SAS Journal of Medicine
Abbreviated Key Title: SAS J Med
ISSN 2454-5112
Journal homepage: https://saspublishers.com

OPEN ACCESS

Pediatric Surgery

Spontaneous Regression Neuroblastoma: A Case Report

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DOI: 10.36347/sasjm.2023.v09i04.026 | **Received:** 02.03.2023 | **Accepted:** 17.04.2023 | **Published:** 23.04.2023

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Abstract **Case Report**

Neuroblastoma is a malignant tumor characterized by great clinical heterogeneity, ranging from spontaneous regression to progressive tumor evolution. It is already known that the prognosis of neuroblastoma varies according to the age of the child at the time of diagnosis, the stage of the tumor and the amplification of the oncogene MYCN, but there are certainly other factors involved not yet elucidated. Indeed, several teams of researchers are exploring other avenues, immunological, genetic and molecular biology, with the aim of better understanding this phenomenon of spontaneous regression. We report a case of neuroblastoma aged 6 months, and classified as stage 1, having spontaneously evolved towards regression with a review of the literature to underline the crucial importance of further research on this subject to better understand the mechanisms and factors intervening in this favorable evolution with the aim of improving the management and prognosis of neuroblastoma in general, including those classified as high risk.

Keywords: Neuroblastoma, Stage, Malignant tumor, Spontaneous regression, Case report.

INTRODUCTION

Neuroblastoma is an embryonal malignancy of the sympathetic nervous system [7] and it is the most common type of *extracranial solid tumour in children* [10]. Neuroblastomas are characterized by heterogeneous clinical behavior, from spontaneous regression or differentiation into a benign ganglioneuroma, to relentless progression despite aggressive, multimodality therapy [5] Spontaneous regression has been observed in different type of cancers including hepatocellular carcinoma, malignant melanoma, thoracic malignancies, lung cancer, and neuroblastoma. However, NB is generally considered the malignancy, in which this phenomenon is most prevalent [2, 3].

Despite that, the prevalence of spontaneous regression has been well documented by mass screening programs undertaken in Japan, North America and Europe [1].

The mechanism underlying the spontaneous regression of neuroblastoma is unclear. Although it was hypothesized that this regression occurs via an immunological mechanism, there is no clinical evidence, and no animal models have been developed to investigate the involvement of immune systems, especially natural antibodies, against neuroblastoma [4].

We report a case of neuroblastoma with spontaneously regressive evolution, followed and treated jointly, in 2020. The report of this case is an important complement to the study of the spontaneous regression of neuroblastoma.

CASE PRESENTATION

A 6-month-old child, admitted, for management of a right retroperitoneal abdominal mass, which is revealed, One month, by abdominal ultrasound examination.

The patient has no significant personal or family history.

On admission, he has good staturoweight and psychomotor development for his age (8 kg / 71 cm). The abdomen was soft and painless on palpation and there was no palpable mass or hepatosplenomegaly.

The superficial lymph node areas are free.

The Urinary catecholamines are normal (Adrenaline = 0.02 µmol/l and Noradrenaline = 0.21

µmol/l), the Ferritin at 3 ng/ml and the Lactic dehydrogenase (LDH) at 393 ng/l.

Thoraco-abdomino-pelvic CT: finds a lesional process of the right adrenal lodge measuring 31 x 34 x 37 mm and evoking, firstly, an adrenal neuroblastoma. Furthermore, there is no secondary abdomino-thoraco-pelvic location (Figure 1).

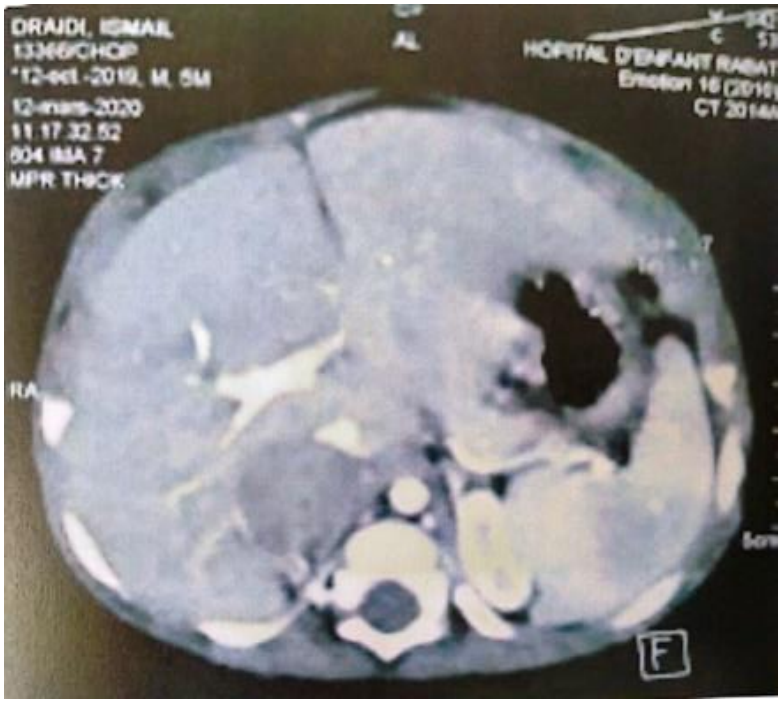


Figure 1: Thoraco-abdomino-pelvic CT, finds a lesional process of the right adrenal lodge measuring 31 x 34 x 37 mm and evoking an adrenal neuroblastoma

MIBG scintigraphy found the focus of right adrenal hyperfixation, with no other secondary location, neither bone nor visceral (Figure 2).

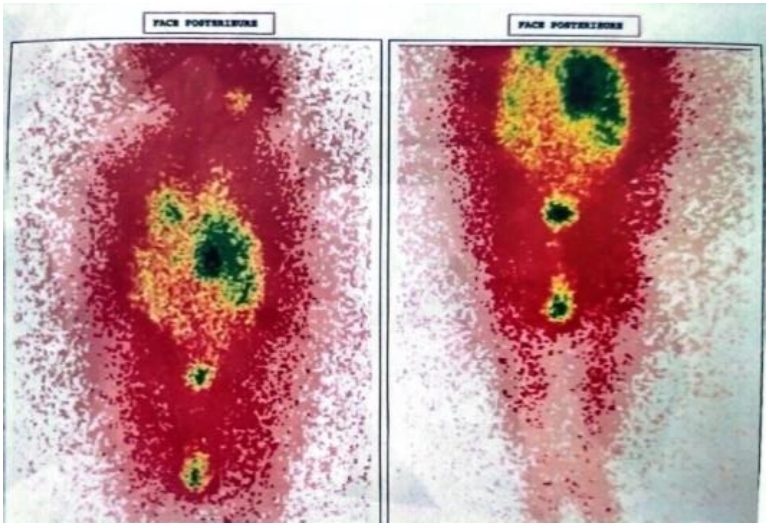


Figure 2: MIBG scintigraphy found the focus of right adrenal hyperfixation, with no other secondary location

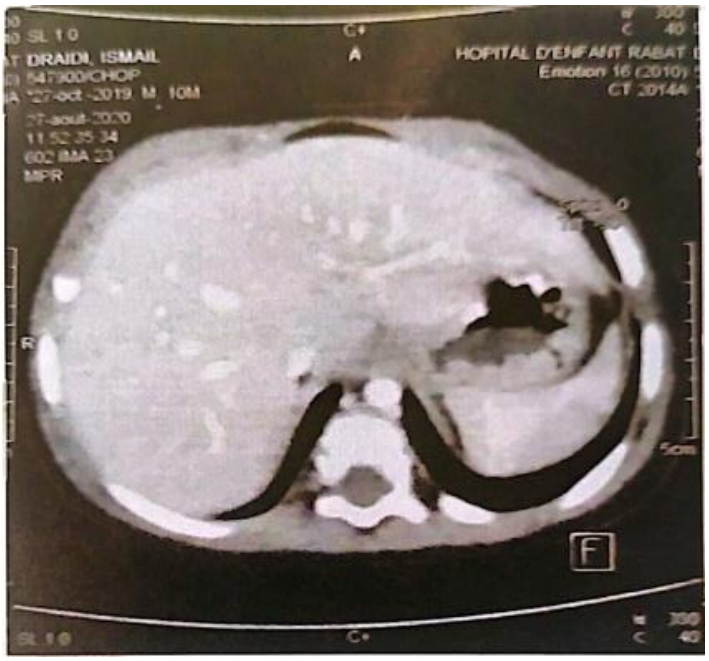
Diagnostic Conclusion: On the clinical and imaging data, the diagnosis of right adrenal neuroblastoma stage I was retained (low risk).

During the meeting of the multidisciplinary consultation, the first surgical resection of the tumor was decided, however this was deferred, due to technical constraints related to the COVID-19 pandemic.

A month later, a new thoraco-abdomino-pelvic CT scan was done as part of the update of the preoperative assessment. This revealed a remarkable

regression of the tumor volume, estimated at 87% (12 x 19 x 21 Vs 31 x 34 x 37) (Figure 3).

It is therefore a spontaneous regression of the tumor.



Figures 3: Thoraco-abdomino-pelvic CT one month later revealed a remarkable regression of the tumor volume, estimated at 87%

DISCUSSION

Spontaneous regression of malignant tumors is defined as the shrinking or disappearance of primary or metastatic disease without therapeutic intervention [17].

It's has been documented in different cancer types for decades. Regression has been observed in renal cell carcinoma, malignant melanoma, choriocarcinoma and lymphoid malignancies [1]. However, neuroblastoma is generally considered the disease in which this phenomenon is most prevalent [3]. The actual prevalence of neuroblastoma regression is not unknown but recent studies have provided evidence that regression may be at least as common as clinically detected neuroblastoma [1].

The most common age of neuroblastoma presentation is between 18 and 22 months, with the majority of cases diagnosed prior to 5 years of age. Age at diagnosis is an important indicator of clinical course, with infants less than 18 months of age more likely to have disease that spontaneously regresses or is successfully treated with surgery alone [8, 9, 11, 6]. However, it is clear that spontaneous regression is not restricted to stage 4S, because regression can be seen in infants with virtually any stage of disease if they have biologically favorable tumors [10, 16].

Our patient was 6 months old at the time of diagnosis, and he was stage 1.

A genetic and biological investigations conduced by several researchers on patients with stage 4 and 4S .Showed that there was essentially no overlap of genes (or proteins) that were differentially expressed by regressing 4S versus non-regressing infant tumors among these studies, so more studies are needed [13-15].

Our case had a favorable biological analyzes (ferritin, LDH, urinary catecholamines).

To understand the mechanisms that regulate the spontaneous regression of neuroblastomas, several studies have been carried out by several teams focusing on theimmunological, genetic and molecular biology aspects of this phenomeno [5, 7, 12].

Brodeur *et al.*, introduced four major pathways that may explain, together or in part, the spontaneous regression of neuroblastoma:

1- Immune-mediated cell killing by antibody-dependent cellular cytotoxicity (ADCC) or by natural killer (NK) cells,
2- Deprivation of neurotrophin and the activation of programmed apoptosis,
3- Dpoptosis caused by low levels/absence of telomerase, and
4- Epigenetic changes in gene expression. However, there has been no clear evidence in support of these or any other mechanisms of spontaneous NB regression [4].

CONCLUSION

By better understanding the mechanisms underlying the phenomena that occur in low-risk

disease, potential new paradigms for therapy may be developed to improve the cure rate for high-risk neuroblastoma [5].

Conflicts of Interest : The authors declare no conflicts of interest.

Authors Contribution: Tous les auteurs ont également contribuée à ce travail et ont lu et approuvé la version finale du manuscrit.

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