

Case Report

Paratesticular Neuroblastoma Presenting as Bilateral Paratesticular Tumors

Makoto Morozumi^{1,2*}, Yoshihide Ogawa^{1,3}, Minoru Miyazato¹, Seichi Saito¹, Takeshi Higa⁴, and Nubuyuki Hyakuna⁴

¹Department of Urology, University of the Ryukyus, Japan

²Department of Urology, Saitama Medical University, Japan

³Department of Urology, Musashino Tokushukai Hospital, Japan

⁴Department of Pediatrics, University of the Ryukyus, Japan

*Corresponding author

Makoto Morozumi, Department of Urology, Saitama Medical Center, Saitama Medical University, 1981 Kamoda, Kawagoe, Saitama, 350-8550, Japan, Fax: 81-49-228-3671; Tel: 81-49-226-9944; Email: morozumi@saitama-med.ac.jp

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- Bilateral paratesticular neuroblastoma

Abstract

We describe a case of simultaneous bilateral paratesticular neuroblastoma presenting as spermatic cord tumors in a 6-month-old boy. He was diagnosed as having stage IV neuroblastoma originated from right adrenal gland with metastases to the paratesticular region, right femur, and right maxilla. The tumor showed favorable biological features according to Shimada's classification and had no N-myc gene amplification, but several unfavorable features were also present such as a diploid karyotype and TrkA mRNA null status. After intensive treatment including multi-drug chemotherapy and cytoreductive surgery, the patient obtained partial remission. At 3 years after diagnosis, he is alive without any progression.

INTRODUCTION

Neuroblastoma is the second most common solid malignant tumor in children and is considered to be an embryonal tumor of neural crest origin that can develop from the sympathetic nervous system in the neck, posterior mediastinum, adrenal medulla, paraspinal ganglia, or pelvis [1]. Therefore, the presentation of neuroblastoma is miscellaneous and depends on the local involvement of structures by the primary tumor as well as the effects of metastasis. This tumor is usually detected as an abdominal mass because the most common site of primary neuroblastoma is the abdomen, including the adrenal gland [1]. It also manifests as Horner's syndrome due to involvement of the stellate ganglion in the neck, "raccoon eyes" resulting from metastasis to the orbits, hepatomegaly with subcutaneous skin nodules characteristic of stage 4S, or generalized symptoms such as weight loss resulting from disseminated disease [1]. Presentation as an intrascrotal mass is uncommon because testicular or paratesticular involvement is rare, even though about 70% of patients have some form of metastasis at the time of diagnosis [2,3].

Here, we report the testis-sparing surgery for a simultaneous bilateral paratesticular involvement by disseminated neuroblastoma presenting as spermatic cord tumors.

CASE REPORT

A 6-month-old boy was referred to our hospital with a right

scrotal mass. His mother reported that he was healthy with a good appetite and that the mass had initially been detected by a local doctor three months before and had not changed in size. Physical examination revealed several firm par testicular nodules near the right spermatic cord and two nodules near the left spermatic cord. These masses were hypo-echoic on ultrasound (Figure 1a). The patient underwent exploration and biopsy after informed consent was obtained (Figure 1b). Intraoperative pathological examination revealed a tumor that was composed of small round cells without atypia. Therefore, we chose testis-sparing surgery and resected the masses as completely as possible from around the spermatic cord, which subsequently required vaso-vasostomy. The final pathological diagnosis was neuroblastoma,



Figure 1a Sonogram of the right scrotal region reveals a hypoechoic mass in the spermatic cord, which is distinct from epididymis and testis.



Figure 1b Arrow indicates the largest of the right paratesticular tumors. T and E indicate the right testis and the right epididymis, respectively. The tumor was separate from both of these structures.

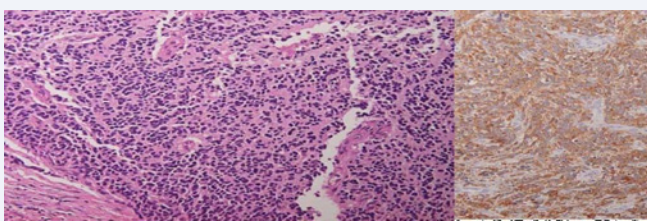


Figure 2 HE-stained section shows the proliferation of small round cells without atypia. The tumor cells with scanty cytoplasm are positive for neuron-specific enolase (NSE) by histochemical staining and there is pseudo-rosette formation.

with the tumor being positive for neuron-specific enolase (NSE) (Figure 2). Although urinary levels of vanillyl mandelic acid (VMA) and homovanillic acid (HVA) were within normal limits when initially measured, both parameters were high on repeat measurement. Some tumor markers such as serum NSE or serum ferritin were elevated as well. CT scans showed a bulky mass surrounding the inferior vena cava and abdominal aorta, which had been impalpable and was not detected by ultrasound prior to surgery. Bone scintigraphy and bone marrow aspiration showed no evidence of metastasis, but MIBG scintigraphy revealed abnormal uptake in the right femur and right maxilla. Therefore, he was diagnosed as having stage IV neuroblastoma and underwent biopsy of the primary abdominal lesion to obtain additional information about N-myc activation, DNA ploidy, and TrkA mRNA expression. The biopsy specimen showed favorable biological features according to Shimada's classification [4] and there was no N-myc gene amplification, but some unfavorable features were also present such as a diploid karyotype and TrkA mRNA null status. The patient underwent 4 courses of chemotherapy with cyclophosphamide (CPA), vincristine, cisplatin, and THP-Adriamycin (THP-ADM) according to the Japanese neuroblastoma study group protocol. Subsequently, exploratory laparotomy detected residual viable cells, so the patient was given two more courses of the same regimen, 1 course of chemotherapy with CPA and dacarbazine, and 1 course of CPA, THP-ADM, and carboplatin. At 3 years after diagnosis, the patient is alive without elevation of any tumor markers including VMA,

HVA, NSE and ferritin, but the abdominal mass is still present around the IVC and aorta without evidence of progression.

DISCUSSION

Paratesticular neuroblastoma occurs in the paratesticular tissues involving the epididymis, spermatic cord, and tunica vaginalis. Paratesticular neuroblastoma among paratesticular tumors, such as lipoma or juvenile form rhabdomyosarcoma, is a rare tumor that can either be primary or metastatic [2,3,5,6]. While primary paratesticular neuroblastoma is considered to arise from the transformation of migrating primitive neural crest cells in paradidymal tissue, metastatic paratesticular neuroblastoma is regarded as a manifestation of disseminated disease [6]. Metastatic paratesticular neuroblastoma was more common than primary and unilateral paratesticular neuroblastoma was more frequent than bilateral. Only three cases including our case, which were composed of one primary case and two metastatic cases, have been reported as a bilateral paratesticular neuroblastoma [3,7]. Two bilateral and metastatic paratesticular cases presented as a scrotal mass and the rest was diagnosed as inguinal hernia.

In general, neuroblastoma is usually a silent tumor at an early stage. At the time of diagnosis, about 70% of patients have metastatic disease. In order to detect neuroblastoma at an early stage, vigorous efforts such as mass screening in infants have been attempted because the prognosis depends on patient's age and the stage of the disease [1,8]. According to recent studies, however, screening of infants for neuroblastoma does not appear to reduce either mortality, or the incidence of disseminated disease [9]. Therefore, mass screening of infants for neuroblastoma is currently being reconsidered. In case of the abolishment of mass screening, it seems possible that clinical neuroblastoma will increase in the future and clinicians will have more chance to encounter symptomatic patients. With respect to paratesticular involvement of neuroblastoma, this entity does not seem to be so rare in patients with disseminated neuroblastoma because it was reported in 4/289 and 6/1,076 neuroblastoma patients [2,7]. In addition, paratesticular involvement by neuroblastoma at initiate diagnosis is not always associated with a poor prognosis, although involvement at relapse bears a poor prognosis and has a fatal outcome [2].

As mentioned above, the survival of neuroblastoma patient is influenced by age and stage. For all stages, overall survival of children less than 1 year old was 76%, while that of children older than 1 year was only 32% and there was a significant difference between the two age groups [1]. Overall survival was nearly 100%, 90%, 37%, 12 % and 81% in stage I, II, III, IV and Vs, respectively [1]. There are several risk factors for neuroblastoma, such as serum NSE, serum ferritin, and histologic type, according to the criteria of Shimada [4]. In addition, there are various genetic characteristics of the tumor like loss of heterozygosis (LOH) at 1p, a diploid karyotype, over expression of the N-myc oncogene, and expression of TrkA mRNA. Especially, amplification of the N-myc oncogene is an important indicator of a poor prognosis because more than 90% of patients with N-myc amplification have rapidly progressive tumors that are resistant to therapy [1,10]. Our patient's tumor had no N-myc amplification and showed favorable features according to Shimada's classification,

and he is still alive without progression despite other unfavorable features.

Making a correct preoperative diagnosis of neuroblastoma may be difficult, even in patients with disseminated disease like our case, because this tumor has miscellaneous, even bizarre manifestations. In particular, paratesticular neuroblastoma as paratesticular mass is not so familiar because most paratesticular tumors in children are composed of lipoma or juvenile form rhabdomyosarcoma. Therefore, we suggest that paratesticular neuroblastoma should be included in the differential diagnosis of a paratesticular mass in infants. We also suggest that molecular analysis should be done at the first operation to avoid unnecessary repeat biopsy as well as delay in starting treatment.

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