Is the Association between Crescentic Glomerulonephritis and Renal Cell Carcinoma Coincidental?

A.		Kagan ^a
L.		Sinay-Trieman ^{a,b}
B.		Czernobilsky ^c
N.		Barzilai ^d
Y.		Bar-Khayim ^a

^aDivision of Nephrology, ^bDepartment of Pediatrics B, ^cDepartment of Pathology, and ^dDepartment of Radiology, Kaplan Hospital, Rehovot, Israel

Alexander Kagan, MD, Division of Nephrology, Kaplan Hospital, Rehovot 76100 (Israel)

Dear Sir,

Glomerular lesions have been frequently described in patients with malignancy [1, 2]. The most common lesion associated with solid tumors is membranous glomerulonephritis [3], whereas crescentic glomerulonephritis occurs very rarely [4, 5].

Although renal cell carcinoma (RCC) is relatively common [6], the reported incidence of glomerular involvement with this tumor is rare. Predominant glomerular complications of hypernephroma are amyloidosis, which accounts for 2-4% of all cases [7, 8], and mesangioproliferative glomerulonephritis [7, 9].

To date, only 1 case of crescentic glomerulonephritis associated with RCC has been reported [10]. We present another case of crescentic glomerulonephritis in which RCC presumably was the trigger for its development.

A 42-year-old White Jewish man was referred to our clinic because of hypertension, proteinuria and mild renal failure. For the previous 15 years, he had been treated with cimetidine for duodenal ulcer, but was otherwise in good health, with no previous history of respiratory tract infection or acute pharyngitis. Physical examination on admission was normal, except for an elevated blood pressure of 170/100 mm Hg.

Laboratory values showed serum creatinine of 229.8 $\mu\text{mol/l}$ (2.6 mg/dl) with a creatinine clearance of 0.67 ml/s (40 ml/min).

Serum electrolytes were normal. Total protein was 58 g/l, albumin 37 g/l, cholesterol 7.29 mmol/l (282 mg/dl) and triglycerides were 2.25 mmol/l (199 mg/dl). Hemoglobin was 120 g/l and hematocrit 38%. Urinalysis revealed a specific gravity of 1.020, 3+ protein (4.0 g/24 h), 5-10 red blood cells and 6-8 white blood cells per high-power field, and no casts. Urine culture was negative. Liver function tests, immunoglobulins, serum complement fractions and serum protein electro-phoresis were normal. Antinuclear antibody, hepatitis surface B antigen, VDRL and cryoglobulins were negative. Chest X-ray and bone survey were normal. Gastrointestinal tract studies revealed the presence of a duodenal ulcer. Renal ultrasonography disclosed a neoplasm in the lower pole of the right kidney which was reaffirmed by abdominal computerized tomography and selective right renal artery angiography. The renal veins were normal. The patient underwent right partial nephrectomy.

The specimen taken for pathological examination consisted of a portion of the right kidney measuring $3.5 \times 3.5 \times 5.5$ cm. The outer surface was granular. Cut section revealed a mass of $3.5 \times 3.0 \times 3.0$ cm containing a yellowish well circumscribed with hemorrhagic areas. On microscopic examination, the mass represented a RCC of the clear cell type. The remaining kidney tissue showed widespread interstitial lymphocytic infiltrates. There was arterial and arteriolar ne-phrosclerosis. More than 50% of the glomeruli showed crescents of various degrees of severity with some glomeruli being completely obliterated (fig. 1A, B). Direct immunofluorescence studies showed that the capillary walls contained granular depositions of IgG 3 + , IgM 1 + , IgA 1 + , complement component C3 3 + and fibrin. In addition, mesangial electron-dense deposits were seen on electron microscopy (fig. 1C).

Recovery after surgery was unremarkable, but because of progressive deterioration of renal function, the patient was started on hemodialysis 6 months after the operation. Three years later, there were no signs of tumor metastasis.

Drugs such as penicillamine, hydralazine, phenylbutazone, enalapril, rifampicin and streptokinase may provoke crescentic nephritis [5]. Our patient had received cimetidine, which has been known to cause acute interstitial nephritis [11, 12]. As far as we are aware, no case of crescentic glomerulonephritis related to cimetidine treatment has been reported. Crescentic glomerulonephritis may be caused by acute respiratory disease, vasculitis or systemic disease [5, 13], but these were excluded in our case.

The association of idiopathic crescentic glomerulonephritis with RCC in our patient may be a mere coincidence. Nevertheless, the frequently observed occurrence of renal dis-

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Fig. 1. A RCC of the clear cell type. HE. $\times 60$. B Section of kidney with interstitial lymphocytic infiltrates and crescentic glomerulonephritis. HE. $\times 150$. C Electron micrograph of the glomerulus showing electron-dense deposits in the mesangium and fusion of foot processes. $\times 20,000$.

ease with malignancy [1, 2] suggests that this association is more than coincidence. The granular deposition of immunoglobulins and complement along the capillary loops revealed by immunofluorescence as well as the electron deposits in the mesangium seen on electron microscopy strongly suggest an immune complex pathogenesis of crescentic glomerulonephritis in our patient [13]. It is

well known that RCC as a potential source of antigen-antibody complex(es) may initiate glomerular injury [9]. Moreover, crescentic glomerulonephritis related to solid tumor has recently been described [4]. Therefore, despite the lack of direct evidence of tumor antigen deposition in the glomeruli, immune-mediated crescentic formation due to RCC cannot be excluded. We do not know why in some

cases RCC is associated with amyloidosis, while in other cases, the predominant picture is one of mesangioproliferative or crescentic glomerulonephritis. It is possible that the release of different forms and amounts of tumor antigens, as well as differences in immuno-logical reaction(s) of the host, may explain this variability.

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