

[CASE REPORT]

Paraneoplastic Polymyositis Due to Renal Cell Carcinoma in a Patient with Autosomal Dominant Polycystic Kidney Disease

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Abstract:

We herein report a 70-year-old man with malaise and muscle weakness that had developed within a month. The patient also had abdominal fullness due to polycystic kidney disease. Severe proximal skeletal muscle weakness and mild elevation of creatinine kinase to 301 IU/L were noted. A muscle biopsy of the right bicep showed polymyositis. Computed tomography showed a right renal mass, and an analysis after right nephrectomy identified clear cell carcinoma. The muscle weakness subsided one month after nephrectomy and intravenous immunoglobulin therapy. Therefore, we suspect that the development of polymyositis in this patient was closely related to renal cell carcinoma.

Key words: polymyositis, paraneoplastic syndrome, renal cell carcinoma, autosomal dominant polycystic kidney disease

(Intern Med 60: 3577-3580, 2021)

(DOI: 10.2169/internalmedicine.7417-21)

Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is a multisystem hereditary disease characterized by the formation of cysts in the ductal organs. Renal cell carcinoma (RCC) has been reported to be a complication of ADPKD (1). RCC shows the signs and symptoms of a paraneoplastic syndrome, including constitutional symptoms (i.e., a fever, cachexia, fatigue, and weight loss) and specific metabolic and biochemical abnormalities (including hypercalcemia, nonmetastatic hepatic dysfunction, and amyloidosis). Most paraneoplastic syndromes associated with localized RCC are definitively treated by nephrectomy only, but they reappear if RCC metastasizes outside the kidney (2). Polymyositis has been reported to be a paraneoplastic syndrome caused by RCC, but the pathogenic mechanism remains unknown (3).

We herein report a patient with ADPKD who developed both RCC and polymyositis. The relationship between RCC

and polymyositis is discussed.

Case Report

A 70-year-old man was admitted to our hospital for the evaluation of abdominal fullness and progressive fatigue. At 63 years old, the patient had been diagnosed by computed tomography (CT) as having ADPKD. At 69 years old, hemodialysis was started for chronic renal failure. Three months ago, he underwent hepatic cyst drainage because of abdominal fullness and malaise. However, these symptoms did not improve. The patient then developed muscle weakness within one month. He was therefore referred to our hospital for an evaluation.

On admission, the patient was 171 cm tall, his dry weight was 61.9 kg, and his blood pressure was 160/101 mmHg. He was emaciated, particularly in his face, thoracic region, and both upper and lower extremities. His abdomen was markedly distended and hard. No edema was present in the lower extremities. The patient had severe proximal skeletal

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Received: February 24, 2021; Accepted: April 13, 2021; Advance Publication by J-STAGE: May 29, 2021

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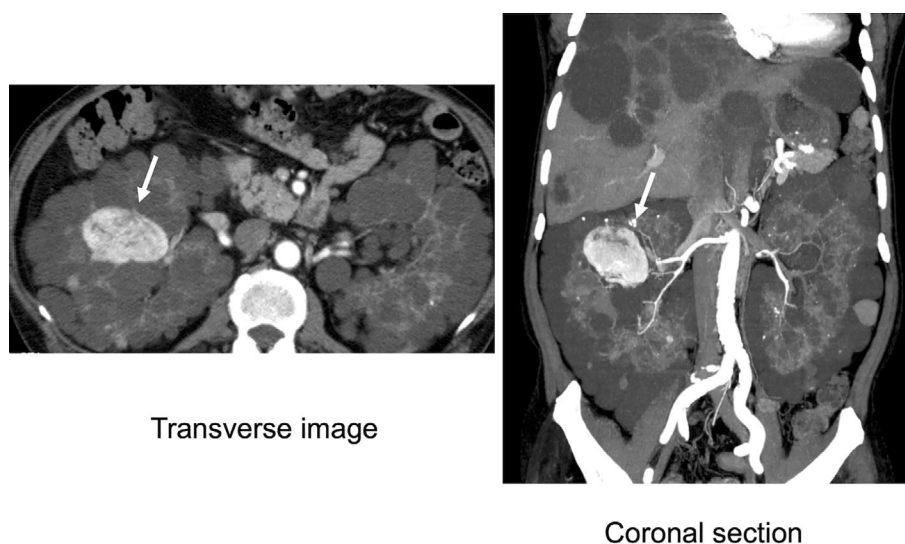


Figure 1. Computed tomography (CT) images of the abdomen. CT showed marked enlargement of both kidneys, with numerous cysts, consistent with autosomal dominant polycystic kidney disease. In addition, contrast enhancement showed a hypervascular stain of 5×6 cm in diameter (arrow) on the right kidney.

muscle weakness, which affected his ability to walk and raise his upper limbs. Furthermore, he also had severe atrophy in the intrinsic muscles. No skin lesion suggestive of dermatomyositis nor arthritic symptoms were observed.

Laboratory tests were performed at admission. The findings of the complete blood count were as follows: erythrocytes, $3.99 \times 10^6/\mu\text{L}$; hemoglobin, 7.2 g/dL; hematocrit, 11.7%; leukocytes, 5,400/ μL ; and thrombocytes, $20.2 \times 10^4/\mu\text{L}$. The blood chemistry values were as follows: total protein, 6.0 g/dL; albumin, 2.4 g/dL; urea nitrogen, 28 mg/dL; creatinine, 7.4 mg/dL; sodium, 138 mmol/L; potassium, 5.4 mEq/L; chloride, 105 mmol/L; calcium, 8.8 mg/dL; phosphate, 3.7 mg/dL; and C-reactive protein, 2.8 mg/dL. The erythrocyte sedimentation rate was 10 mm/h. The creatinine kinase (CK) level was 301 IU/L (normal level, <100 IU/L), and the aldolase level was 12.1 U/L (normal range, 2.7-7.5 U/L). Rheumatoid factor, anti-nuclear antibodies, anti-Jo-1 antibody, anti-M2 antibody, anti-transcriptional intermediary factor (anti-TIF)1- γ antibody, anti-Mi-2 antibody, and other myositis-associated autoantibodies were all negative.

CT showed marked enlargement of both kidneys and numerous cysts, consistent with ADPKD. The left kidney measured 13.0×13.4×19.0 cm, and the right kidney measured 11.4×14.0×21.8 cm. In addition, contrast enhancement showed a hypervascular stain 5×6 cm in diameter on the right kidney (Fig. 1).

A needle electromyogram examination indicated myogenic response with spontaneous activity. CT showed severe fat replacement of the lower limb muscles, predominantly on the posterior side of thigh. A muscle biopsy was performed to evaluate the presence of a myogenic disorder.

Muscle biopsy findings

A muscle specimen from the right bicep showed variation

in fiber size, inflammatory cells in the perimysium, phagocytosis of necrotic fiber, and regenerating fibers (Fig. 2a), enhanced expression of class I major histocompatibility complex antigens by muscle fibers, and infiltration of CD8-cytotoxic T lymphocytes, predominantly in the fascicle (Fig. 2b); these findings led to a diagnosis of polymyositis. Rimmed vacuoles and ragged red fibers, which would suggest a diagnosis of inclusion body myositis, were not identified, even by Gomori-Trichrome staining. No fibers were positive on p62 or anti-ubiquitin staining.

Clinical course

Transcatheter arterial embolization was performed with a platinum microcoil, followed by right surgical nephrectomy. After nephrectomy, the CK level temporarily increased to 1,639 IU/L but subsequently decreased to a normal level. The C-reactive protein (CRP) value also normalized. To avoid the risk of renal cyst infection specific to ADPKD, we did not use corticosteroid therapy as standard treatment of myositis. The patient received 400 mg/kg/day of intravenous immunoglobulin (IVIG) for 5 consecutive days for his severe muscle weakness (4). His muscle power improved, which allowed him to take steps with walking sticks within one month. After the surgery and IVIG therapy, the patient did not show relapse of either clinical symptoms or laboratory parameters (Fig. 3).

A histological evaluation of surgical nephrectomy

The tumor was 4.0×2.5×5.0 cm in size and diagnosed as clear cell carcinoma. Complete resection was confirmed (Fig. 4).

The final diagnosis

The patient was diagnosed with polymyositis based on the

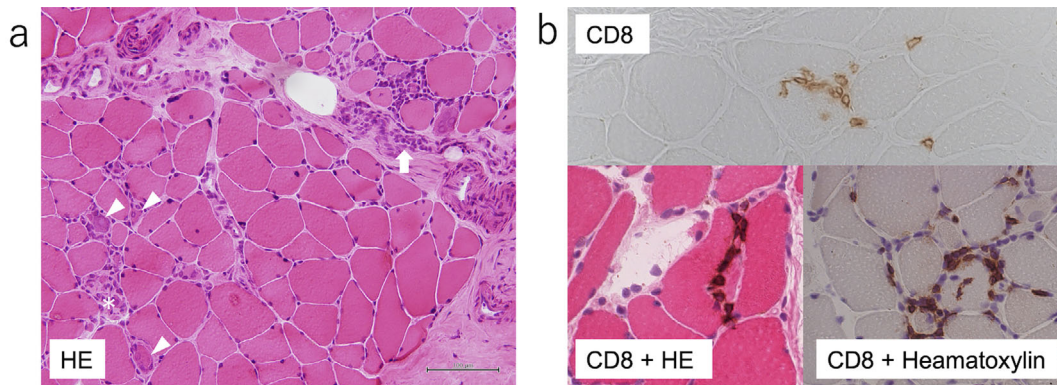


Figure 2. Muscle biopsy findings of the right bicep. (a) The muscle biopsy showed variations in fiber size, inflammatory cells in perimysium (arrow), phagocytosis of necrotic fiber (*), and regeneration (arrowheads). (b) CD8 T cell immunostaining (upper image) and hematoxylin and CD8 double staining (lower right image) show the infiltration of CD8-cytotoxic T lymphocytes around the fascicle. Hematoxylin and Eosin staining (HE) and CD8 double staining (lower left image) shows the infiltration of CD8 cytotoxic T lymphocytes dominant in the endomysium.

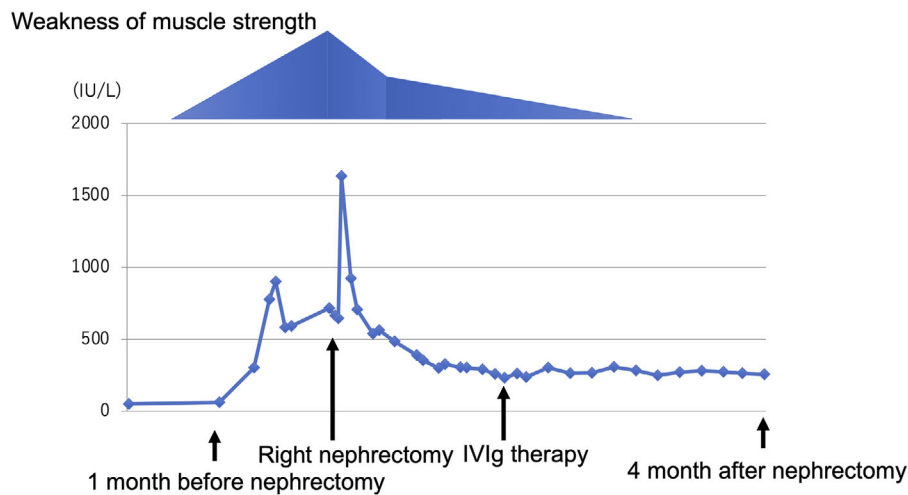


Figure 3. Clinical course of the creatinine kinase (CK) levels. The CK level increased to 1,639 IU/L immediately after nephrectomy but then decreased to a normal level of 200 IU/L.

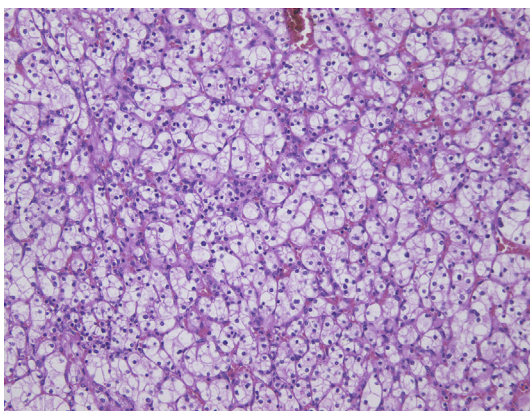


Figure 4. Histology of the right nephrectomy specimen. Clear cell carcinoma was diagnosed.

the development and resection of RCC, resulted in a final diagnosis of paraneoplastic polymyositis due to RCC.

Discussion

We encountered a patient with paraneoplastic polymyositis due to RCC. Inflammatory myopathies due to malignancy are referred to as paraneoplastic syndrome (5). Among the reported inflammatory myopathies, dermatomyositis carries the highest risk of malignancy and has been reported to be closely related to anti-TIF1- γ antibody. The relative risk of malignancy is considered to be lower in polymyositis than in dermatomyositis (6, 7), and only a few reports have been published concerning myositis associated with RCC. Klausner et al. described a 45-year-old patient who developed polymyositis. The patient underwent CT because of suspected occult malignancy. A left renal mass was seen and treated successfully by laparoscopic radical

muscle biopsy findings, and the clinical course of the onset and improvement of muscle weakness, which coincided with

nephrectomy, and clear cell carcinoma was diagnosed. The patient's muscular symptoms subsided after surgery. Therefore, the authors suggested that RCC may have contributed to the disease process of polymyositis in a paraneoplastic fashion (3). Naert et al. presented a 49-year-old patient with concurrent necrotizing myopathy and a right renal mass. After laparoscopic radical nephrectomy, remission of the myopathy was seen. A pathologic evaluation of the nephrectomy specimen identified clear cell RCC. Relapse of the myopathy six months after the operation coincided with a diagnosis of liver metastasis. After the initiation of treatment with a mechanistic target of rapamycin (mTOR) inhibitor, the myopathy became less active, so the authors suggested that it had been closely related to the RCC (8). Nevins et al. reported on a 77-year-old woman who developed severe muscle weakness and was diagnosed with dermatomyositis; a solid mass in the left kidney was also noted. Left laparoscopic nephrectomy confirmed conventional (clear cell) RCC. The patient recovered slowly after the operation but had almost completely returned to her normal life by six months later. The early detection of the typical skin rash associated with dermatomyositis may provide a clue to the diagnosis, and screening for neoplasm may improve the prognosis (9). Terakawa et al. published the case of a 74-year-old Japanese woman diagnosed with ADPKD accompanied by polymyositis and well-differentiated squamous cell carcinoma. Immediately after surgical resection of the right kidney, the patient's serum CK level decreased to within the normal range. These authors hypothesized that the occurrence of squamous cell carcinoma in patients with ADPKD is closely related to the development of polymyositis (10). Although there have been some reports describing other types of myositis related to RCC (8, 9), these are the only reports of polymyositis with RCC as a paraneoplastic syndrome.

In contrast to those previous reports, Ytterberg et al. described two patients with concurrent inclusion body myositis and RCC in whom the strength did not improve after nephrectomy. They concluded that there was no etiopathological relationship between inclusion body myositis and malignancy (11).

When we focused on instances of myositis related to RCC accompanied by polycystic kidney disease, the case reported by Terakawa et al. was the only one previously published (10). Although only a few reports have been published concerning myositis associated with RCC, patients with ADPKD have an increased risk of renal carcinoma (1), so we should consider the possibility of RCC with paraneoplastic myositis if those patients develop muscle weakness.

We reviewed this case and the previous literature and found several prominent characteristics. The myositis symptoms improved after the removal of the kidney tumor, suggesting that the tumor had been related to the development

of myositis. The histological types of renal neoplasia are diverse, with no uniformity. The phenotype of myositis is also diverse, which may be a characteristic of neoplastic myositis.

In conclusion, we encountered a 70-year-old man who presented with malaise and severe proximal skeletal muscle weakness that developed within 1 month of each other. He also showed abdominal fullness due to ADPKD. The concurrent occurrence of polymyositis and RCC was diagnosed. After nephrectomy and IVIg treatment, his polymyositis improved. We suggest that polymyositis developed in this patient as a paraneoplastic syndrome due to RCC.

The authors state that they have no Conflict of Interest (COI).

Acknowledgement

The authors would like to thank Dr. Jun Shimizu (Department of Neurology, University of Tokyo, Graduate School of Medicine) for performing the muscle biopsy.

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