IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 19, Issue 8 Ser.12 (August. 2020), PP 41-43
www.iosrjournals.org

Neuroblastoma in India – The underdog

[1.] Dr Puligundla Krishna Chaitanya, [2.] Dr Vishal Toka,
[3.] Dr Radhika Parimkayala
[1,2,3]*Assistant Professor*

Introduction
Neuroblastoma is the most common extracranial solid tumor in childhood. It is considered to have one of the least favourable outcomes among paediatric cancers.
Aims
To assess the outcome of childhood neuroblastoma in a tertiary care centre over the period of 12 years. Number of studies on neuroblastoma with outcome data from India is very limited.
Methods
The study was retrospective analysis of neuroblastoma casesfrom during the period of 2008 to 2019. International neuroblastoma risk group staging system was usedfor Staging and risk stratification. Graphpad prism softwareversion 8.0 was used for the survival analysis.
Results
The study included 107 patientsof neuroblastoma with male and female ratio of 1.14:1.The median age of presentation was 4 years,with 19.6% (21/107) percentage of cases were age less than 12 months.83% (89/107) percentage of the cases had abdominal mass at presentation and 17%(18/107) percentage were extra abdominal.Low risk was observed in 23% (22/96),intermediaterisk in 27% (26/96) and high risk in 50% (48/96) of patients. Risk stratification could not be done in 10% (11/107) patients due to incomplete data. The median overall survivalwas not reached in low risk,22.1 months inintermediate risk and 14.1 months in high risk patients with a median follow up of 11.6 months.
Conclusion
The outcome of the high risk neuroblastoma in India is dismal.The factors contributing to a poor outcome of high-risk neuroblastoma in India include late diagnosis,poornutrition,higher treatment related mortality,limited availability of transplant and treatment abandonment.

Date of Submission: 10-08-2020 Date of Acceptance: 24-08-2020

I. Introduction

Neuroblastoma is the most common extracranial solid tumor in childhood in developed countries accounting for 10% of paediatric cancers[1].Neuroblastoma is the commonest cancer in infancy. Upto 90% of patients are less than five years of age at diagnosis and almost all are less than 10 years of age[1], with male to female ratio of 1.2 :1 in western countries [1,2]. Neuroblastomacan originate from anywhere along the sympathetic chain with presentation of masseither in the neck,mediastinum,abdomenor pelvis . Two-thirds of primary tumorsoccur in the abdomen [1,2]. Abdominal tumors are more frequent in older children compared to infants where thorasicand cervical tumors are common[1]. Metastatic disease is frequent in older children compared to infants[1]. Metastasis can occur to regional lymph nodes,bonemarrow,corticalbone,liver and skin.Paraneoplastic syndromes such as opsoclonus myoclonus ataxia syndrome and watery diarrhoea are seen[1,2].It is considered to have one of the least favourable outcomes among paediatric cancers.The cure rate of the high-risk neuroblastoma in the developed countriesis approximately 40%[1,2]and it is dismal in India. Factors contributing to a poor outcome of high-risk neuroblastoma in India include late diagnosis, poor nutrition with the resultant higher treatment related mortality, limited availability of autologous transplant and treatment abandonment.

II. Methods

This is a retrospective analysis of neuroblastoma casesdone by retrieving case records from 2008 to 2019 in a tertiary care centre.All the patients who were diagnosed with neuroblastomaincluded in the study and analysed.Demographic data and clinical presentation were recorded. Biopsy and IHC was used for the diagnosis of neuroblastoma. Contrast-enhanced CT scanning/ FDG-PET CTscan,bone scan and bone marrowwereused for the staging purpose.Risk stratification was done by using age,stage,histopathology, NMYC analysis. International risk group staging system was used to stage and risk stratify the disease.Treatment was

administered based on risk stratification.Chemotherapy regimens commonly used were CADO and OPEC.Survival analysis was done by using graphpad prism software version 8.0.

III. Results

Our study population comprised hundred and seven (107) neuroblastoma patients of which 53.2% (57/107) percentage were males and 46.8%(50/107) were females with ratio of 1.14:1. The median age of presentation was 4 years.19.6% (21/107) of cases were age less than 12 months.83% (89/107) of the cases had abdominal mass at presentation and 17%(18/107)were extra abdominal. 14.5% (14/96), 27%(26/96) and 58.3%(56/96) had L1,L2,metastatic stage respectively based on international risk group staging system.Low risk was observed in 23%(22/96),intermediate risk in 27%(26/96) and high riskin 50%(48/96) of patients. Risk stratification could not be done in 10% (11/107) patients due to incomplete data.Surgery was done in 19.6% (21/107)of cases. 13%(14/107) of patients had received radiation. Autologous stem cell transplant was done in 3.7%(4/107) of cases.The median overall survivalwas not reached in low risk, 22.1 months in intermediate risk and 14.1 months in high risk patients with a median follow up of 11.6 months.

IV. Discussion

In contrast to the number of patients with neuroblastoma the number of studies with outcome data from India is very limited.Median age of presentation in our study was 4 years similar to most studies.19.6%(21/107) of cases were age less than 12 months and it was 26%in AIIMS study[3]. Male to female ratio was1.14 :1 in our study compared to 1.2:1 in western data[1,2] and 2.8 :1 in PGIMER data[4].Commonest presentation was mass per abdomen in 83% percentage of cases compared to 78% in AIIMS study[3]. 14.5%(14/107) , 27%(26/107) and 58.3% (56/96) had L1 , L2, metastatic stage respectively in our study, whereas stage 3 and 4 disease noted in 75% cases in otherseries [5,6,7,8]. Low risk, intermediate and high risk was noted in 23%, 27% and 50% percentage of patients respectively compared to 8%, 24% and 68% inVenkatraman Radhakrishnan etal. study[10]. Median overall survival for low risk intermediate and high risk wasnot reached, 22.1 months and 14.1 months with 11.6 months of median follow up. Whereas 3 year overall survival of 100%,77% and 34% respectively in Venkatraman Radhakrishnan etal study[9]. In AIIMS study overall survival was 70% for those under 12 months of age and 72% for stage 3 patients and 36% for stage 4 papatients[3] .In PGI Chandigarh study, out of 103 children only 4 children were disease free for a period of 16.5 +/ – 6.7 months[4].In the Bangalore Cancer registry, Nadakumaret al., reported a 28 % and 23 % ,5 and 10 y overall survival (OS) respectively in 22 patients with neuroblastoma[10] .From the Chennai registry, 64 patients with neuroblastoma and ganglioneuroblastoma had a 5 and 10 y overall survival (OS) of 36.9 % and 26.9 % respectively[11].

Financial support and sponsorship
Nil

Conflicts of interest
There are no conflicts of interest.

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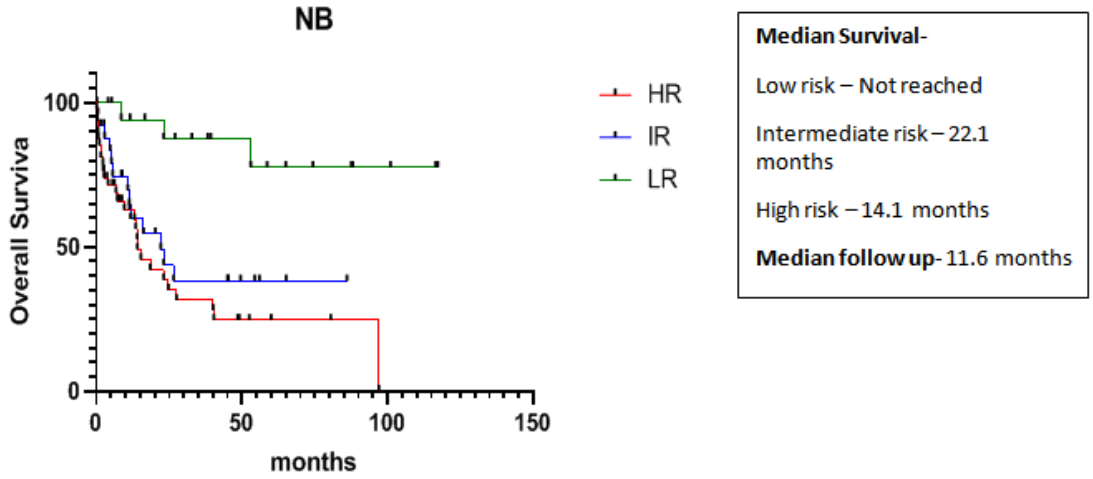
Supplementary Table:1 Demographic and clinical features

Parameter	n (%)
Total number of cases	107(100)
Male 57(53.2)	
Female	50(46.7)
Stage at presentation	96(100)
L1 stage	14(14.5)
L2 stage	26(27)
Metastasis	56(58.5)
Risk stratification	96(100)
Low risk	22 (23)
Intermediate risk	26 (27)
High risk	48 (50)

Table 2: Comparison with other studies from India

Study (Institute)	Mandelia et al. AIIMS	Bansal et al. PGIMER	Radhakrishnan V et al	Present study
Number	144	103	85	107
Stage III and IV	87.5% (126/144)	98% (101/103)	NA	NA
Risk Low Intermediate High	NA	NA	8% (7/85) 24% (20/85) 68% (58/85)	14.5% (14/96) 27% (26/96) 58.5% (56/96)
EFS	NA	NA	3 y EFS LR – 100% IR – 54% HR – 18.9%	NA
OS	Stage 3 - 72% Stage 4 – 36%	In CR – 8%	3 y OS LR – 100% IR – 77% HR – 34%	Median OS – Median f/u (11.6 mo) LR – Not reached IR – 22.1 mo HR – 14.1 mo

Figure 1: Kaplan-Meier estimates of overall survival



. Dr Puligundla Krishna Chaitanya, et. al. "Neuroblastoma in India – The underdog." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(8), 2020, pp. 41-43.