Case Report

Renal Cell Carcinoma Occurring in a Child 2 Years After Chemotherapy for Neuroblastoma

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Improvements in diagnosis, supportive care, and treatment have led to an increasing number of persons surviving childhood cancer [1]. In a small proportion of patients, however, a second malignant tumor develops [2]. We report an infant who had a stage IV-S neuroblastoma diagnosed when 10 weeks old and subsequently had a renal cell carcinoma of the right kidney develop 2 years after completing a short course of chemotherapy. Two other cases of renal cell carcinoma developing in survivors of neuroblastoma have been reported previously. However, this is the first case we know of that involved such a short latency period between the development of the two tumors.

Case Report

A 10-week-old male infant had had increasing abdominal swelling for 10 days. Physical examination showed an enlarged abdominal girth with a smooth, firm mass in the upper abdomen extending into both lower quadrants.

Plain radiographs showed a large soft-tissue mass without calcification occupying the abdomen. Sonography showed the mass to be an enlarged liver, with an associated left adrenal mass. CT of the abdomen confirmed the sonographic findings (Fig. 1A). A wedge biopsy of the liver confirmed the diagnosis of neuroblastoma. Bone marrow aspirate did not show any marrow involvement. Urine levels of catecholamines, both homovanillic acid (HVA) and vanillylmandelic acid (VMA), were markedly elevated. The DNA index was 1.0 and the n-myc copy number was one, indicating no amplification. The tumor was classified as a stage IV-S neuroblastoma. The patient was treated with two courses of chemotherapy (doxorubicin/cyclophosphamide alternating with teniposide/cisplatin). The left adrenal mass resolved, and the liver metastases regressed, with levels of HVA and VMA in the urine decreasing to normal. The patient was followed up until 18 months old without tumor recurrence. No radiotherapy was done, and the patient was subsequently lost to follow-up for the next 17 months.

When he was 3 years old, he returned for evaluation, and on physical examination a mass was noted in the right upper quadrant extending to the umbilicus. A spot check revealed a normal VMA level in the urine. Sonography showed a mass of heterogeneous echogenicity arising from the right kidney and extending into the right iliac fossa (Fig. 1B). Abdominal CT confirmed the renal mass and associated retrocaval adenopathy (Fig. 1C).

A right nephrectomy, proximal right ureterectomy, and regional lymph node resection were performed. Histopathologic examination revealed a renal cell carcinoma with metastatic involvement of regional lymph nodes. The patient had an uneventful postoperative course and has received no additional therapy. The patient has been followed up for 12 months without evidence of tumor recurrence.

Discussion

Neuroblastoma is the most common malignant tumor of infancy and the most common extracranial solid tumor of childhood. It arises from cells of the neural crest that form the sympathetic ganglia and adrenal medulla [3]. In contrast, renal cell carcinoma is rare in children; it has 1/30 the prevalence of Wilms' tumor in the first decade of life. It arises from the renal tubular epithelial cells, probably from the proximal convoluted tubules [4].

Second malignant tumors (including neuroblastoma) developing in survivors of childhood cancer are increasingly

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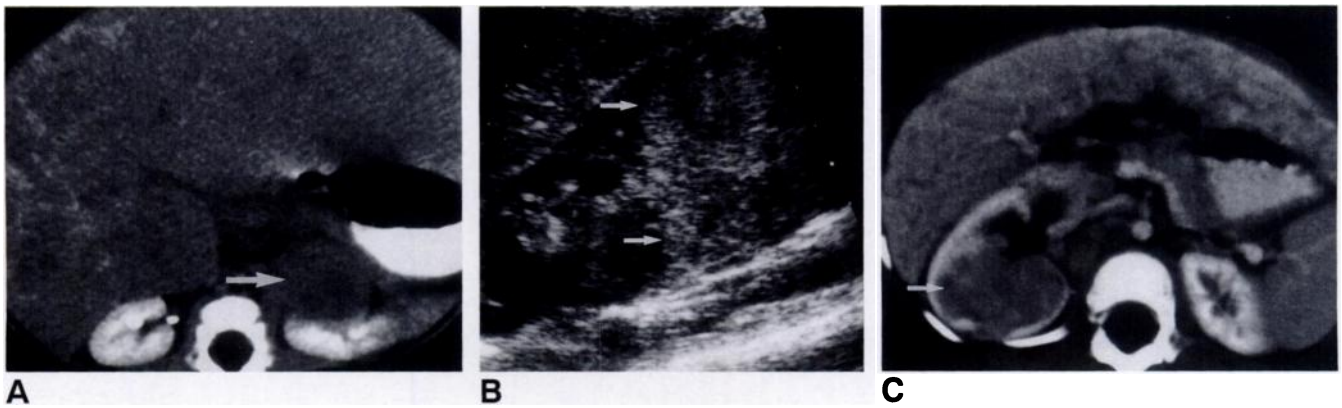

Fig. 1—*A*, Contrast-enhanced CT scan shows left adrenal mass (*arrow*) and enlarged liver with heterogeneous attenuation consistent with diffuse metastases.
***B*, Sagittal sonogram shows solid mass (*arrows*) arising from lower pole of right kidney.**
***C*, Contrast-enhanced CT scan shows intrarenal mass (*arrow*) at lower pole with retrocaval adenopathy at level of right renal hilus.**

being reported [2]. In a recent series of 303 adult patients, Schmahl et al. [5] reported that two thirds of the second tumors were leukemias; only three in their series were renal cell carcinoma. Li et al. [6] first reported a patient with stage IV-S neuroblastoma treated with radiotherapy, with subsequent development of renal cell carcinoma 14 years later. Fairchild et al. [7] reported a woman who had had an abdominal neuroblastoma when she was 9 months old, had been treated with local radiotherapy, and then had renal cell carcinoma 25 years later. In the current child, renal cell carcinoma developed less than 3 years after a short course of chemotherapy for stage IV-S neuroblastoma.

Because this patient did not receive radiotherapy, only the chemotherapy can be implicated as a causative agent in the development of the renal cell carcinoma, in particular, the alkylating agent (cyclophosphamide) and epipodophyllotoxin (teniposide). The other possibility is that certain persons have an inherent biologic predisposition to the development of second malignant tumors. Malkin et al. [8] reported that among 59 patients with second malignant tumors and no family history of the Li-Fraumeni syndrome, four had germline mutations of the p53 tumor suppressor gene. This patient has no family history of malignant syndromes; mutations of the p53 tumor suppressor gene were not assessed.

Whether these two tumors in this child are related to multioncogenic potential or a consequence of chemotherapy is speculative. Nevertheless, an awareness of this association is important in the diagnostic follow-up of neuroblastoma.

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