Clin Kidney J (2014) 7: 90–91

CKJ

From the Clinic

Anti-glomerular basement membrane glomerulonephritis after radiotherapy for early prostate cancer

Anti-glomerular basement membrane (GBM) glomerulonephritis is characterized by rapidly progressive glomerulonephritis (RPGN) with anti-glomerular basement antibodies. Although the underlying pathogenesis is not completely understood, factors such as smoking, cocaine, silica or mechanical stress are known to induce auto-antibody production. Moreover, studies have reported that radiotherapy may trigger auto-immunity: some cases revealed increased immune response to tumour antigens after local radiotherapy. Here, we describe a case of anti-GBM glomerulonephritis which developed post-radiotherapy for early prostate cancer. A 68-year-old Japanese male was admitted to our hospital for acute kidney injury (AKI) with serious rectal bleeding, which was thought to be the adverse effects of previous radiotherapy for prostate cancer. He had been well until he complained of gross haematuria, with increasing prostate-specific antigen (PSA) levels (8.74 ng/mL)(8.74 μg/L).

Histological prostate specimens revealed a well-differentiated adenocarcinoma (Gleason score, 3 + 4 = 7). Abdominal and pelvic computed tomography (CT) and magnetic resonance imaging (MRI) indicated that the primary lesion was localized in the prostate, no metastatic expansion was evident in any nearby organ. The clinical stage was classified as T1, and radiotherapy was recommended for this early-stage cancer. His laboratory data showed no renal impairment including serum creatinine and urinalysis before treatment.

Intensity-modulated radiation therapy was administered using a total of 76 Gy radiotherapy divided over a 2-month period. No major adverse effects were observed during radiotherapy, and because his PSA levels gradually decreased to 1.73 ng/mL (1.73 μg/L), hormonal therapy was not added.

Three months post-radiotherapy, he visited the emergency unit at our hospital complaining of severe rectal bleeding. The cause of this bleeding was examined by colonoscopy, which revealed erosive rectal mucosa and bleeding. His laboratory data revealed serious AKI, with serum creatinine levels of 13.34 mg/dL (1179.26 μmol/L), blood urea nitrogen levels of 125.4 mg/dL (44.77 mmol/L) and cystatin C levels of 6.74 mg/L. At the end of radiotherapy, his serum creatinine levels were 1.0 mg/dL, with no manifestation of congestive lung oedema. Urinalysis revealed albuminuria and microhaematuria including red-blood cell casts. Oligonuria was already present, and therefore, renal replacement therapy using haemodialysis was immediately initiated. The serological findings were as follows: ANA titre, ×80; IgG, 1071 mg/dL (10.71 g/L); IgA, 171 mg/dL (1.71 g/L); IgM, 65 mg/dL (0.65 g/L); anti-dsDNA antibody, negative; C3, 98 mg/dL (0.98 g/L); CH50 48.1 U/mL and anti-GBM antibody positive, 96 U/mL. Anti-cytoplasmic antibodies, anti-myeloperoxidase ANCA and PR-3 ANCA were all negative.

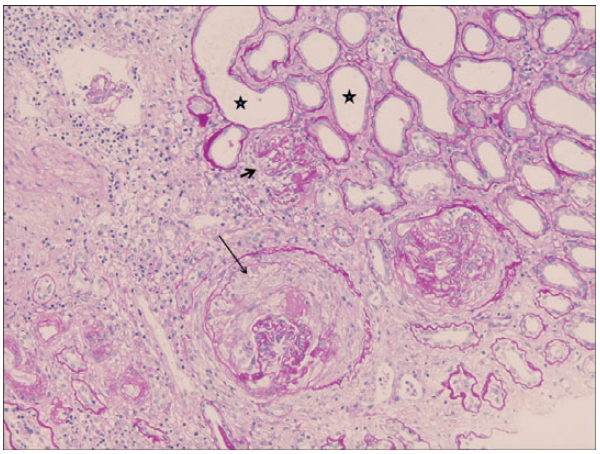

Fig. 1. Renal histopathology (periodic acid-Schiff staining ×200) revealing cellular and cellular-fibrotic crescent formation (long arrow), with necrotizing glomerulonephritis, collapsed glomeruli (short wide arrow) and damaged dilated tubule-s (star).

Renal histopathology revealed massive necrotizing glomerulonephritis with cellular or cellular–fibrous crescent formation (Figure 1). The greater part of the glomeruli was sclerotic and collapsed. Pulmonary haemorrhage was not observed, although slight inflammation was observed with C-reactive protein levels of 2.52 mg/dL (24.00 nmol/L). Low-dose oral predonisolone was initiated (20 mg/day), although aggressive immunosuppressive therapy was not administered, including plasma exchange or cyclophosphamide, because he was elderly and did not reveal evidence of respiratory failure.

Despite therapy, his renal failure did not improve, and he has required haemodialysis since the onset of this disease.

The coexistence of RPGN and a malignant tumour has been described in several cases [1]. Moreover, a case with deposition of tumour antigen for prostate cancer in the glomerulus, which caused crescentic glomerulonephritis, has been reported as well [2]. However, in our case, AKI developed 3 months after the completion of radiotherapy, with the PSA levels being normal (1.73 ng/mL) (1.73 μg/L) at that time.

Although the mechanism of anti-GBM antibody production still remains unknown, in some cases, anti-GBM glomerulonephritis has been associated with exposure to silica, hydrocarbons or smoked cocaine [3]. It was suggested that tissue damage caused by cocaine may expose the pulmonary basement membrane antigens with subsequent antibody formation. Few cases of anti-GBM glomerulonephritis have also been reported after extra-corporeal shock wave lithotripsy (ESWL). Iwamoto *et al.* [4] described ESWL-induced alterations in the structure of GBM, which may have exposed the GBM antigens, leading to the onset of anti-GBM glomerulonephritis.

Radiotherapy-induced expression of inflammatory and immune-stimulatory molecules and an antigen-specific immune response in prostate cancer management has been described [5]. Further, our patient complained of rectal bleeding, which indicated radiation proctitis [6].

© The Author 2014. Published by Oxford University Press on behalf of ERA-EDTA. All rights reserved.
For permissions, please email: journals.permissions@oup.com.

Auto-antibody production may be initiated by impaired tissue, because it has been reported that anti-GBM antibodies which react with basement membrane antigens exist not only in the kidney, but also in the lung, placenta, aorta and intestine [7].

To our knowledge, the association of anti-GBM glomerulonephritis with radiotherapy has not been previously reported.

However, in our patient, we speculate that auto-antibody production was the result of an adverse effect of radiotherapy rather than the existence of prostate cancer.

Conflict of interest statement. None declared.

[1]Department of Nephrology, Hashima Municipal Hospital, Hashima-city, Gifu, Japan
[2]Department of Hematology and Rheumatology, Kinki University Faculty of Medicine, Osakasayama city, Osaka, Japan
[3]Department of Urology, Hashima Municipal Hospital, Hashima-city, Gifu, Japan

Masafumi Sugiyama[1,2]
Yoshiteru Yamada[3]
Yuji Nozaki[2]
Koji Kinoshita[2]
Masanori Funauchi[2]

Correspondence and offprint requests to: Masafumi Sugiyama; E-mail: m-sugi@med.kindai.ac.jp

References

1. Lorenz M, Regele H, Kovarik UJ *et al*. Rapidly progressive glomerulonephritis and carcinoma of the hypopharynx. *Am J kidney Dis* 2001; 37: E3
2. Haskel LP, Fusco MJ, Wadler S *et al*. Crescentic glomerulonephritis associated with prostatic carcinoma: evidence of immune-mediated glomerular injury. *Am J Med* 1990; 88: 189–192
3. Perez GM, Garcia BF, Puras GA. Pulmonary hemorrhage and antiglomerular basement membrane antibody-mediated glomerulonephritis after exposure to smoked cocain (crack): a case report and review of the literature. *Pathol Int* 1997; 47: 692–697
4. Iwamoto I, Yonekawa S, Takeda T *et al*. Anti-glomerular basement membrane nephritis after extracorporeal shock wave lithotripsy. *Am J Nephrol* 1998; 18: 534–537
5. Nancy JN, Robert AS, Brad S *et al*. Standard treatments induced antigen-specific immune responses in prostate cancer. *Clin Cancer Res* 2007; 13: 1493–1502
6. Takemoto S, Shibamoto Y, Ayakawa S *et al*. Treatment of patients with late rectal bleeding after intensity-modulated radiation therapy for prostate cancer. *Radiat Oncol* 2012; 7: 87
7. Weber M, Pullig O, Köhler H. Distribution of Goodpasture antigens within various human basement membranes. *Nephrol Dial Transplant* 1990; 5: 87–93

doi: 10.1093/ckj/sft154
Advance Access publication 12 January 2014