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Case Report

Adult-onset Renal Neuroblastoma: Case Report and Literature Review

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Abstract

Neuroblastoma is an extremely rare neoplasm in adults, with a poorer prognosis compared to pediatric neuroblastoma. Due to its rarity, there are no specific treatment guidelines for adult neuroblastoma. Here, we report a case of adult renal neuroblastoma presenting initially with painless and gross hematuria. Enhanced computed tomography revealed an infiltrative, heterogeneously enhanced renal mass at the lower pole of the right kidney, accompanied by regional lymphadenopathies. The initial impression was renal cell carcinoma, and a right nephroureterectomy with regional lymph node dissection was performed. Pathologic examination confirmed the diagnosis of primary renal neuroblastoma with a differentiating subtype. The patient was classified as having International Neuroblastoma Staging System stage 2B or International Neuroblastoma Risk Group Staging System stage L2. The patient underwent six courses of adjuvant chemotherapy, and no disease recurrence was observed during a 7-year follow-up period.

Keywords: Adult, chemotherapy, kidney, nephrectomy, neuroblastoma

Introduction

Neuroblastoma is a type of neuroendocrine tumor arising from the primitive embryonic sympathoadrenal lineage of the neural crest.[1] Due to genetic and epigenetic alterations, these tumors can develop in the adrenal gland or sympathetic ganglia.[2] The incidence of neuroblastoma is around 6–10 cases per million people.[2] The median age at diagnosis is 18 months, and 90% of cases occur in children under 10 years of age.[3,4]

Neuroblastomas are unique due to their broad spectrum of clinical behavior, ranging from spontaneous regression to aggressive metastatic spread. The Children's Oncology Group (COG) revised the most recent risk classification based on tumor stage, age at diagnosis, histologic features, chromosome aberrations, and molecular markers.[5] High-risk neuroblastoma is associated with the worst prognosis. Despite multimodal therapies, including multiagent chemotherapy, surgical resection, consolidative high-dose chemotherapy with autologous stem cell transplant, and postconsolidation immunotherapy, the survival rate remains low in children, at approximately 50% at 5 years.[4,6]

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Adult-onset neuroblastomas account for <5% of all cases, and they have a significantly worse outcome compared to pediatric cases.[7] Most adults diagnosed with neuroblastoma present with metastatic disease initially.[8] Due to its rarity, there is no standard therapy or standardized staging for adults with neuroblastoma. Here, we report a case of adult renal neuroblastoma successfully treated with nephrectomy and adjuvant chemotherapy.

Case Report

A 41-year-old female (height: 160 cm, weight: 53 kg) presented with painless and gross hematuria for 1 month. She was a homemaker without a significant medical history, and she had been in good health. Painless and visible hematuria developed over 1 month with no history of traumatic injury, and she also reported mild abdominal pain over the right upper quadrant region approximately 2 weeks before this presentation. She did not report fever, diarrhea, vomiting, dysuria, or shortness of breath. A urine culture was negative for bacterial growth, and urine cytology did not reveal malignant cells. A contrast-enhanced computed tomography scan revealed an infiltrative renal mass measuring approximately 5.02 cm in the lower pole of the right kidney. The mass exhibited perirenal fat invasion, heterogenous enhancement, and an enlarged right para-aortic lymph node with encasement of renal vessels. Initially, the radiologist suspected renal cell carcinoma with a metastatic lymph node [Figures 1 and 2].

The patient underwent right nephroureterectomy and regional lymph node dissection. Pathologic examination revealed a grayish-white, elastic renal mass measuring 5.8 cm × 5 cm × 4.7 cm, with evidence of vascular invasion and regional lymph node metastasis. Microscopic examination showed a tumor composed of undifferentiated cells in a fibrillary background, with focal immature neuroepithelial and ganglionic differentiation. Immunohistochemical studies were negative for CD45, PAX8, GATA3, CD99, and WT1. The ganglion cells and Schwannian stroma expressed chromogranin A, synaptophysin, and neuropil. This led to a diagnosis of an unusual primary renal neuroblastoma. The tumor exhibited a differentiating subtype with a high mitotic-karyorrhectic index, classified as unfavorable histology according to the International Neuroblastoma Pathology Classification. The final diagnosis was primary renal neuroblastoma with regional lymph node metastasis, classified as stage 2B according to the International Neuroblastoma Staging System (INSS) and stage L2 according to the International Neuroblastoma Risk Group Staging System (INRGSS).

Following surgery, the patient received six cycles of adjuvant chemotherapy, including cisplatin (60 mg/m^2 on day 1), doxorubicin (30 mg/m^2 on day 2), etoposide (80 mg/m^2 on day 2 and day 5), and cyclophosphamide (750 mg/m^2 on day 3 and day 4). Over a 7-year follow-up period, there was no evidence of disease recurrence.

Discussion

Neuroblastoma accounts for approximately 7% of all cases of childhood cancer.[4,8] Its occurrence in adults is exceedingly rare, with an estimated incidence of 1 case per 10 million adults per year.[8,9] Adults with neuroblastoma typically have poorer outcomes than children, even with intensive multimodal therapies.[7] There is increasing evidence indicating that adult neuroblastoma presents with distinct clinical and biological features compared to pediatric neuroblastoma.[8,10,11]

Clinical features

Neuroblastomas originate from the sympathetic nervous system, with the adrenal gland being the primary site in 40% of pediatric patients. Other common sites include the abdomen (25%), thorax (15%), cervical region (5%), and sympathetic ganglia in the pelvis (5%).[4]

Conter *et al*. reviewed data from the MD Anderson Cancer Center from January 1994 to September 2012, encompassing 118 adults ranging from 18 to 82 years old.[8] The most

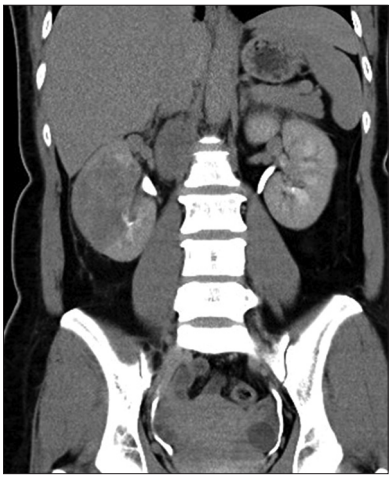

Figure 1: Abdominal contrast computed tomography showed a right renal mass and an enlarged right para-aortic lymph node

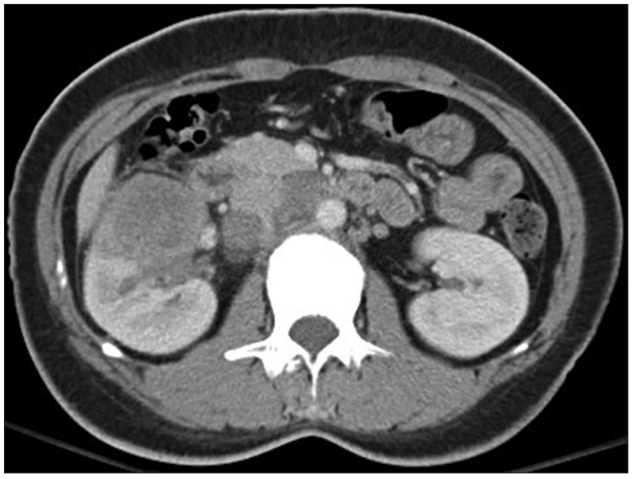

Figure 2: Abdominal contrast computed tomography showed a right renal mass and a right para-aortic lymphadenopathy with renal vessel encasement

frequent primary sites were found to be in the head and neck (69.5%), followed by the genitourinary tract (11.01%), soft tissue (7.62%), chest cavity (4.23%), and central nervous system (3.38%).[8] Common presentations are abdominal mass, abdominal pain, systemic symptoms such as weakness, fever, and weight loss, as well as complications such as spinal compression, hematuria, and hypertension.[8,12]

Intrarenal neuroblastomas are exceptionally rare in adults. Our case presented with painless gross hematuria and mild abdominal pain as the initial symptoms.

Molecular genetic characterization

Several genetic changes are known to have a negative prognostic impact in pediatric neuroblastoma, including amplification of the MYCN gene,[13] segmental chromosome aberrations such as loss of heterozygosity at 1p and gain of 17q,[14] mechanisms related to telomere maintenance.[15]

MYCN oncogene amplification is a well-known poor prognostic factor, occurring in approximately 20% of pediatric neuroblastomas.[9] In contrast, MYCN gene amplification is rare in adult-onset neuroblastomas, found in only 3% of cases.[12] Deletion of chromosome 1p is the most common chromosomal abnormality observed in pediatric neuroblastoma, associated with a poorer prognosis and present in about 35% of cases.[16] In adult-onset neuroblastoma, approximately 20% of cases exhibit deletion of chromosome 1p.[11]

Furthermore, alterations in the anaplastic lymphoma kinase (ALK) gene have been reported to be independent predictors of a poorer prognosis.[14] In addition, early-phase and preclinical trials have shown the promising efficacy of ALK inhibitors.[17] ALK mutations have been reported in around 14% of pediatric neuroblastomas,[14] Data on adult-onset neuroblastomas are limited; however, one study reported that 42% of cases (10/16) had ALK mutations.[11]

Stage

Two staging systems are used for neuroblastomas: The INSS and INRGSS. The INSS, initially proposed in 1988 and revised in 1993, considers factors such as resectability, lymph node involvement, and distant metastases.[18] Assessment, according to the INSS, occurs after the initial surgical resection has been completed.[13] On the other hand, the INRGSS is a pretreatment classification system that incorporates pretreatment imaging parameters. It is widely used for prospective research and serves as the basis for risk classification by the COG.[5] The COG neuroblastoma risk classifier categorizes patients based on the INRGSS, MYCN gene status, histologic status, DNA index, segmented chromosomal aberrations, and age.[5]

Studies have explored the feasibility of using the INRGSS pediatric classification for adult-onset neuroblastoma, and shown similar survival outcomes to those seen in pediatric patients.[8] Therefore, the INRGSS is recommended for stratifying adult-onset neuroblastoma. However, the COG neuroblastoma risk classifier has not been validated for use in adult-onset neuroblastomas.

In our case, the patient was classified as INSS stage 2B and INRGSS stage L2. The COG neuroblastoma risk classification was intermediate-risk disease.

Treatment

In pediatric neuroblastoma, treatment decisions hinge on the COG neuroblastoma risk classifier. Patients with low-risk disease typically undergo surgery alone without additional chemotherapy,[5,19] whereas those with intermediate-risk neuroblastoma are managed with neoadjuvant chemotherapy involving multiple agents followed by surgery.[19,20] Patients with high-risk disease require a more aggressive treatment approach combining chemotherapy, surgical resection, high-dose chemotherapy with autologous hematopoietic stem-cell rescue, radiotherapy, and immunotherapy plus isotretinoin, which has been shown to significantly improve survival outcomes.[19]

The COG neuroblastoma risk classifier has not been validated for adult-onset neuroblastoma. Due to the rarity of adult-onset neuroblastoma, there is currently no established standard of care. Conter *et al*. retrospectively reviewed 118 cases at the MD Anderson Cancer Center, focusing on treatment strategies based on the INRGSS staging system.[8] Their findings revealed that for L1-stage disease, combining surgery and radiation showed a trend toward better progression-free survival (PFS) (median = 11.1 months) compared to surgery or radiation alone (median = 6.4 months).[8] Adding chemotherapy to local therapy did not significantly improve the PFS for patients with L2 neuroblastomas (median PFS = 4 months vs. 5.2 months with local therapy alone).[8] In patients with untreated M-stage disease, common chemotherapy regimens included cisplatin/carboplatin, etoposide, cyclophosphamide, and vincristine. Notably, high-dose chemotherapy with autologous hematopoietic stem-cell rescue did not improve survival outcomes.[8]

Regarding our case, the patient was classified as INSS stage 2B, INRGSS stage L2, and intermediate-risk according to the COG risk classification. After surgical resection, she received adjuvant chemotherapy with cisplatin, doxorubicin, etoposide, and cyclophosphamide, and no recurrence was observed during a 7-year follow-up period.

Conclusion

Adult neuroblastoma is extremely rare, and the diagnosis requires a tissue biopsy and pathologic examination. Molecular characterizations, clinical symptoms, and prognosis in adult neuroblastoma differ from those in pediatric cases. Even though adult patients with neuroblastomas generally have a poorer prognosis than pediatric patients, the INRGSS has been validated retrospectively for predicting the prognosis in adults. Due to its rarity, the standard treatment for adult neuroblastoma remains unknown. Further studies are necessary to establish specific treatment guidelines for this rare condition.

Declaration of patient consent

This study was performed in accordance with and conforming to the Declaration of Helsinki. The authors certify that they

have obtained all appropriate patient consent form. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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