International Journal of Contemporary Pediatrics
Kumar RA et al. Int J Contemp Pediatr. 2016 Nov;3(4):1469-1471
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291
DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20163703

Case Report

Response to 13 cis retinoic acid in metatstatic neuroblastoma

R. Arun Kumar[1], S. Lakshmi Narasimhan[1], J. Muthukumaran[2]

[1]Department of Medical Oncology, Institute of Obstetrics and Gynaecology, Egmore, Madras Medical College, Tamil Nadu, India
[2]Department of Paediatric Surgery, Institute of Child Health, Madras Medical College, Egmore, Chennai, Tamil Nadu, India

Received: 21 August 2016
Revised: 28 September 2016
Accepted: 04 October 2016

***Correspondence:**
Dr. Lakshminarasimhan Srinivasan,
E-mail: drnarasimhan@rediffmail.com

ABSTRACT

Neuroblastoma is the most common extra cranial solid tumour of childhood, with 5 year survival rate of 40%-50% in high risk group. Surgery, chemotherapy, radiotherapy, high dose chemotherapy with stem cell transplant and retinoid therapy are treatment options for neuroblastoma. Here we present a 5 year female child presenting with abdominal pain for 1 month and abdominal distension for 3 weeks, and underwent biopsy after necessary investigations, and diagnosed to have high risk neuroblastoma and treated with multiple lines of chemotherapy and attained complete response after retinoid therapy. The case is presented because of complete response achieved with retinoid therapy with tolerable side effects.

Keywords: Complete response, Neuroblastoma, Retinoid therapy

INTRODUCTION

For high-risk patients, the treatment has been intensified to include chemotherapy, surgery, radiation therapy, hematopoietic stem cell transplantation, differentiation therapy and immunotherapy, so that the survival rates of 40% to 50% could be achieved.[1,2]

Neuroblastoma arises from primordial neural crest cells. Asymptomatic abdominal mass is the most common presentation. Surgery, Radiation therapy, chemotherapy, HSCT are various treatment options for neuroblastoma. The differentiation agents are commonly used after HSCT.

CASE REPORT

A 12 year old female child, known case of metastatic neuroblastoma, diagnosed at the age of 5 years, after repeated lines of chemotherapy, now with complete response is presented. At the age of 5 years, the child was brought with complaints of abdominal pain for 1 month, abdominal distension for 3 weeks, low grade fever 3 weeks and history of loss of appetite and loss of weight. On clinical examination the child had 6× 8cm ill-defined mass in right hypochondrium, firm in consistency, tender and not bimanually palpable. Ultrasound abdomen showed a large lobulated hypoechoeic mass of 10.6×7 cm in the retroperitoneal region above right kidney in the region of right adrenal gland and crosses midline. The left kidney was in left iliac fossa, the infra hepatic portion of IVC appears to be encased. CT scan abdomen confirmed the ultrasound findings. The Child underwent laparotomy and biopsy as it was inoperable. HPE showed poorly differentiated neuroblastoma.

Patient received 16 cycles of PCV regimen (once in 21 days) from April 2009 to April 2010 after discussion in tumour board (cisplatin D1-D3 (19mg/19mg/19mg), cyclophosphamide D1-D3 (190mg/190mg/190mg) and

(vincristine 0.8mg). Patient was on regular follow up till March 2013. During follow-up period there was no residual disease in abdomen clinically and as per ultrasound. In March 2013 child presented with left side neck nodes and abdominal pain. Ultrasound revealed a mass in retroperitoneal area (2.7×2.1×4.3 cm) in aortocaval region. Neck node FNAC was positive for metastasis. The Patient was started on doxorubicin D1, D2 (20mg/10mg) and etoposide D1, D2 (90 mg/90 mg) from March 13, 2013. The patient received three cycles.

Ultrasound in May 2013 showed 2×1 cm mass in paraaortic region. Neck nodes were clinically persisting. Hence after discussion in tumour board, the patient was started on ICE chemotherapy. (ifosfamide 1g d1-d3; mesna 200mg 0, 4, 8 hrs d1-d3; carboplatin 150mg d1-d2 and etoposide 80mg D1-D3). After 2nd cycle ultrasound abdomen showed no mass and neck nodes disappeared completely. After the 3rd cycle, the child was anaemic and treated with packed cells transfusion. PET CT was done in August 2013 after the 3rd cycle.

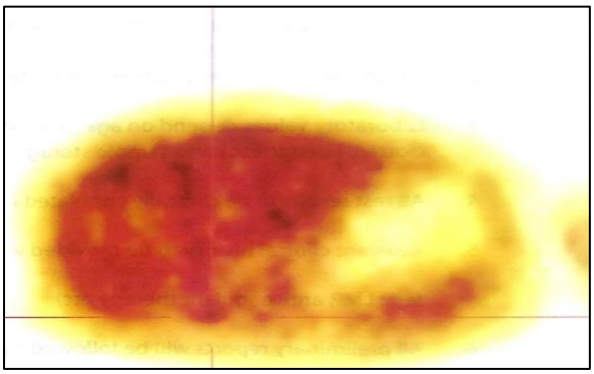

Figure 1: PET image of soft tissue thickening in the retrocrural region.

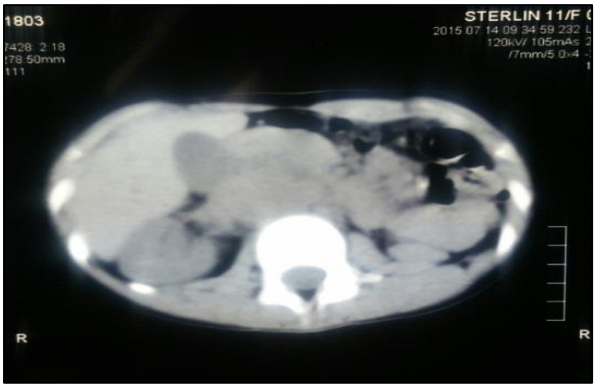

Figure 2: CT scan of pre and paravertebral mass.

It showed metabolically active disease in right retrocrural region. Hence patient was continued on ICE chemotherapy. During 4th cycle patient had thrombocytopenia and got corrected. The Patient completed 6th cycle in November 2013. In December 2013 ultrasound showed 1.7×1.7cm residual mass in Right adrenal region. No paraaortic nodes identified. Patient was started on oral cyclophosphamide 50 mg D1-D7 once in a month from December 2013 and 6 cycles were completed till April 2014 during which patient was asymptomatic and ultrasound was normal. Patient was disease free till July 2015, after which patient had abdominal pain and CT abdomen showed 10×6×4 cm mass in the prevertebral and paravertebral region encasing IVC.

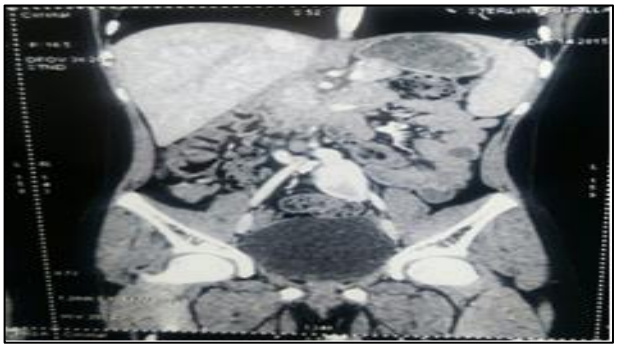

Figure 3: CT scan of pre vertebral mass.

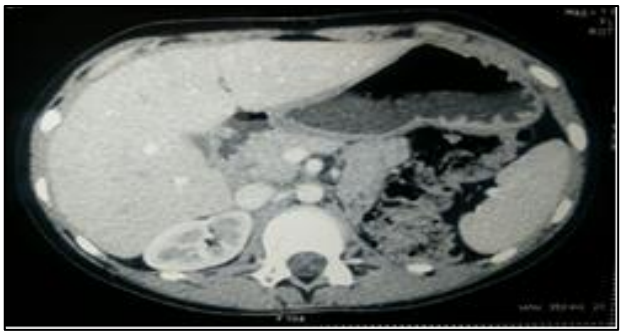

Figure 4: CT scan of retroperitoneal node encasing inferior vena cava (before retinoid therapy).

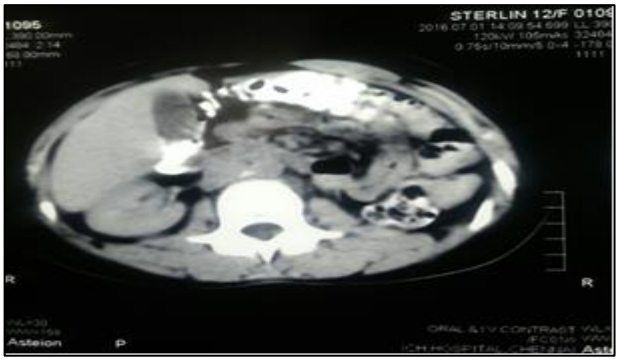

Figure 5: CT scan of no residual disease (after retinoid therapy).

Patient was rechallenged with (cisplatin d1-d3 (20 mg/20 mg/10 mg) cyclophosphamide (300 mg/300 mg) and vincristine d1 (1 mg) from July 2015. During 4th cycle ultrasound showed 0.7 cm residual mass, patient completed 6 cycles in November 2015. Evaluation by CT abdomen in December 2015 showed 5×1.3 cm mass in retroperitoneal region encasing IVC.

The case was again discussed in tumour board and started on 13-cis-retinoic acid (4 mg/kg/day) for 14 days once in a month. Patient received 6 cycles from December 2015 to June 2016. Patient was evaluated with CT abdomen in July 2016 which showed no residual mass. Clinically patient was asymptomatic and clinical examination is normal.

DISCUSSION

Neuroblastoma patients were divided in to a low-risk, intermediate-risk or high-risk group based on the following according to COG risk system:

- International neuroblastoma staging system (INSS) stage
- Age
- International neuroblastoma pathologic classification (INPC)
- DNA ploidy
- NMYC oncogene amplification within tumor tissue.

The International neuroblastoma risk group (INRG) system was based on whether the tumor is low, intermediate, or high risk to decide the treatment.

The approach is either observation or resection for INRG L1 or COG low-risk tumors. Five-year overall survival (OS) was 97% in a large COG study.

Chemotherapy is often given before definitive resection, for INRG L2 or COG intermediate-risk tumors. It depends on clinical and tumor biological risk factors and response to therapy. The 3-year OS rate for intermediate-risk patients was about 96% in a large COG study.

Differentiation therapy with 13.cis retinoic acid is used to treat minimal residual disease following HSCT.[3] After treating with myeloablative chemotherapy and stem cell rescue, patients were treated with the differentiating agent oral isotretinoin for 6 months. Immunotherapy is also tried along with differentiated therapy in the post-HSCT differentiation therapy regimen. Chimeric anti-GD2 antibody ch14 combined with GM-CSF and IL-2 are given with isotretinoin and have been shown to improve EFS in high risk patients following HSCT remission.[4,5] In our case we used the differentiating agent 13-cis retinoic acid in metastatic setting after various lines of chemotherapy and achieved complete response. The neuroblastoma cell lines can be induced to terminally differentiate on exposure to retinoid compounds.[6]

Neuroblastoma is the third most common malignancy in paediatric age group after leukemia and brain tumours.[7] Most tumours are diagnosed before 5 years. It is more common among boys slightly. Neuroblastoma is reported less frequently in India.[8]

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Kumar RA, NarasimhanSL, Muthukumaran J. Response to 13 cis retinoic acid in metatstatic neuroblastoma. Int J Contemp Pediatr 2016;3:1469-71.