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Adrenal Insufficiency: An Extremely Rare Complication Due To Bilateral Neuroblastoma

Bilateral Nöroblastom ve Adrenal Yetmezliği Olan Nadir Bir Vaka

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INTRODUCTION

Neuroblastoma originating from neural crest cells is the most common extracranial solid tumor in childhood. Primary tumor is most commonly seen in the adrenal medulla, but the neck, posterior mediastinum, paraspinal sympathetic chain may also be the origin of the tumor (1). Incidence of neuroblastoma is approximately 8-10% among childhood cancers. It is most commonly diagnosed between 0-4 years of age (2). It has shown a wide clinical presentation from spontaneous regression to rapid progression. Age over 18 months, advanced disease stage, poor Shimada pathology, hypodiploidy and n-myc amplification are poor prognostic factors. Information about clinical features and outcomes of bilateral neuroblastoma is still insufficient. Adrenal insufficiency has almost never been reported in patients with neuroblastoma. We did not encounter this complication in neuroblastoma patients in English literature.

CASE

A seven- year- old male patient without previously known disease was admitted to Cukurova University Faculty of Medicine, Department of Pediatric Oncology. Patient was admitted to the external center with abdominal pain two months ago. The parents are distant relatives. There is no known family history of inherited disease or malignancy. USG reported solid mass lession in the right adrenal gland. Computed tomography showed 22x16 mm mass lesion in the left adrenal gland and 42x30 mm mass lesion on the right. Neuroblastoma was suspected. Bone marrow aspiration and biopsy showed no metastasis. Ki67 6-7% and synaptophysin were positive in right surrenal biopsy material. The neck and thorax were reported normal in PET. The patient was directed to us for further examimation and treatment. Initial VMA value was 13.2 mg/day (3.3- 6.6 mg/day). It was decided to undertake surgical resection after neo-adjuvant chemotherapy. Intermediate risk chemotherapy protocol including cisplatin, cyclophosphamide and etoposide and vincristine, ifosfamide,adriamycin and dacarbazine were given to patient alternately (Turkish Pediatric Oncology Group Protocol). The patient did not receive radiotherapy. Adrenal gland sparing surgery was performed by laparotomy, after six cycles of chemotherapy, total surrenalectomy on the right, tumor excision with preserving normal tissue

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on the left. Pathological examination revealed neuroblastoma with poor histology. Synaptophysin and neuroblastoma marker were positive in the right and left surrenal materials (Figure 1). Ki67 proliferation index was 30% on the right and 10% on the left. N-myc amplification was negative in the examined preparations. The VMA value measured was 2 mg/day (3.3-6.6 mg/day). Thorax-abdomen tomography and PET scan showed no recurrence or residual tumor; therefore, maintenance protocol was started.

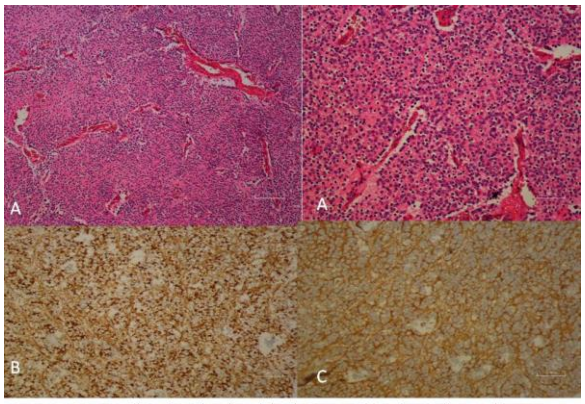

Figure 1. A: Tumor cells in the right adrenal gland B:Immunohistochemically neuroblastoma marker staining C: Immunohistochemically synaptophysin staining

However, the control abdominal USG and CT imaging of the patient at this time revealed a mass in the left adrenal gland region, which may be compatible with recurrence. USG reported as a well- circumscribed ovoid, hypoechoic lesion, 11.5x9 mm in size, in the longutidinal plane in the left surrenal region; CT reported a milimetrik nodular soft tissue lesion in the left adrenal gland region. Mass excision was performed by laparotomy. Pathologic examination revealed "no focus compatible with neuroblastoma. No calcification and histiocytic focus". However, postoperative adrenocorticotropic hormone was 1067 pg/mL (10- 50 pg/mL), cortisol was 5.1 µg/dL (6.7- 22.6 µg/dL). Fludrocortisone and hydrocortisone were initiated for the patient who was found to have developed surrenal insufficiency.

The patient who completed 13- cis retinoic acid treatment 5 months ago is currenltly followed up with control VMA values and imaging methods without medication.

DISCUSSION

Although unilateral neuroblastoma is more common, bilateral neuroblastoma is rarely seen. (10%) (2). Median age at diagnosis for bilateral neuroblastoma was found to be 2.75 months and most of the patients were infants (3). 45 cases were reported in the literature with a mean age of 3 months at diagnosis. One of these cases was diagnosed during intrauterine period. Only 7 cases were of age 1 and over and only 6 cases age 5 and over in the published literature (2). Our case is the first bilateral neuroblastoma case over 5 years among total 155 neuroblastoma cases in the last 8 years in our department. In situ bilateral adrenal neuroblastomas may occur in neonates and premature infants (1). The reason for its occurrence in our case in seven years (over 1 year) is not known. Bilateral adrenal tumor or multifocal primary familial neuroblastoma occurring in 20% of patients with neuroblastoma are usually diagnosed under 18 months (4,5). Systematic USG performed in the third trimester of pregnancy have been beneficial for the diagnosis. Some studies have reported cases diagnosed during the intrauterine period (6). Although most cases are followed as stage 4S, their clinical course is more complex. A significant proportion of cases reported with bilateral neuroblastoma die, due to metastases and/ or aggressive clinical course. Total colonic aganglionosis, VACTERL, microcephaly, Fanconi anemia have been reported in some patients (1,2). There was no myc- n amplification or a syndromic condition in our patient.

Bilateral neuroblastoma cases have a higher rate of metastases than unilateral cases. In a study, this rate was observed to be 88.5% (3). In the studies performed, although the rate of metastasis is high in bilateral neuroblastoma, patients have a highersurvival rate than unilateral neuroblastomas. It is more commonly associated with 4S stage disease and good prognostic factors were observed in bilateral neuroblastomas more than unilateral neuroblastomas (3). Our patient also is well and being followed- up in outpatient clinic.

Adrenal insufficiency is almost never seen in neuroblastoma cases. This complication seen in our case is very rare and there are no case reported before in English literature. In our case, although he was followed up without adrenal insufficiency after the surgery at the time of the diagnosis, adrenal insufficiency developed after the surgery with suspicion of recurrence one year later. In our literature search, we did not find a case report of adrenal insufficiency similar to our case. Adrenal insufficiency that developed in our case probably occured as a result of two surgeries.

In conclusion, staging, treatment and unclear prognosis of bilateral neuroblastoma separate it from unilateral neuroblastoma. Individual treatment and molecular studies for bilateral neuroblastoma are especially required. In addition, especially in bilateral neurobalstoma cases, it is necessary to avoid aggresive surgery as much as possible in order to prevent adrenal insufficiency.

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