NEUROBLASTOMA: OUTCOME OVER A 14 YEAR PERIOD FROM AIIMS NB 96 PROTOCOL

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Neuroblastoma: Introduction

- Neuroblastoma - most frequent extracranial childhood tumor
- Various clinical presentations and diverse prognosis of subsets
- Chance of cure in children older than 1 year with metastatic disease remains poor
Neuroblatoma : Introduction

- Limited reports on the outcome of children with neuroblastoma from India
- Few studies have documented survival by reporting large series of patients diagnosed over a long period

Bansal D et al. Indian Pediatrics 2008; 45: 135-139
AIIMS – NB 96 : Aim

• To evaluate the outcome of children with neuroblastoma treated at AIIMS with AIIMS NB 96 protocol
Prospective study:
- Follow up till Dec 2010

Inclusion
- All NB patients registered in solid tumour clinic

Diagnosis
- Pathological diagnosis of biopsy samples
- Bone marrow aspirate / trephine biopsy positive + increased urinary VMA/HVA

MIBG scan
AIIMS – NB 96 : Patients and Methods

• **Staging**
  – The International Neuroblastoma Staging System (INSS) was used for staging

• **Treatment**
  – based on stage and presentation
  – children with stage 1 and 2 received 3 weekly courses of cyclophosphamide and doxorubicin
  – Stage 3 and 4 patients received cyclophosphamide, doxorubicin, etoposide and cisplatin
Neuroblastoma: Response to therapy
Treatment

- RT to the primary site given to all stage 3 and 4 abdominal and pelvic tumors
- Surgical resection attempted only when radiological findings suggested resectability (either upfront or following 4-6 courses of chemotherapy)
- $^{131}$I MIBG therapy given for metastatic non-responsive neuroblastoma (4 cases)
- Myeloablative therapy with autologous BMT
• **Patient categorization**
  - Two age groups defined: < 12 months and > 12 months
  - Primary site groups: abdominal and extra-abdominal
  - Final outcome: CR / PR / NR / PD

• **Statistical Analysis**
  - 3-year OS calculated using Kaplan Meier survival curves
  - log rank test of significance (\(P\)-values below 0.05 were considered statistically significant)
AIIMS – NB 96 : Patients and Methods

Pre chemo

Post chemo
AIIMS – NB 96 : Results

- Total no. of patients: 144
- Median age at diagnosis: 36 months
- Age range: 1-132 months
AIIMS – NB 96: Age at diagnosis

Age of patients (n = 144)

>12 months: 106 (73.6%)

<12 months: 38 (26.4%)
Sex distribution of patients:

- Female: 41 (28.5%)
- Male: 103 (71.5%)
AIIMS – NB 96: Site distribution

% distribution of patients

- Abdominal: 112 (77.8%)
- Extra-abdominal: 32 (22.2%)
Chart Title

- Adrenal: 56.3%
- Extra-Adrenal: 16.3%
- Pelvic: 4.9%
- Thoraco-Abd: 15.9%
- Cervical/thoracic: 2.1%
- Occult: 6.9%

Primary tumor site
AIIMS – NB 96: Stage distribution

87.5% Stage III & IV

% distribution of patients

Stage of Disease

1  2  3  4  4s

0  20  40  60  80  100

2.1  2.1  40.3  47.2  8.3
AIIMS – NB 96: n = 144

% distribution of patients

- **Excision**: 83 (57.6%)
- **Biopsy only**: 4 (2.8%)
- **Not operated**: 57 (39.6%)

Total patients (n=144)
AIIMS – NB 96 : Outcome

n = 144

Operated
87 (60.4%)

Excision
83 (57.6%)

CR
47 (32.6%)

PR
20 (13.9%)

PD/NR
16 (11.1%)

Biopsy only
4 (2.8%)

CR
14 (9.7%)

Not operated
57 (39.6%)

PR
24 (16.7%)

PD/NR
19 (13.2%)

PD/NR
4 (2.8%)
n = 144

Alive
- 100 (69.4%)
  - CR 60 (41.7%)
  - PR 33 (22.9%)
  - PD/NR 7 (4.9%)

Dead
- 44 (30.6%)
  - CR 1 (0.7%)
  - PR 11 (7.6%)
  - PD/NR 32 (22.2%)
AIIMS – NB 96 : Overall survival

- 3- Yr OS: 60.7% [95CI: 50.4-69.5]
- 41.7 % achieved CR
- 22.9 % achieved PR

3-year OS for the whole cohort
Kaplan-Meier survival estimates

- <12 months: 69.7% [95CI 51.8-82.0]
- ≥12 months: 55.3% [95CI 42.2-66.6]

P = 0.73
**AIIMS – NB 96 : 3-yr OS by tumor site**

Kaplan-Meier survival estimates

- **Extra-abdominal**: 82.6% [95CI; 62.6-92.3]
- **Abdominal**: 54.9% [95CI; 42.9-65.3]

P = 0.07
Kaplan-Meier survival estimates

Stage 1+2: 100%

Stage 4s: 83.3% [95CI; 48.2-95.6]

Stage 3: 71.5% [95CI; 55.3-82.7]

Stage 4: 35.7% [95CI; 19.3-52.4]

$P = 0.001$
AIIMS – NB 96 : OS & CR by stage

% distribution of patients

Stage of Disease

- Stage 1
- Stage 2
- Stage 3
- Stage 4
- Stage 4s

3-Yr OS
CR (%)

- Stage 1
- Stage 2
- Stage 3
- Stage 4
- Stage 4s
AIIMS – NB 96 : Conclusions

- Significant proportion of our patients present in advanced stages (87.5 %)
- All of children with stage 1&2 achieved CR and were alive
- 57% of stage 3 could achieve CR and had an OS of 71.5%
- OS (35.7%) and CR (17.6%) for stage 4 was significantly less (p=0.001)
<table>
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<tr>
<th>Author</th>
<th>Year</th>
<th>Group</th>
<th>n</th>
<th>OS (%)</th>
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<tr>
<td>Bernstein et al.</td>
<td>1992</td>
<td>North America</td>
<td>295</td>
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<td>Kusumakumary et al.</td>
<td>1998</td>
<td>Trivandrum, India</td>
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<td>Sze Mag et al.</td>
<td>1999</td>
<td>Malaysia</td>
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<td>Cotterill et al.</td>
<td>2000</td>
<td>ENSG</td>
<td>1277</td>
<td>45</td>
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<td>Spix et al.</td>
<td>2001</td>
<td>EUROCARE II</td>
<td>1094</td>
<td>51</td>
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<td>Bansal et al.</td>
<td>2008</td>
<td>PGI, India</td>
<td>103</td>
<td>8.7 (CR)</td>
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<td>Juárez-Ocaña et al.</td>
<td>2009</td>
<td>Mexico</td>
<td>68</td>
<td>64</td>
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<td>Schroeder et al.</td>
<td>2009</td>
<td>Denmark</td>
<td>160</td>
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<td>Haupt et al.</td>
<td>2010</td>
<td>Italy</td>
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<td><strong>Present</strong></td>
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