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An Uncommon Presentation of Neuroblastoma

Manish Kumar, Krutarth Thakar, Aditya Joshipura, Mukul Trivedi, SJ Pandya
From the Department of Surgical Oncology, Gujarat Cancer and Research Institute, B.J. Medical College, Ahmedabad, India.

Abstract:

Neuroblastoma (NB) is the most common extra-cranial solid malignancy in children but rarely described in adults, being 10% of all cases diagnosed after the first decade of life. Currently, there are no standard treatment guidelines for adult NB patients. We report the case of 26 year old man who presented with a retroperitoneal neuroblastoma. Treatment included chemotherapy and radiotherapy. The patient remains asymptomatic 1 year after completion of chemotherapy.

Key words: Neuroblastoma, Neoplasms, Retroperitoneal Space, Nervous system neoplasms.

Introduction

Neuroblastoma is an uncommon malignancy in adult life as compared to childhood. In literature, few cases have been reported and management protocol for adult cases is still evolving. Neuroblastoma is the most common extra-cranial solid tumor in childhood that originates from the neural crest representing 7.7% of all pediatric cancers, with an incidence of 2.26 cases per million/year [1]. The mean age of diagnosis is 2 years, with 36% of patients diagnosed before age 1 year, 75% before 5 years and over 90 % for 10 years. The condition is very rare among adolescents and young adults. Less than 10% of all cases are diagnosed after the age of 10 years. We report a 26 year-old man with retroperitoneal neuroblastoma who presented with symptoms of abdominal distension.

Case Report

In November 2010, a previously healthy 26 year old man presented with abdominal distension and generalized body-ache of 1 month duration. Physical examination revealed an abdominal mass. There were no comorbidities including hypertension. Computed Tomography (CT) showed 17x12x13 cm mass in the retro-peritoneum from the level of the diaphragm to the upper border of the sacrum. Mass was encasing the aorta and inferior vena cavae. There were multiple paraaortic, retrocrural and mediastinal nodes. Guided needle biopsy of the lesion revealed adult neuroblastoma upon histopathological examination. Histologically, the tumor consisted of small and round-shaped pseudorosette forming cells with hyperchromatic nuclei. Immunohistochemistry showed cytoplasmic

Corresponding Author: Dr. Manish Kumar
Email: manish_surg@yahoo.com
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positivity for neuronal specific enolase (NSE), chromogranin A and synaptophysin. A bone scan showed extensive skeletal metastasis. Bone marrow biopsy was positive for metastasis. The serum levels of catecholamine metabolites, including dopamine, were in the normal range.

The patient was diagnosed as having stage IV neurolastoma. Combination Chemotherapy was started with OPEC (Vincristine, Cisplatin, Etoposide and Cyclophoshamide) regimen according to the pediatric protocol. A follow-up CT scan after 6 cycles showed 13/9 cm residual mass in the retroperitoneum encasing the major vessels and with metastatic adenopathy. The patient was then given palliative external beam radiotherapy 35 Gray (Gy) with 1.8 Gy per day, 5 days per week. A repeat CT scan showed 10.5/ 15 cm residual lesion in the retroperitoneum encasing major vessels with right pleural based lung metastasis. The patient was subsequently given ICE (Ifosfamide, Carboplatin and Etoposide) regimen.

The last CT scan done after completion of 6 cycles of ICE showed residual disease with minimal decrease in size and no further advancement of disease. The patient was labeled as having stable disease and was put on observation. The patient is on regular follow-up and is symptom free till date.

Discussion

Neuroblastoma (NB) refers to a malignancy derived from primitive neural crest cells arising in the sympathetic nervous system. Neuroblastomas are the most common extracranial solid malignancy of childhood [1]. Up until September 2007, no more than 60 neuroblastomas in adults had been reported in the literature. Neuroblastoma shows an incidence of 2.26 cases per million inhabitants/ year; 60% of the cases are diagnosed within the first 2 years of age, and 75% within the first 5 years of age. Case reports of this neoplasm over 18 years of age are rare, and this disease shows no preference for gender [2].

A large percentage of neuroblastomas undergo spontaneous regression, and this could possibly account for the scarcity of its presence among the adult population [3]. The clinical features of neuroblastoma in adults are similar in children. Symptoms associated with the diagnosis are usually unrelated to any catecholamine imbalance. However, on rare occasions, compression of the renal artery may lead to hypertension as a presenting manifestation. The most common symptoms are a hard, asymptomatic mass in the abdomen, or bone pain resulting from metastatic spread. The exception is that the bone marrow involvement occurs less frequently in adults, and there is a higher frequency of metastases at unusual sites such as lung or brain [4].

The most common site of neuroblastomas in children is the adrenal medulla. While in adults, considering the last 30 reported cases (>18 years) [5], extra adrenal sites are more common like retroperitoneum (30%) followed by adrenal, pelvis and mediastinum, other rare sites include head and neck, mesentery, thoracic spine, epidural space and extremities. There has been a single case report of ovarian metastasis (unilateral) with primary in the adrenals [6].

Although neuroblastoma is among the curable tumors in young children, it is associated with a worse prognosis in adults, with a 5-year median survival rate after diagnosis <40% [7]. There is no consensus regarding the treatment of neuroblastoma in adults. It seems that, in some studies, the treatment is similar to the protocol in children. Treatment options include surgical resection, chemotherapy or radiotherapy [8]. There are limitations in the longitudinal studies focusing on adult's neuroblastoma treatment due to the rare reports of this neoplasm in adults.

Our 26 year old patient showed an inadequate response to chemotherapy treatment. This is in line with previously reported adult or adolescent patients with neuroblastoma, for whom the ultimate outcome is generally poor, regardless of the initial disease stage [9]. The prognosis of neuroblastoma strongly depends on the age at diagnosis, with significantly better survival rates for younger children [10]. Thus, the treatment of neuroblastoma not only depends on the disease stage, but also on the patient's age. More aggressive or innovative therapeutic approaches are needed for older patients. Ablative chemotherapy followed by autologous stem cell transplantation leads to prolonged survival in advanced stage diseases [11]. Tandem transplants show some promise with progression-free survival rates of over 50% at up to seven years. However, for children older than 18 months with disseminated disease, the survival rates remain low at approximately 30%. Therefore, new tumor-specific strategies are under investigation. Immunotherapy with antibodies targeted at GD2 (a disialoganglioside on the surface of neuroblastoma) produced promising preliminary results [12]. The radioisotope iodine-131-MIBG in conjunction with hematopoietic stem cell transplantation is effective in the treatment of advanced stage disease. Novel approaches like MYC-targeting therapies; radioisotope iodine-131-MIBG in conjunction with hematopoietic stem cell transplantation; knockdown of XAB2, a part of the co-receptor complex that inhibits differentiation induction by retinoic acid; allogeneic stem cell transplantation are recent modalities of treatment of advanced neuroblastoma.

As long as remission is not an accessible intent, a satisfactory aim may also be disease stabilization, avoiding more serious therapeutic side effects. The patient described here had a long disease course with few symptoms and retained a good life quality beside the disseminated malignant disease for now more than 20 months after the first diagnosis. To properly evaluate the efficacy and toxicity of new or more aggressive therapeutic strategies for adolescent and adult patients with neuroblastoma, a central collection of the data is necessary.

Conclusion

The diagnosis in adults presents a worse outcome than that in children. Currently, there are no standard treatment guidelines for patients with adult NB. In patients with metastatic disease and at late stages of disease, multimodal therapy should include surgical resection, radiotherapy, and outpatient chemotherapy.

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