MEDWIN PUBLISHERS
Committed to create value for Researchers

Open Access Journal of Cancer & Oncology

Neuroblastoma above 5 Years Old

Baddouh N*, Elbaz M and Elhoudzi J

Department of Pediatric Hematology and Oncology, Mohammed VI University Hospital, Faculty of medecine, Cadi Ayyad University, Morocco

Clinical Note

Volume 2 Issue 3

Received Date: May 19, 2018

Published Date: May 28, 2018

***Corresponding author:** Naima Baddouh, Department of Pediatric Hematology and Oncology, Mohammed VI University Hospital, Marrakesh, Morocco, Tel: 212672050984; Email: naima_102@hotmail.com

Abstract

Neuroblastoma (NB) occurs rarely among 5 years old, and information is scarce on its characteristics and clinical course in this age group.

Objective: to investigate the clinical features and outcomes of neuroblastoma (NB) children aged between 5 and 10 years, and to provide a theoretical basis for improving prognosis.

Methods: a retrospective analysis was performed for the clinical data of 8 previously untreated NB children, and their clinical features and outcome were analyzed.

Results: we collected 8 cases, representing 12.1 % of all patients diagnosed with neuroblastoma in our center. The average age was 7.1 years (between 5 and 10 years). A male predominance was noted: five of the patients. The adrenal location was the most common: 4 of the cases. The average admission time was 1.8 months with extremes between 15 days and 3 months. Clinically five patients were admitted with a poor status and abdominal pain. In 5 of the cases an abdominal mass was found. There was a predominance of advanced stages, 7 patients had metastases at diagnosis. Bone metastases were the most frequent, followed by bone marrow and in 6 patients multiple sites were affected. MIBG was positive in 5/8 patients (62%); Ferritinemia and LDH were elevated in 7 cases, and catecholamine in 5 cases. In the histological study one case corresponded to poorly differentiated and one to differentiated NB. Moreover, 6 tumors were considered undifferentiated. According to the INSS classification our patients were classified all stage IV except one stage III. NMYC was not done in our patients. Partial primary resection of the tumor was possible in one patient. In all other metastatic cases, chemotherapy was initiated according to HR-NBL-MA-10 regimen. Fifty courses of induction have been completed in all except one who was died in the first cure. Four of seven patients undergoing chemotherapy required the palliative treatment for progression of the mass and / or metastases, without the possibility of a surgical cure. The death rate in our series was 50%. One patient died during the first course of vasovagal syncope probably under etoposide, and 3 of the patients under palliative treatment were died with a life expectancy of 2 years on average after diagnosis. The other patients are still under treatment.

Conclusion: At the age between 5 and 10 years, the neuroblastoma is associated with a poor prognosis in our series. High dose chemotherapy does not seem to be useful in these patients, hence the need for new therapeutic approaches in this age group.

Keywords: Children; Neuroblastoma; 5 years old

Introduction

Neuroblastoma (NB) is a childhood malignancy arising from the embryonic sympathetic nervous system. It accounts for 8–10% of all pediatric cancers, but is responsible for 15% of cancer-related deaths in children. Mean age at diagnosis is 2 years, and 47% of cases are diagnosed before 1 year of Age. Its incidence declines sharply within the first 3-5 years of life, until it becomes very rare after 5 years. Less than 5% of cases occur in patients older than 10 years of age at diagnosis [1,2]. Age at diagnosis is an important risk factor, children older than 18 months having a worse prognosis [3,4]. Some studies have treated NB in adolescent, whereas NB in the age between 5 and 10 years is often ignored in these studies. The aim of this study is to investigate the clinical features and outcomes of neuroblastoma (NB) children aged between 5 and 10 years, and to provide a theoretical basis for improving prognosis.

Methodology

We reviewed all NB cases aged between 5 and 10 years of age at diagnosis registered in the department of pediatric oncology from 2013 to 2017. Staging included studies of the primary tumor by thoracic, abdominal and pelvic CT scan; 2 bone marrow aspirates and biopsies; MIBG scan; and mTc-99 if MIBG was negative or unavailable. Disease extension was classified according to INSS criteria in all patients. Samples of fresh tumor were referred to anatopathological department.

Data concerning demographics, disease characteristics, treatment received and outcome were retrieved from patient's records. We included in the study only the complete patient files that contain all data on the clinical, biology and evolution of patients, so we excluded incomplete data and lost to follow-up.

Descriptive statistics were reported as absolute frequencies and percentages for qualitative data.

Results

We collected 8 cases, representing 12.1% of 70 patients diagnosed with neuroblastoma in our center during this period.

The characteristics of patients are summarizing in (Tables 1 & 2). The average age was 7.1 years (between 5 and 10 years). A male predominance was noted: 5 of the patients. The adrenal location was the most common: 50% (the right was the most affected), followed by pelvic: two cases and abdominal non-adrenal two cases. The average admission time was 1.8 months with extremes between 15 days and 3 months, with the particularity of a patient who was treated as Acute rheumatic fever for bone pain 9 months before diagnosis and another who was operated on for appendix 3 months before.

Clinically five patients were admitted with poor status and abdominal pain. Five cases of abdominal mass were found, in addition to five cases of adenopathies of significant size especially of cervical localization and five cases of bone pain. A fever was reported in 3 cases. One case of Hutchinson syndrome was noted.

There was a predominance of advanced stages, 7 patients had metastases at diagnosis. Bone metastases were the most frequent, followed by bone marrow and 6 patients had multiple sites of metastasis.

MIBG was positive in 5/8 of patients (62%). Anemia was found in three cases. Ferritinemia and LDH were elevated in 7 cases, and catecholamines in 5 cases.

Pathology studies showed one case of poor differentiation, one c as with differentiated NB, and 6 tumors were considered undifferentiated. According to the INSS classification our patients were classified stage IV except one stage was stage III. NMYC was not done in our patients because it is not available yet.

Partial primary resection of the tumor was possible in one patient and was followed by chemotherapy. In all

other metastatic cases, chemotherapy was initiated according to HR-NBL-MA-10 regimen witch associated cisplatin, etoposide, vincristin, cyclophosphamide, doxorubicin, ifosfamide and carboplatin. No patient had a contraindication to chemotherapy. Five courses of induction have been completed in all except one who was died at the beginning of first course. Four of seven patients undergoing chemotherapy required the palliative treatment for progression of the mass and / or metastasis in the control report after the end of the courses, without the possibility of a surgical treatment. No patient was treated with radiation.

The death rate in our series was 50%. One patient died during the first course of vasovagal syncope probably, and 3 patients under palliative treatment were died with a life expectancy of 2 years on average after diagnosis. Only one patient, alive, is still under metronomic protocol.

Number of case	Age st Diagnosis	Sex	Location	Metastasis	Stage
1	5	F	SR (L)	LN	IV
2	5	F	SR(R)		III
3	10	M	Pelvic	BM, B, hepatic	IV
4	6	M	Abd n A	BM, B	IV
5	6.5	F	Pelvic	LN, B, Orbit, Lung	IV
6	10	M	SR(R)	BM, B	IV
7	10	M	SR (R)	BM, B, Pleura	IV
8	5	M	Abd n A + thoracic	BM, B, LN, Lung	IV

Table 1: Clinical characteristics and stage of patients.
Abdn A, abdominal non-adrenal; SR, adrenal; L: left; R: right ; B, bone; BM, bone marrow; LN, lymphnodes;

Number of case	HP	LDH	Ferritin	Outcome	Follow-up time (months)
1	uNB	Increased	Increased	On treat	4
2	dNB	normal	normal	On treat	6
3	uNB	Increased	Increased	On treat	11
4	uNB	Increased	Increased	AWD	19
5	uNB	Increased	Increased	DOD	15
6	uNB	Increased	Increased	DOD	31
7	uNB	Increased	Increased	DOD	32
8	pdNB	Increased	Increased	DOD	25

Table 2: Pathological, biological characteristics and outcome of the patients.
HP: histopathological; uNB: undifferentiated NB; pdNB: Poorly differentiated; dNB: Differentiated NB; DOD: Died of disease; AWD: Alive with disease.

Discussion

Less than 5% of cases of neuroblastoma occur in patients older than 10 years of age at diagnosis [3,5]. In addition to tumor extension, age at diagnosis is a very well known prognostic factor for NB. In fact, infants (ages 0–11 mos) fare remarkably better than older patients at any stage [6].

However, because of the rarity of these tumors among 5 years old, little information is available on the characteristics and clinical course of patients with NB in this age group. We collected 8 cases of neuroblastoma diagnosed between 5 and 10 years old, representing 12.1% of 66 patients diagnosed with neuroblastoma in our center during 5 years.

An age threshes old that predicts more indolent disease in older patients has not been defined. Most studies, although rare, have studied neuroblastoma in children over 10 years of age. Few have tried to isolate an age group of 5 to 10 years in large series including different age groups. To our knowledge, the current series represents the second cohort of children aged from 5 to 10 years with NB described to date. [7].

Compared to the only study done in 54 children aged 5 to 10 years, our clinical data match those reported by the Chinese team; boys are twice affected than girls. All patients were class III and IV of the INSS classification. Also the retroperitoneal localization is the most predominant.

Biologically, all our patients' classified stage IV had high levels of LDH and ferritinemia. The rate was normal at the girl with stage III. They were considered high risk criteria in our patients. These two settings are reported correlated with a poor prognosis in the literature too. They can be used as a prognostic factor defining so high risk groups [8].

We note the particularity of the atypical revelation of the disease in two of our patients. One patient was treated, 9 months before admission, by corticosteroids for suspicion of acute rheumatic fever. The other one was operated, 3 months before admission, for suspicion of appendicitis.

We, therefore, draw the attention of clinicians to the need to evoke neuroblastoma among the diagnostic eventualities on the occasion of abdominal pain or bone pain in children.

The death rate in our series was 50%; a close ratio of 44% was reported in the Chinese series [7]. This reflects the aggressiveness of the tumor in this age group compared to other age groups especially those aged less than 18 months where the tumor is of good prognosis in general [8]. When compared with adolescents, the authors of a large Italian series including 1116 children and 53 adolescents were able to identify a group of patients with a cut-off age between 6 years and 10 years that had more indolent course but a worse prognosis: a significantly worse overall survival rate and a slower decrease in the 5-year survival was documented in this age group [9].

A report from the international neuroblastoma risk group in 2014 had concluded that despite indolent disease and infrequent MYCN amplification, older children (5 to 15 years old) with advanced disease have poor survival, without evidence for a specific age cut-off [10]. The genetic study was not done for our patients.

Seven of our patients were treated according to the HR-NBL-MA -10 regimen that combines high dose chemotherapy. Despite that 4 of them had showed persistence or progression of the tumor and / or metastasis after the end of the induction chemotherapy. Therefore, there was no possibility for surgery or radiotherapy in these cases. Authors suggest that antilogous hematopoietic cell transplantation (AHCT) may provide a survival benefit in older children with metastatic response to induction chemotherapy. L'AHCT is not available in our training. After Current standard treatments, maintenance treatment with 13-cis-retinoic and immunotherapy are also used. In spite of this intensive multimodal therapy, outcome for patients with high-risk neuroblastoma is still very poor with a 5-year OS <50% [11].

Conclusion

At the age between 5 and 10 years, the neuroblastoma in our patients is revealed at the stage of metastases in the majority of the cases, with an unfavorable histological type and a high lethality. High LDH and ferreting levels are associated with a poor prognosis in our series. High dose chemotherapy does not seem to be useful in these patients. In the last decade, several new therapies and combinations have been tested, mostly with quite disappointing results. Deeper understanding of tumor biology and new therapies is urgently needed.

Conflicts of Interest

The authors have declared no competing interest.

Funding

Auto financing by the authors

Acknowledgements

The authors acknowledge all the members of the department of Pediatric Hematology and Oncology, Mohammed VI University Hospital of Marrakesh, where teamwork and expertise together benefit our patient, and the parents of the patients for their cooperation.

References

1. Spix C, Pastore G, Sankila R, Stiller CA, Steliarova-Foucher E (2006) Neuroblastoma incidence and survival in European children (1978-1997): report from the automated childhood cancer information system project. Eur J Cancer 42(13): 2081-2091.

2. Maris JM (2010) Recent advances in neuroblastoma. N Engl J Med 362(23): 2202-2211.

3. Brodeur GM, Maris JM (2002) Neuroblastoma. In: Pizzo PA, Poplack DG (Eds.), Principles and practice of paediatric oncology. 4th (Edn.), JB Lippincott, Philadelphia, pp: 895-938.

4. London WB, Castleberry RP, Matthay KK, Look AT, Seeger RC, et al. (2005) Evidence for an age cut-off greater than 365 days for neuroblastoma risk group stratification in the Children's Oncology Group. J Clin Oncol 23(27): 6459-6465.

5. Victoria Castel, Eva Villamón, Adela Cañete, Samuel Navarro, Amparo Ruiz, et al. (2010) Carmen Neuroblastoma in adolescents: genetic and clinical characterisation. Clin Transl Oncol 12(1): 49-54.

6. Valteau-Couanet D, Michon J, Boneu A, Rodary C, Perel Y, et al. (2005) Result of induction chemotherapy in children older than 1 year with a Stage 4 neuroblastoma treated with the NB 97 French Society of Pediatric Oncology (SFOP) protocol. J Clin Oncol 23(3): 532-540.

7. Zhang Y, Zhang WL, Huang DS, Han T, Zhi T, Li J et al. (2016) Clinical features and outcomes of neuroblastoma patients aged above 5 years. Zhongguo Dang Dai Er Ke Za Zhi 18(12): 1217-1221.

8. Pérel Y, Valteau-Couanet D, Michon J, Lavrand F, Coze C, et al. (2004) Prognosis of neuroblastoma in childhood. Methods of assessment and clinical use. Archives de pédiatrie 11: 834-842.

9. Conte M, Parodi S, De Bernardi B, Milanaccio C, Mazzocco K, et al. (2006) Neuroblastoma in Adolescents: the Italian Experience. Cancer 106(6): 1409-1417.

10. Mossé YP, Deyell RJ, Berthold F, Nagakawara A, Ambros PF, et al. (2014) Neuroblastoma in Older Children, Adolescents and Young Adults: A Report From the International Neuroblastoma Risk Group Project. Pediatr Blood Cancer 61(4): 627-635.

11. Berlanga P, Cañete A, Castel V (2017) Advances in emerging drugs for the treatment of neuroblastoma. Expert Opin Emerg Drugs 22(1): 63-75.