

ORIGINAL ARTICLE

Neuroblastoma in Sudan: experience of a single institute

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ABSTRACT

Neuroblastoma (NBL) is the most common malignant solid extracranial tumour in children. It accounts for about 8%–10% of overall childhood malignancies in developed countries and only 1%–3% in developing countries. We aim to study the clinical presentation and outcome of NBL in children treated at the National Cancer Institute (NCI), University of Gezira, Wad Madani, Sudan. This is a retrospective, descriptive, hospital-based study, where patients' records were reviewed from the years 2004–2015. During this period, 38 paediatric patients were treated in the Paediatric Oncology Unit at the NCI, accounting for about 4% of the overall childhood malignancies. Of them, 24 (63%) were males and 14 (37%) were females with a ratio of 1.7: 1. The age at presentation ranged between 2 months and 7 years with a mean age at the presentation of 3 years. Twenty-nine (76%) of them were classified as high-risk disease, no one received high-dose chemotherapy, 33(87%) died and only 5 (13%) achieved complete remission. This study reflects the poor outcome of NBL among

Sudanese children which can be explained by the late presentation of the patients, lack of the diagnostic modalities and lack of the sophisticated treatment modalities for high-risk NBL.

KEYWORDS

Neuroblastoma; Child, Outcome; Sudan.

INTRODUCTION

Neuroblastoma (NBL) is the most common malignant solid extracranial tumour in children. It accounts for about 8%–10% of overall childhood malignancies in developed countries [1]. However, it accounts for only 1%–3% in developing countries, but the true incidence is unknown [2,3]. It affects children younger than 10 years of age. About 50% of affected children are younger than 2 years. The disease is more prevalent in males than females with a ratio of 1.2:1. About 70% of patients have an abdominal primary [4]. The prognosis of NBL depends on the age of the patient, staging and N-myc oncogen amplification [5,6]. The children older than 1 year of age with stage 4 NBL constitute the majority of the high-risk category. The 5-year

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survival rate of NBL is very disappointing as it is only 50% in spite of chemotherapy intensification, stem cell transplantation and using advanced surgical procedures [7,8]. The main aim is to study the clinical presentation and outcome of NBL among Sudanese children treated at the National Cancer Institute (NCI), University of Gezira, Wad Madani, Sudan.

MATERIALS AND METHODS

This was a retrospective, facility-based study, in which the data were obtained from the records of all paediatric patients attending the NCI during the period from 2004 to 2015. A total number of patients seen during the study period were 964 patients aged between 0 and 15 years. Thirty-eight (4%) of them were the cases of NBL, who attended the Paediatric Oncology Unit at the NCI in the period from 2004 to 2015.

Patients

The diagnosis of NBL was based on the histopathological examination of tissue biopsies from the primary tumour with the interpretation of the clinical and radiological findings. The staging and risk stratification of the disease were based on the International Neuroblastoma Pathology Classification and the International Neuroblastoma Staging System according to the size and location of the primary tumours by ultrasonography and X-ray computed tomography in addition to presence or absence of distant metastasis. The patients were treated according to their assigned stage and risk group (low, intermediate and high risk) by modified Children's Oncology Group-based protocols. The patients were treated by chemotherapy, surgery and/or radiotherapy. The chemotherapy regimen consisted of vincristine, cyclophosphamide, carboplatin/cisplatin and etoposide. None of the patients had received high-dose chemotherapy in this study. Complete remission was defined as the absence of disease after the completion of treatment and during the follow-up period.

Statistical analysis

All the data were entered into the computer and analysed using the Microsoft Excel program.

RESULTS

During the period from 2004 to 2015, 38 (4%) children out of 964 with childhood malignancies were diagnosed and treated as the cases of NBL at the NCI, University of Gezira, Wad Madani, Sudan. Twenty-four (63%) of them were males and 14 (37%) were females, with a male to female ratio of 1.7: 1. The age at presentation ranged between 2 months and 7 years with a median age at the presentation of 3 years. Eight (21%) of them were less than 2 years, 5 (13%) were less than 1 year and 25 (66%) were more than 2 years of age. Half of the patients (19, 50%) were from Gezira State, 2 (5%) from White Nile State, 8 (22%) from Gadaref State, 4 (11%) from Sinnar State, 2 (5%) from Kordofan and 3 (9%) from Damazin.

The diagnosis was made by trucut biopsy in 25 (66%) of the cases, cytology plus radiological interpretation in 8 (22%) and by excisional biopsy in 4 (11%). All patients had a high level of Lactate dehydrogenase (LDH) more than three figures. Clinical staging showed no child with stages I and II. In stage III, there were 18 (47%) patients, whereas, in stage IV, 20 (52%) patients. The most common sites of involvement were the abdomen in 29 (76%), chest in 7 (18%) and neck in 2 (4%).

There was no histopathological description of the biopsy according to Shimada classification. Twenty-nine (76%) of them were classified as high risk and 9 (24%) as intermediate risk; 29 (76%) received chemotherapy, 4 (11%) received the combination of chemoradiation and 5 (13%) did not receive any treatment as they died before starting treatment. Thirty-three (87%) died, and only 5 (13%) achieved complete remission. The most common cause of death was sepsis in 23 (70%), and 10 (30%) patients died at home without obvious causes.

DISCUSSION

This is a descriptive, retrospective, hospital-based study, conducted at the NCI, University of Gezira, Wad Madani, Sudan. In this study, NBL cases accounted for 4% of the overall childhood malignancy in NCI. This result is less than the international data [1] but approximating results from low- and middle-income countries, where

the incidence ranged from 1% to 3% [2,3]. In NBL, disease staging, N-MYC amplification, DNA ploidy and histopathological classification were the most important factors that affect the outcome and prognosis [9,10]. In this study, 76% of cases were classified as high-risk neuroblastoma (HR-NB) using the modified criteria for risk stratification, which depend mainly on the age of the patients, LDH level and presence of metastasis that is responsible for the poor prognosis even with the uses of aggressive treatment [11]. The best outcome for high risk (HR)-Neuroblastoma (NB) was achieved by high-dose chemotherapy and surgery, followed by myeloablative therapy and hematopoietic stem cell transplantation and cis-RA as a differentiating agent [12]. Unfortunately, the last two are not available in Sudan. All patients in this study had high LDH levels, which goes with international results which proved that an increased level of LDH is a strong prognostic indicator of poor outcome and is associated with unfavourable histopathology [13,14]. The median age of presentation was 3 years, which is one of the poor prognostic features, and it does not fit with the international data [15] and studies from Saudi Arabia [16] but approximated results from Egypt, which was 2.8 years [4,17]. The gender of the patients does not affect the outcome in this study. Males were more affected than females, which goes with the international data. The majority of the patients were from Gezira State, where the NCI is located. The majority were also diagnosed by trucut biopsy, which reflected that the tumour was not accessible to primary surgical reduction. Half of the cases were stage IV (52%) which reflects the late presentation of the patients to the oncology centres, either due to the lack of health facilities or because of seeking treatment earlier with traditional healers. About one-third (30%) of patients died at home without obvious cause, which means a lack of adherence to treatment and follow-up.

CONCLUSIONS

These results showed that NBL cases accounted for 4% among overall childhood malignancies in Sudan with a very poor outcome. This is mainly due to the late presentation of the patients, limited diagnostic modalities, lack of knowledge of the caregivers and the majority of primary healthcare

providers about childhood malignancy, lack of trained personnel in the field of paediatric oncology and lack of some chemotherapeutic agents, as some of them are not available in Sudan. Furthermore, there are no facilities for high chemotherapy doses and stem cell transplantation.

RECOMMENDATIONS

1. Raise awareness of the public and medical personnel about childhood malignancy.
2. Avail chances of training in the field of paediatric oncology.
3. Strengthening of collaboration with international hospitals, institutes and the NCI
4. Working in multidisciplinary teams including paediatric oncologist, paediatric surgeons, radiation oncologists, histopathologists, radiologist and oncology nurses to improve the outcomes.
5. Involvement of the stakeholders to avail training, diagnostic modalities and drugs which are very expensive, i.e., the Ministry of Health, health insurance and community members.

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CONFLICT OF INTEREST

There is no conflict of interest

ETHICAL APPROVAL

Ethical approval was cleared from the Ethics Committee of the National Cancer Institute, University of Gezira, Sudan. Informed consent for participation and publication was obtained

from the guardian of the patients. Confidentiality was maintained at all levels.

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