A FIVE YEAR REVIEW OF CHILDREN WITH NEUROBLASTOMA AT
Dr. SARJITO HOSPITAL, YOGYAKARTA, INDONESIA: 1999-2004

Mulataih S', Sutaryo', Ali K', Purwanto1
1Division of Hematology-Oncology, Department of Pediatric, Sarjito Hospital/Faculty of Medicine, Gadjah Mada University, Indonesia;
2Saskatchewan Cancer Agency and University of Saskatchewan, Canada

ABSTRACT

Background: The prevalence and outcome of childhood cancers in developing countries is not well documented. In 2001, the Yogyakarta Pediatric Cancer Registry (YPCR) was developed in collaboration with the Saskatchewan Cancer Registry in Canada. Its purpose was to collect and analyze demographic, treatment and outcome data in children newly diagnosed with cancer at Dr. Sarjito General Hospital, Indonesia.

Objective: The objectives of this study were to analyze clinic profiles and treatment responses in children under 15 years of age diagnosed with neuroblastoma in 1 January 2001 – 31 December 2004.

Materials and Method: A retrospective review of health records was conducted. Information on all patients diagnosed with cancer from 1998 onwards was transcribed into a standardized data capture form, and then entered into the computerized YPCR data base for review and analysis.

Result: A total of 27 children with neuroblastoma were identified within the 5 year study period. Twenty two patients (81.5%) had stage IV disease, 4 (14.8%) had stage III, and 1 (5.7%) stage I. Male to female ratio was 1.5:1. Mean age at diagnosis was 3.1 years. Nineteen patients (70%) were treated on the OPEC protocol, 3 (11%) per the NIH protocol, and 1 (4%) on the N54E protocol; 4 (15%) were not treated. Of the OPEC treated group, 15 (55%) patients are surviving, 6 (18%) relapsed and 3 (42%) were lost to follow up.

Conclusion: In keeping with published reports, the majority of children with neuroblastoma presented with advanced stage disease. The 3-Years free survival was 20% for patients treated on the OPEC protocol. More effective treatment protocols and improved surveillance of children following discharge from hospital are challenges that need to be addressed.

Keywords: Neuroblastoma-Sarjito Hospital-outcome

INTRODUCTION

Neuroblastoma is the most common extra cranial solid tumor in children, accounting for approximately 6-10% of all childhood malignancies in European registries.1

There is evidence for an increase in the incidence of neuroblastoma in the past decades, possibly due to better health care, screening programmes and the increasing availability of ultrasound devices for paediatricians.2

However, the prevalence and outcome of childhood cancers in developing countries is not well documented. In 2001 the Yogyakarta Pediatrics Cancer Registry (YPCR) was developed in collaboration with the Saskatchewan Cancer Registry in Canada. Its purpose was to collect and analyze demographic, treatment and outcome data in children newly diagnosed with cancer at Dr. Sarjito Hospital, Yogyakarta, Indonesia.

The objectives of this study were to analyze clinical profiles and treatment response in children under 15 years of age diagnosed with neuroblastoma in 1 January-31 December 2004.

MATERIALS AND METHODS

A retrospective review of health records was conducted. Information on all patients diagnosed with cancer from 1998 on wards was transcribed onto a computerized data capture form and then entered into the computerized YPCR database for review and analysis. Medical records reviews were conducted for 27 patients aged 0-15 years at diagnosis who presented with neuroblastoma in Pediatric Institution, Dr. Sarjito Hospital,

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Yogyakarta, Indonesia during the period 2000-2004. Most patients received their original diagnosis at that hospital.

RESULTS
During 2000-2004 periods, 486 newly diagnosed malignant neoplasms were registered among children from 0-15 years of age new cases. The percentage of new cases according to tumor types is presented in Figure 1. As it follows from that: the most common types is leukemia, accounted over 50%. However, it can be seen that neuroblastomas are counted for 7%. In addition, 25% of others patients were included renal tumor, other intracranial tumor (such as medulloblastoma, ependimoma), teratoma, rhabdomyosarcoma etc.

Figure 1. Total Pediatric Cancer Patients; 2000-2004 (N=486)

From 27 neuroblastoma patients, accounted for 62% with stage IV, for 7% with stage II and III, while stage I disease just for 4%. Metastasis of these patients at diagnosis were observed in bone marrow, lymph node, in the pleura, and intracranial (Figure 2).

Figure 2. Neuroblastoma Patients By Stage; 2000-2004 (N=27)

Chemotherapy treatment included OPEC protocol for 19 of 27 patients (70%), N8 protocol for 3 of 27 patients (11%), NB4E protocol for 1 of 27 patients (4%). While for 4 of 27 patients (15%) were no treatment (Figure 3). Most of our patients come from poor family, and usually they asked went to the alternative treatment.

Figure 3. Treatment Protocols for Neuroblastoma: 2000-2004 (n=27)

The regimen OPEC protocol contains the combination of 1.5-mg/m2 vincristine, 600 mg/m2 Cyclophosphamide, 50 mg/m2 cytarabine, and 150- mg/m2 etoposide. These drugs were given for 8 cycles with interval 3-4 week in between.
Nineteen of 27 patients with OPEC protocol were analyzed for the outcome of that treatment. It can be seen that for 15 of 27 patients (52%) still survive, even they just got partial remission, and developed relapse. For 2 of 27 patients (7%) were died either during the treatment period or after it was done. The most important data was for 12 of 27 patients (41%) were lost of followed up. The most of our patients come from remote area, with far distance from the hospital, and low in come, and have no good communication (no telephone), so it was very difficult to follow them (Figure 4).

Figure 4. Status of Neuroblastoma Patients After Got Therapy Opec Protocol
Survival analysis was carried out on 27 cases of neuroblastoma diagnosed in children aged 0-15 years in 2000-2004. Survival rates were presented by the regimen of treatment. Figure 5 shows that the 3-year survival rate was achieved for 20% in OPEC protocol. Our study demonstrated that there was low in survival rates Indonesia, especially in our hospital from 2000-2004.

DISCUSSION

The annual rate for childhood cancers in developed countries amounts to 105-130 new cases per 1 million children. Thus, in region inhabited by 50-75 thousand children, 5 to 10 new cases can be expected to occur every year. Our study found 466 new childhood cancers during five years (2000-2004), than every year the average were 100 new cases. Leukemias, mainly of acute lymphoblastic type, and most frequent form in Poland. There were accounted for about 42% of all childhood cancers. Malignant lymphomas, bone tumor, and germinal tumors are more frequently diagnosed in Poland, but the incidence of central nervous system tumor is lower than in other countries. Similarly, in this study found 51% new leukemia cases with mostly acute lymphoblastic leukemia type.

Neuroblastoma is an embryonal malignancy of the sympathetic nervous system that is derived from primordial neural crest cells and occurs almost exclusively in infants and young children. The other research mentioned that neuroblastoma is a rare cancer and its reported incidence varies by country. High incidence rates have been observed in the Nordic countries and in the countries Western Europe and Shorten Europe. If no increase in other childhood cancers occurs in the coming generations, then rates for childhood cancer may soon be significantly lower than those in US white children. Rates are low for all lymphomas, largely because of very low rates of Hodgkin's disease. Rates are also low for neuroblastoma. The rate for all Alaska Native children is also lower for neuroblastoma compared with US white (1% vs. 5%). Our study demonstrated higher than both Alaska Natives and US white, whereas neuroblastoma accounted for 7% of 486 new childhood cancer cases in 2000 to 2004. In 1998, SENSE (the study group the evaluation of neuroblastoma screening in Europe) investigated differences between neuroblastoma in Germany, France, UK and Australia over the time period of 1987-1991. The incidence was lower in the UK compared with the other countries; age at diagnosis was significantly higher as was the proportion of metastatic disease (stage IV). In addition, the incidence of metastatic disease in the UK was significantly higher compared with the other countries; while the incidence of stage I – III and IVs was significantly lower (especially in the first year of life. The SENSE paper makes it seem likely that high overall incidence is correlated with a lower age at diagnosis and lower incidence and fraction of metastatic cases (no stage data are available for EUROGARE). Relatable population-based data on the survival of children with neuroblastoma is available only for few countries, where a large enough population is covered by a childhood cancer registry or a general cancer registry (such as England and Wales, Germany, USA SEER), respectively. Note that 5-year survival rate, usually chosen to assess cancer treatment in adults, may not be the optimal indicator for treatment success in children, whose life expectancy would normally be far longer. Our Hospital-based study demonstrated that 3-year survival was 20%. The data was not stratified by the age, because there were a few patients. Sips et al, present the data collected for the UROCARE II.
study, describing survival patterns for children diagnosed in Europe 1985-1989 in detail, and exploring time trend from 1978 to 1992. On average, the mean 5-year survival rate was considerably higher in infant (79%) compared with older children (30-33%). There is pronounced difference between countries, with Scotland and England and Wales having two of the lowest survival rates (28% and 36% 5-year survival rates, respectively). The survival rates in France, Germany and Italy (48-66% 5-year survival) were among the highest. Age greater than 1 year is highlighted as an unfavorable prognostic factor, particularly in disseminated disease where the outcome remains poor despite the intensification of treatment regimens and even the use of bone marrow transplantation highest. There were no report concerning the lost of follow patients in other countries, even in Europe, UK and Asia. Our study reported for 42% patients lost from our followed up. Thus, we did not report the high mortality, because they just accounted for 5%.

CONCLUSION

Neuroblastoma is one of the most common solid cancers in children. In keeping with published, the majority of children (> 1year) with neuroblastoma present metastatic disease at diagnosis with poor outcome, despite intensive treatment protocols. The 3-years survival was 20% for patients treated on the OPEC protocol. More effective treatment protocols and improving surveillance of children following discharge from hospital are challenges that need to be addressed. An international comparison of population-based mortality would be a more valid basis for decision than comparison of survival.

REFERENCES