Concurrent Renal Cell Carcinoma and Central Nervous System Lymphoma in a Patient with Autosomal Dominant Polycystic Kidney Disease

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Key Words

Polycystic kidney disease · Lymphoma · Renal cell carcinoma

Abstract

Objective: To report an unusual case of synchronous renal cell carcinoma and CNS lymphoma in a patient with autosomal dominant polycystic kidney disease (ADPKD). **Case Presentation and Intervention:** A 58-year-old woman presented with progressive right hemiparesis of 2 months' duration. A brain CT scan revealed multiple enhanced lesions in the basal ganglia and the right occipital lobe. CNS lymphoma was confirmed by a stereotactic biopsy. Polycystic kidneys and a right renal mass were found incidentally. It was decided to treat the patient with cranial radiotherapy and chemotherapy first. The patient achieved complete remission of CNS lymphoma after 3 months, but the renal mass remained unchanged. A needle biopsy of the renal mass revealed renal cell carcinoma and unilateral nephrectomy was performed successfully. The patient remained in complete remission at 6-year follow-up. **Conclusion:** The patient was treated successfully with a combination of chemotherapy, radiotherapy, and unilateral nephrectomy. This report highlights the need for clinicians to remain alert to the possibility of double malignancies while caring for ADPKD patients, especially when multiple unexplained manifestations exist.

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Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is caused by mutations of *PKD1* or *PKD2*, and has an incidence of 1/1,000 individuals [1]. Common complications of ADPKD include renal insufficiency, hypertension, liver cysts, and cerebral aneurysms [1]. Renal cell carcinoma is infrequent in ADPKD and may be difficult to identify due to its non-specific symptoms such as hematuria, flank pain and palpable large kidneys [2, 3]. Primary CNS lymphoma is a rare cancer that accounts for less than 3% of all brain tumors and is more commonly seen in immunocompromised patients [4]. Here, we present an unusual case of ADPKD with synchronous CNS lymphoma and renal cell carcinoma.

Case Report

A 58-year-old previously healthy woman had experienced progressive right hemiparesis for 2 months. She became confused and was brought to the hospital for further treatment. There was no fever, flank pain, or gross hematuria. Her parents had died of unknown causes, and her 3 children gave no history of systemic disease. On admission, her Glasgow Coma Score was E4V4M6 (E: eye opening, V: verbal response, M: motor response). She was afebrile and normotensive. The muscle power of the right arm was 1, and that of the right leg was 3. She had left ptosis and pupil size was asymmetric (left: 5 mm, right: 3 mm). The abdomen was soft on examination without palpable mass. The patient had no skin

Fig. 1. Synchronous CNS lymphoma and renal cell carcinoma in a patient with ADPKD. **a** Brain CT showing a hyperdense mass (arrowhead) over the left midbrain. **b** Brain biopsy of the right occipital lobe showing infiltration of large lymphoid cells with atypical nuclei (arrowhead). HE. $\times 400$. Using other stains (data not shown), the cells were positive for leukocyte-common antigen and L26 (B-cell marker) and negative for MT1 (T-cell marker) and AE1/AE3 (cytokeratin), confirming a diagnosis of B cell lymphoma. **c** Abdominal CT showing a renal mass (arrowhead) over the right kidney and multiple renal cysts in both kidneys. **d** Brain CT showing complete remission of the CNS lymphoma after radiotherapy and chemotherapy. **e** Percutaneous biopsy of the right renal mass showing renal cell carcinoma (arrowhead). HE. $\times 400$.

lesions suggestive of tuberous sclerosis or von Hippel-Lindau disease. Hemogram and serum biochemistry were within normal limits. She was seronegative for HIV antibody. A CT scan showed multiple enhanced lesions in the left basal ganglia, the left subthalamic region, the left midbrain (fig. 1a) and the right occipital lobe. A stereotactic biopsy of the right occipital lesion showed clusters of cerebral parenchyma with foci of small blue neoplastic cell aggregations (fig. 1b). Immunohistochemistry revealed that the tumor cells were positive for leukocyte common antigen and B cell marker (L26). A diagnosis of malignant B cell lymphoma was made. In situ hybridization for Epstein-Barr virus-encoded RNA was negative in the lymphoma cells.

A subsequent bone marrow biopsy revealed no evidence of lymphomatous involvement. An abdominal CT scan revealed multiple cystic lesions of variable size in the liver and bilateral kidneys, which is consistent with ADPKD. A solid lobular tumor (4 × 3 cm) with contrast enhancement was found incidentally in the lower pole of the right kidney (fig. 1c). The renal mass was hypovascular on angiography. In view of the possibility of lymphoma with renal involvement, it was decided to first institute cranial radiation therapy (6,120 cGy in 34 fractions over 7 weeks), intravenous dexamethasone (15 mg/day, then gradually tapered), and chemotherapy, including 2 cycles of high-dose intravenous methotrexate (1 g/m²) with leucovorin rescue, 6 doses of intrathecal therapy with methotrexate (12 mg per dose) via lumbar puncture over 3 weeks, followed by 2 doses of cytosine arabinoside (3 g/m²). Her hemiplegia improved partially after 3 months of treatment. A repeated CT scan showed complete remission of the CNS lymphoma with no evidence of tumor recurrence (fig. 1d). However, the tumor in the right kidney was unaffected. A subsequent CT-guided needle biopsy showed that the tumor was composed of clear and granular cells (fig. 1e) and a diagnosis of renal cell carcinoma was made. The patient survived a right nephrectomy uneventfully. She remained in complete remission at 6-year follow-up.

Discussion

We report a rare case of ADPKD complicated by synchronous CNS lymphoma and renal cell carcinoma. To our knowledge, the concurrence of these 3 diseases has not been previously reported. The presence of multiple malignancies is uncommon, and the association is considered to be 'synchronous' if 2 unrelated malignancies occur within 6 months [5]. Renal cell carcinoma is the most commonly reported malignancy in patients with ADPKD [6]. It was speculated that tubular epithelial hyperplasia may represent a premalignant lesion in ADPKD kidneys. Indeed, ADPKD-associated renal cell carcinoma was more often concurrently bilateral, multicentric and sarcomatoid in type, and occurred at a younger age than in the general population [6]. However, whether or not the incidence of renal cell carcinoma in patients with ADPKD is higher than that in the general population is still controversial [2].

Interestingly, a higher risk of coexisting renal cell carcinoma and non-Hodgkin's lymphoma has been reported by several investigators [7, 8]. The pathogenesis of synchronous renal cell carcinoma and non-Hodgkin's lymphoma is not clearly understood. A breakdown of tumor surveillance has been proposed as a predisposing factor in the development of renal cell carcinoma in lymphoma patients [8]. A recent study demonstrated that Epstein-Barr virus infection could be one of the pathogenic mechanisms for the occurrence of renal cell carcinoma in non-Hodgkin's lymphoma related to AIDS [9]. Immunodeficiencies in post-transplant patients and AIDS are risk factors for primary CNS lymphoma [4]. However, we found no evidence of infection by Epstein-Barr virus or HIV in this patient, and she was not taking any immunosuppressive drug. Possible links between ADPKD and CNS lymphoma remain to be determined. Interestingly, a microarray analysis of gene expression patterns in diffuse large B cell lymphomas revealed a trend toward downregulation of *PKD1* mRNA [10]. *PKD1* was found to be associated with important cell functions, such as cell proliferation and apoptosis [1]. The pathophysiological significance of this observation is currently unclear and merits further investigation.

The diagnosis of malignancies could be difficult in ADPKD as the symptoms related to malignancies may be obscured by systemic manifestations of ADPKD, such as hematuria, palpable abdominal mass or ruptured cerebral aneurysm. In our case, the presence of an incidental renal mass in addition to the CNS lymphoma complicated our treatment plan; it was decided to spare the patient from nephrectomy and start radiotherapy and chemotherapy first, but a nephrectomy was eventually required once renal cell carcinoma was confirmed. Our case demonstrated that renal lymphoma may be difficult to differentiate from renal cell carcinoma on imaging studies, and that a renal biopsy or nephrectomy is required if the tumor does not respond well to the standard chemotherapy for lymphoma. The differential diagnosis of a solitary renal mass includes renal cell carcinoma, transitional cell carcinoma, lymphoma, metastasis, angiomyolipoma and other etiologies. Renal lymphoma is very rare in patients with ADPKD and has only been reported in a post-transplant patient who was on immunosuppressive therapy [11]. It is worth noting that primary CNS lymphoma with systemic metastasis has also been reported [12].

Conclusion

The patient was treated successfully with a combination of chemotherapy, radiotherapy and unilateral nephrectomy. Clinicians must remain alert to the possibility of double malignancies while caring for ADPKD patients, especially when multiple unexplained manifestations exist.

Acknowledgement

We thank Dr. Tse-Ching Chen for performing the in situ hybridization for Epstein-Barr virus-encoded RNA.

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