks [11]. It is important to stress that a high rate of neuroblastoma in situ in comparison with rarely encountered clinically apparent neuroblastomas, was attributed to the suggestion that a substantial number may undergo spontaneous regression and degeneration or maturation [12]. Improvements in prenatal imaging and widespread use of fetal ultrasonography have increased its diagnosis. Neuroblastomas commonly present with a palpable abdominal mass, abdominal pain, fever, bone pain, opsoclonus, cerebellar ataxia, orbital ecchymosis or intractable diarrhea, and less commonly with myoclonus [3]. Ultrasound is a useful screening tool and prognosis depends on the sonographic features, which could be variable: cystic, mixed or completely solid with or without calcification. Patients with a cystic neuroblastoma usually have a better outcome than those with no cystic tumors [7,13] and generally tend to a spontaneous regression, [14] especially when there's an antenatal diagnosis. In addition, fetal MRI performed during the third fetal scan can support diagnosis; also, it is useful in cases where liver metastases are suspected, for staging and evaluating metastases and to exclude adrenal hemorrhage [15]. Recently Davis et al. performed a postmortem MRI, in a case where the patient's family had declined traditional autopsy. In this report, they gathered significant information about neoplasm without limitations of prenatal imaging as artefacts [16]. Many studies suggested several maternal factors that may be associated with the subsequent development of a neuroblastoma. Some of these are: folate deficiency, toxic exposures, congenital abnormalities and gestational diabetes mellitus. In our case, the mother was diagnosed with gestational diabetes at 25.3 weeks of gestation. A control case study of 240 children with neuroblastoma showed a correlation with the presence of maternal gestational diabetes mellitus [17].

Although ultrasonography can be an important tool in the diagnosis of neuroblastoma, sometimes it can be missed and only a fetal autopsy with ancillary techniques could play a crucial role [18].

4. Conclusion

In our case, during pregnancy there wasn't evidence of neuroblastoma on ultrasonography or cardiotocography. The only element related to this data was a gestational diabetes that was diagnosed during the third quarter.

However, according to international literature, diabetes mellitus is an unspecific disease related to neuroblastoma, and was not considered a risk factor for this case.

Neuroblastoma is a frequent pathology, considering international literature, however, this case shows how it can grow silently despite regular pregnancy monitoring and traditional autopsy remains the gold standard for postmortem diagnosis. On the basis of the histopathological study, diagnosis of a disseminated malignant tumor was established.

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