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Original Article

Low-stage pediatric neuroblastoma: A 20-year single institution review

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ABSTRACT

Background: Neuroblastoma is a common childhood cancer with poor prognosis. This is a retrospective review of the outcomes in children with low-stage neuroblastoma in Taiwan.
Methods: We reviewed the charts of all children with International Neuroblastoma Staging System (INSS) stages 1 and 2 diagnosed at the Mackay Memorial Hospital between November 1994–December 2013. The patients' demographic data, age of diagnosis, treatment, and survival rates were analyzed.
Results: A total of 75 children with all stages of neuroblastoma were identified, of which 23 children in the low stage were enrolled. There were 12 (16.0%) patients in stage 1, and 11 (14.6%) patients in stage 2. The mean age of diagnosis for stage 1 and stage 2 was 5.4 months and 10.2 months, respectively. A total of 18 (78.3%) patients received initial complete surgical excision, and 5 patients received initial biopsy. The site of the tumor was the adrenal gland in 19 (82.6%) patients. Total or near-total resection was possible in 18 (78.3%) patients; all children with stage 1 were treated by complete surgical resection. Seven patients (63.6%) in stage 2 received chemotherapy. Children in both stages 1 and 2 had the same 5-year overall survival of 100%. The event-free survival rate for patients in stage 1 and stage 2 was 91.7% and 81.8%, respectively.
Conclusion: This retrospective study confirmed that children with stage 1 and 2 neuroblastoma had good outcomes. Specifically, children with stage 1 disease are best treated by surgery alone, but selected patients in stage 2 need additional chemotherapy.

1. Introduction

Neuroblastoma is the third most common cancer in children under one year of age. In fact, it is the most common extracranial solid tumor in childhood,[1] and most commonly found in the retroperitoneal cavity. The incidence of neuroblastoma is about 10 cases per million in children under 15 years of age.[2,3] It accounts for 10–15% of all pediatric cancer fatalities[4]; the overall 5-year survival rate is poor, at less than 50%.[5] However, patients with low-stage disease typically have excellent outcomes.[6] The purpose of this study was to evaluate the clinical characteristics and treatment outcomes of children with stages 1 and 2 neuroblastoma from a single institution in Taiwan.

2. Methods

This was a retrospective study involving all children who were diagnosed with stage 1 and 2 neuroblastoma between November 1994 and December 2013 at the Mackay Memorial Hospital in Taipei, Taiwan. After being approved by the Institutional Review Board, medical records of the children were analyzed. The demographic data, age of diagnosis, surgery, treatment, radiological and laboratory data, and survival outcomes were recorded. Diagnosis was made from biopsy specimens from the primary or metastatic site, or bone marrow biopsy. The location of the primary tumor was based on computed tomography (CT) findings and/or confirmed in surgery. The diagnosis and staging assessments were made according to the International Neuroblastoma Staging System

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(INSS). Patients were treated according to their assigned risk group (low, intermediate and high risk) and according to the protocols of the Taiwan Pediatric Oncology Group (TPOG). Written informed consent was obtained from all patients prior to chemotherapy.

3. Statistical analysis

Event-free survival (EFS) was measured from the date of diagnosis to the date of progression or relapse, or patient death. Overall survival (OS) was calculated from the date of diagnosis until the date of death, or the date of last follow-up. The final outcomes were overall survival (OS) and event-free survival (EFS). Analysis of 5-year OS and EFS were performed using the Kaplan-Meier method and the log-rank test of significance.

4. Results

A total of 75 children with all stages of neuroblastoma were identified, of which 23 children in the low stage were enrolled. There were 12 (16.0%) patients in stage 1, and 11 (14.6%) patients in stage 2. The demographic data was summarized in Table 1. The median follow-up was 13.6 years (range 2.5–19.6 years). There were 8 (34.8%) patients who were under 1 year of age. A total of 18 (78.3%) patients received initial surgical excision, and 5 patients received initial biopsy.

4.1. Stage 1

There were 12 (16.0%) patients in stage 1, with a mean age of diagnosis of 5.4 months (range 0–26.3 months). All children with stage 1 were treated by surgery alone, and total excision was possible in all patients. There was 1 patient who suffered a relapse at 6.1 month of age. However, the patient received salvage chemotherapy and thereafter had long-term disease-free survival.

4.2. Stage 2

There were 11 (14.6%) patients in stage 2, with a median age of diagnosis of 10.2 months (range 0.3–21.1 months). Five patients received initial open surgical biopsy, followed by chemotherapy. Six patients received up-front total or near-total excision, followed by adjuvant chemotherapy, which included carboplatin, etoposide, cyclophosphamide, and doxorubicin. One patient had MYCN amplification, and 2 patients had unfavorable Shimada histology. Seven patients (63.6%) in stage 2 received chemotherapy. There were 2 relapses, at 7.6, and 13.2 months after diagnosis, respectively. The first patient was an 11.7-month-old boy, who had stroma-poor, undifferentiated histology with high mitosis-karyorrhexis index (MKI). The second patient was a 19.1-month-old boy, who had a similar histology, and amplified MYCN oncogene.

Table 1
Clinical characteristics of all patients with stage 1 and stage 2 neuroblastoma (n = 23).

Variable	Stage 1	Stage 2
Age at diagnosis, (months)		
Mean	5.4	10.2
Range	0–26.3	0.3–21.1
≤1 year, n (%)	5 (41.7%)	3 (27.3%)
>1 year, n (%)	7 (58.3%)	8 (72.7%)
Sex, n (%)		
Male	5 (41.7%)	6 (54.5%)
Female	7 (58.3%)	5 (45.5%)
INSS stage, n (%)	12 (15.4%)	11 (14.1%)
Primary tumor site, n (%)		
Adrenal	11 (91.7%)	8 (72.7%)
Extra-adrenal	1 (8.3%)	3 (27.3%)
Surgery, n (%)		
Initial biopsy only	0 (0%)	5 (45.5%)
Initial excision	12 (100%)	2 (18.2%)
Total		
Near total	0 (0%)	4 (36.4%)
Chemotherapy	0 (0%)	7 (63.6%)

5. Survival analysis

All children with stages 1 and 2 were alive at 5 years. The 5-year OS and EFS for stage 1 were 100% and 91.7%, respectively. The 5-year OS and EFS for stage 2 were 100% and 81.8%, respectively (Fig. 1). Both groups of patients older and younger than one year of age had OS of 100%. The 5-year EFS for patients under and over 1 year of age were 95.7% and 91.3%, respectively. (Fig. 2). Results using the log-rank test were not significant.

6. Discussion

This is a 20-year retrospective review which provided information on clinical and outcome analysis in Taiwanese children with low-stage neuroblastoma. All children with stages 1 and 2 disease had good prognosis and were all alive at the 5- year follow-up. All

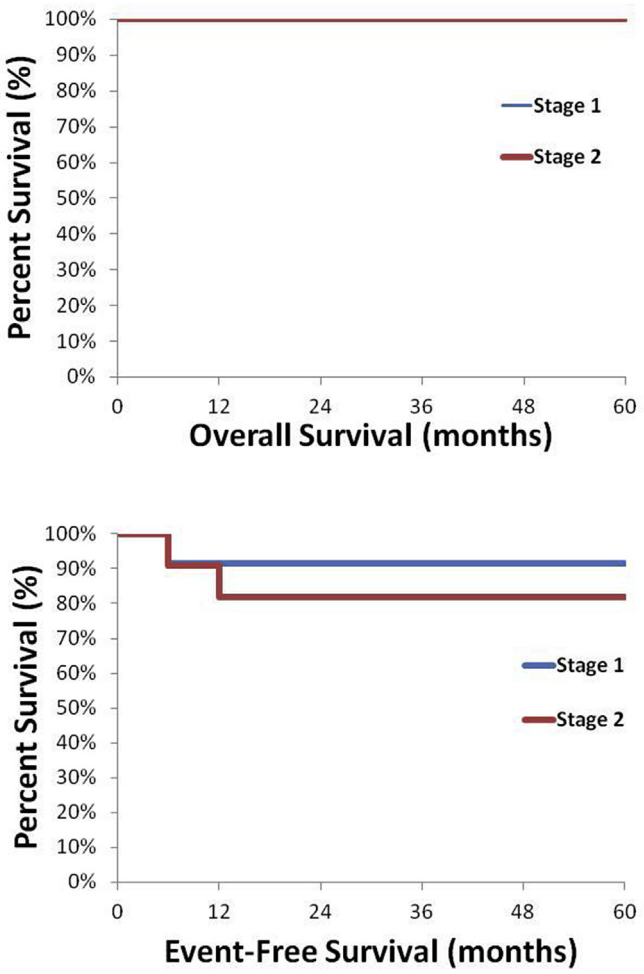

Fig. 1. Survival outcome in patients with stage 1 and stage 2 neuroblastoma (n = 23). Upper graph: overall survival. Lower graph: event-free survival.

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