CASE REPORTS

HISTOLOGICAL FEATURES OF SPONTANEOUSLY REGRESSING NEONATAL NEUROBLASTOMA: A CASE REPORT

Histological Features of Spontaneously Regressing Neonatal Neuroblastoma: A Case Report

Author	Tom Membrez, Jim C. H. Wilde, Oliver Sanchez, Danai Papangelopoulou, Fabienne Gumy-Pause, Anne-Laure Rougemont
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ABSTRACT

Neuroblastoma, the most common malignancy in infancy, accounts for 8% of paediatric cancers and up to 15% of paediatric cancer-related deaths. Up to 50% of tumours may regress spontaneously, yet detailed histological descriptions are limited. We report a case showing edema, mild collagen deposition, prior haemorrhage, and calcifications. Cellularity was minimal, with rare mature ganglion cells and no neuropil or neuroplastic clusters. Recognising these features in surgical specimens is crucial for guiding optimal treatment.

Key Clinical

Localised neonatal neuroblastoma can undergo spontaneous histological regression, which may mimic post-chemotherapy changes. This report provides a valuable reference framework for pathologists diagnosing regression in neuroblastoma.

Introduction

Neuroblastoma is the tumor developing from sympathetic nervous system progenitor cells that develop into benign ganglia. Neuroblastoma is the most common solid tumour in children under the age of 5 years, with a median age at diagnosis of 2 years. Neuroblastomas constitute about 8% of childhood cancers, and up to 15% of paediatric cancer deaths are attributed to neuroblastoma.

Neuroblastoma demonstrates heterogeneous biological characteristics, which include differentiation into a benign ganglioneuroma or an aggressive, metastatic, and therapy-resistant neoplasm. The prognosis of neuroblastoma depends on age, stage, and biological/molecular features. Perinatal neuroblastoma tumours tend to be localised (approximately 90%, mostly located in the adrenal gland), have low stage (L1), and lack poor prognosis markers, including amplification of the MYCN gene. Localised neuroblastoma tumours diagnosed in infants have an excellent prognosis with

spontaneous resolution in almost 50% of untreated cases. [1]

Spontaneously regressed neuroblastoma is an important clinical entity whose pathological features need to be known to properly diagnose and treat the disease. The following is a description of one of such cases that might help other pathologists. [2]

Case History

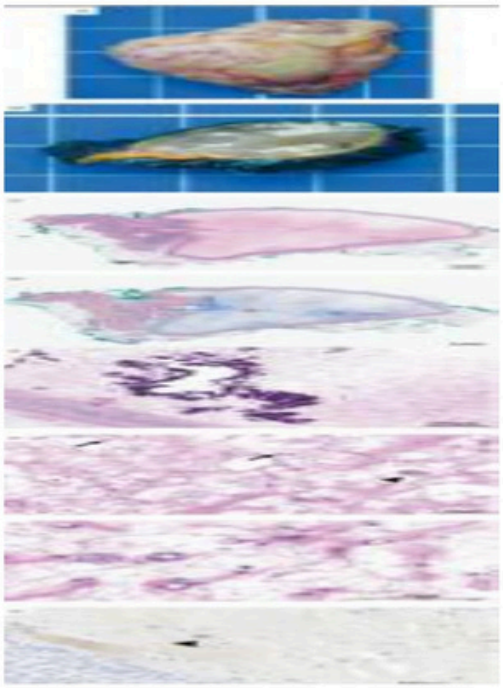
A one-month-old female child, delivered at term following an unremarkable pregnancy without any prior medical history, was subjected to abdominal ultrasonography due to presence of preauricular pits and congenital dislocation of hips. A well-defined, hyperechoic lesion was seen in the right adrenal gland. Mild elevation in urinary levels of catecholamines and increased uptake of MIBG was noted on scintigraphy, with a diagnosis of neonatal neuroblastoma, without any metastatic disease

Investigations, Treatment, and Final Diagnosis

Monthly ultrasound examinations were done based on the SIOPEN Low and Intermediate Risk Neuroblastoma European Study (LINES). Normalisation of urine catecholamines occurred within one month. Within 15 months, there was a spontaneous reduction of the mass from 3.6 x 3.2 x 3.8 cm to 1.9 x 1 x 1.5 cm. The MRI done at 48 weeks showed persistence of a cystic mass with microcalcification. At 15 months, retroperitoneoscopic excision of the mass was carried out based on LINES guidelines.

Pathology Findings

Macroscopic examination revealed a well-circumscribed nodule with a smooth, white, glossy surface. On sectioning, there was a homogenous, myxoid-like translucent mass, with preservation of the adrenal gland at the periphery. Microscopically, there was a poorly cellular tumour with a loose, edematous stroma, some collagen fibres, and abundant blood vessels. The presence of hemosiderin-positive macrophages suggested previous haemorrhage, along with calcifications. There were occasional mature-appearing ganglion cells, with rare immature binucleate ganglion cells. There was no neuropil or neuroplastic cell clusters. Immunohistochemical staining revealed positivity for S100 protein and PHOX2B in ganglion cells (Figure 1).



Final Diagnosis

The diagnosis of the lesion was made to be a peripheral neuroplastic tumour, NOS, with marked spontaneous evolving fibrosis and rare mature ganglion cells, totally excised without any remaining neuroplastic element

Outcome and Follow-Up

The post-operative period was free of complications. Follow-up clinical and ultrasound examinations were recommended every six months for the first two years and once a year for the next five years. No further treatment was required.

Discussion

Neuroplastic tumours can be divided morphologically into neuroblastoma, ganglioneuroblastoma, and ganglioneuroma, further subdivided according to differentiation and neuropil. Ganglioneuroblastoma can be either nodular or intermixed, whereas ganglioneuroma is either maturing or mature.

Post-treatment regression is well-known, characterised by median tumour shrinkage of 77.5% (range 60–100%) with typical histological changes consisting of cellular death, fibrosis, calcification, moderate deposition of hemosiderin, and occasional necrosis.

Spontaneous regression without chemotherapy has been known to occur in 30%-50% of infantile localised neuroblastomas but remains infrequently documented histologically. Reports predating 1990 suggest the following as characteristics of spontaneous regression: necrosis, fibrosis, calcification, stage 4S congenital neuroblastoma regression over three years, and small in situ adrenal tumours in neonates displaying edema and necrosis without remaining oncogenic potential.

Potential mechanisms for spontaneous regression include:

- **Receptor expression of neurotrophins:** TrkA induces differentiation and causes high TrkA-expressing cells to undergo apoptosis in the absence of nerve growth factor.
- **Hypothetical immune cell killing:** Anti-neuroblastoma antibodies and natural killer cell activity have been implicated in cell death.
- **Telomerase enzyme function:** Low telomerase enzyme function with shorter telomeres is associated with apoptosis and decreased tumorigenicity, while high enzyme function has been linked with amplification of MYCN and poor prognosis.

Conclusion

The present case underscores the morphologic changes seen in spontaneously regressing neonatal neuroblastomas, which are very similar to those seen after chemo regression, namely, pluricellular changes, edema of the stroma, fibrosis, calcifications, and infrequent mature ganglion cells. Identifying these changes helps in establishing the diagnosis of spontaneous regression.

References

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