

## Case Report

# Nephrotic syndrome and prostate cancer: an instructive case

Weijie Chen<sup>1</sup>, Weigang Yan<sup>2</sup>, Jianfang Cai<sup>3</sup>

Departments of <sup>1</sup>Surgery, <sup>2</sup>Urology, <sup>3</sup>Nephrology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, P. R. China

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**Abstract:** The associations between nephrotic syndrome and prostate cancer are less reported. We herein describe an instructive case in a 64-year-old male. He was admitted in our hospital because of nephrotic syndrome. The result of renal biopsy was membranous nephropathy stage II. Although steroid and cytotoxic drug were given, the control of proteinuria was poor. One year later, the patient was hospitalized again, accepted transrectal prostatic biopsy because of a 3-month history of dysuria and the high level of PSA (6.86 ng/ml). The pathological result was poorly differentiated prostatic adenocarcinoma (T1aNOMO). Subsequently he underwent radical prostatectomy. After operation the patient went into complete remission of nephrotic syndrome, no proteinuria was subsequently detected. The immunofluorescence and electron microscopy found the decrease of staining of IgG and C3, and absorption of immune-complex by the glomerular basement membrane. No relapse of nephrotic syndrome or prostate cancer was observed during nearly 3 years of follow-up. The observation of clinical remission after radical prostatectomy and pathological findings before and after operation in our study indicate that there is a relationship between prostatic cancer and nephrotic syndrome. This case reminds clinicians that for elder patients with nephrotic syndrome, a diagnosis of prostate cancer should be considered.

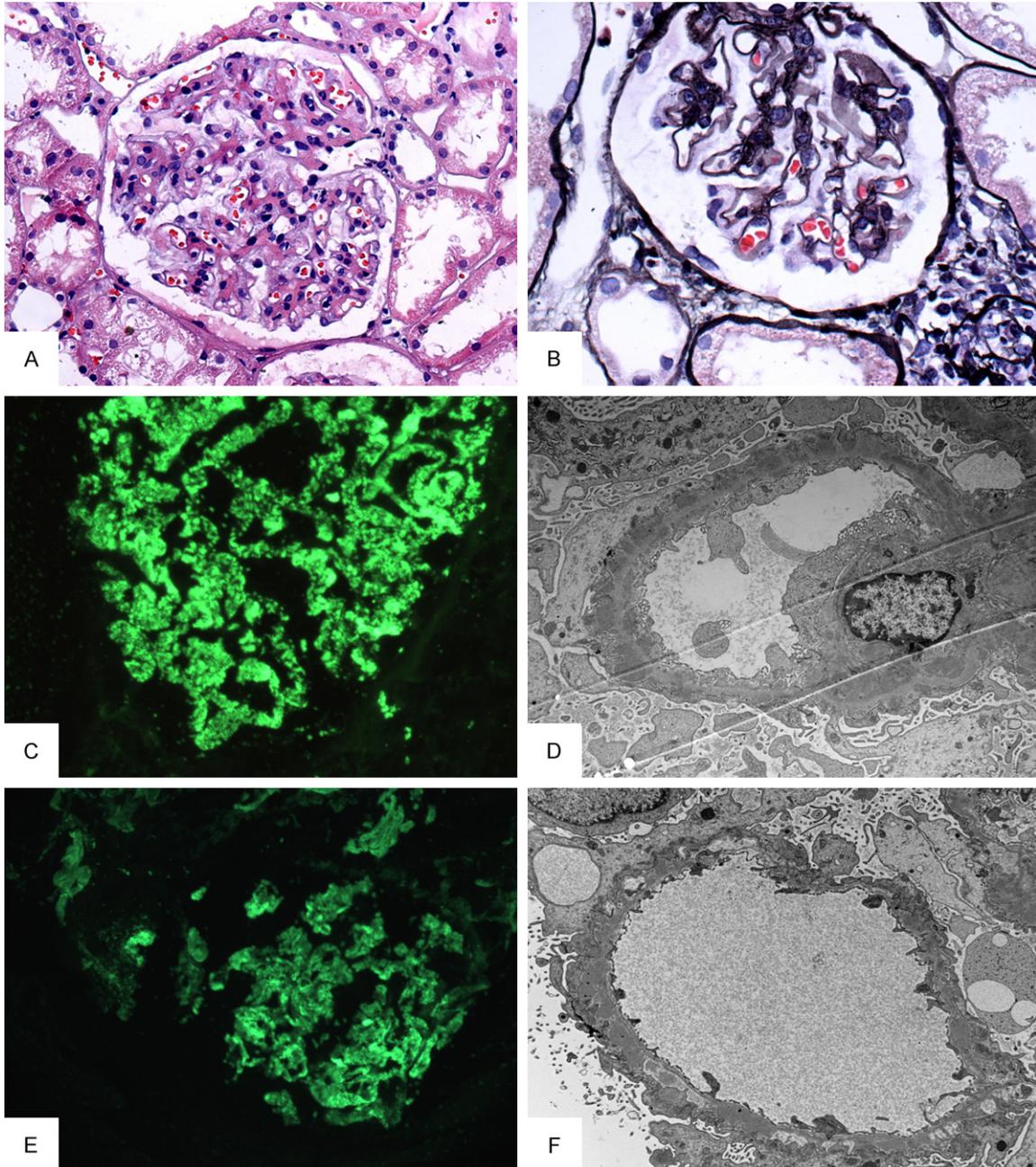
**Keywords:** Nephrotic syndrome, prostate cancer, membranous nephropathy

### Introduction

Membranous nephropathy is a leading cause of nephrotic syndrome in adults with characteristics of the accumulation of immune deposits and thickness of glomerular basement membrane. It may be idiopathic, however, as high as 13% of the cases are secondary to malignancies [1]. Traditionally, the solid organ cancers that are most commonly associated with membranous nephropathy are lung and gastrointestinal cancer [1]; associations between prostate cancer and membranous nephropathy are rarely reported. We herein describe an instructive case of nephrotic syndrome simultaneously complicated by prostate cancer. The patients achieved a clinical remission after complete surgical removal of prostate for prostate cancer, which gives an evidence of the causal relationship between prostatic cancer and nephrotic syndrome.

### Case report

A 64 year old man was admitted presented initially with a chief complaint of a history of anasarca for 2 months. He did not have an infection or hypertension before. His parents and two sons were healthy. We did not identify any special circumstances regarding his family history or personal history related to his presentation. Upon physical examination, he was afebrile with blood pressure of 145/95 mmHg and a regular pulse of 72 beat per minute. The hydrosarca anasarca was obvious, and abdominal cavity effusion was found. The total 24-hours urinary protein was 8.3 g/24 h, and the serum albumin was 22 g/L (normal 35-51 g/L). The other laboratory data were: serum creatinine 95  $\mu$ mol/L (normal 59-104  $\mu$ mol/L), triglyceride 2.5 mmol/L (normal 0.45-1.70 mmol/L), cholesterol 6.03 mmol/L (normal 2.85-5.70 mmol/L), low density lipoprotein 4.03 mmol/L



**Figure 1.** Light microscopy, immunofluorescence and electron microscopy of membranous nephropathy in a patient with prostate cancer. A. HE staining, magnification 200×; B. PASM staining, magnification 400×; C. Strong granular staining of IgG along the glomerular capillary loops and mesangial area with FITC-IgG staining, magnification 400×; D. Subepithelial and intramembranous immune deposits, thickening of glomerular basement membrane and diffuse fusion of podocyte foot processes observed with electron microscopy, magnification 6000×. E. The decrease of staining of IgG along the glomerular capillary loops with FITC-IgG staining after radical prostatectomy, magnification 400×. F. Absorption of immune-complex by the glomerular basement membrane observed with electron microscopy after radical prostatectomy, magnification 6000×.

(normal 2.07-3.63 mmol/L) and high density lipoprotein 0.75 mmol/L (normal 0.93-1.81 mmol/L). He underwent renal biopsy after admission, the immunofluorescence and elec-

tron microscopy revealed thickening of the glomerular basement membrane, diffuse strong granular staining of immunoglobulin G (IgG) and complement factor 3 (C3) along the glo-

## An instructive case

**Table 1.** membranous nephropathy associated with the prostate cancer reported in the literature

Year	Authors	Number	Age	Race	Renal function	Level of proteinuria	Stage of cancer	Treatment	Response to prostate cancer treatment
	Our case	1	64	Chinese	Stage 2	8.3 g/24 h	T1aN0M0		
2012	Yokoyama H	1	NA	Japanese	NA	NA	NA	NA	NA
2007	Bjørneklett R	6	NA	NA	NA	NA	NA	NA	NA
2006	Lefaucheur C	5	NA	NA	NA	NA	T2NxM0	H	C
							T2NxM0	H+Cs+R	P
							T3NxM0	H+R	NA
							T3NxM0	S+H+Cs	NA
							T3NxM0	H	NA
2005	Rihova Z	1	NA	NA	NA	NA	NA	NA	NA
2000	Porush JG	1	68	NA	NA	NA	TxN1M0	H	C
2000	Matsuura H	1	78	Japanese	Stage 1	12.9 g/24 h	TxNxM1	H	C
1986	Stuart K	1	66	NA	NA	NA	TxNxM1	NA	NA

C, complete remission (proteinuria <0.3 g/day or protein to creatinine ratio <0.3 g/g); Cs, chemotherapy including steroids; H, hormonal therapy; NA, not available; P, partial remission (proteinuria <3 g/day and a 50% reduction in proteinuria); R, radiotherapy; S, surgery.

merular capillary loops, formation of spikes on the epithelium, and diffuse fusion of the podocyte foot process (**Figure 1A-D**). Therefore, he was diagnosed as nephrotic syndrome due to membranous nephropathy stage II, and given steroid therapy (prednisone 1.5 mg/kg×d). The control of proteinuria was poor, although the cytotoxic drug (cyclophosphamide 100 mg/d) was given 4 months later. The 24-hours urinary protein was 6.5 g/24 h after steroid therapy and 5.7 g/24 h after 2 months cyclophosphamide therapy. The serum creatinine was 92 µmol/L, and 146 µmol/L after steroid and cyclophosphamide therapy, respectively. One year later, the patient was hospitalized again, accepted transrectal prostatic biopsy because of a 3-month history of dysuria and the high level of prostate specific antigen (PSA 9.86 ng/ml, normal less than 3 ng/ml). The pathological result was poorly differentiated prostatic adenocarcinoma (T1aN0M0). Subsequently the patient underwent radical prostatectomy, and went into complete remission of nephrotic syndrome. The 24-hours urinary protein decreased from 6.3 g/24 h before surgery to 0 g/24 h at 6 postoperative months with no steroid treatment. The serum creatinine restored to 83 µmol/L, and the level of serum albumin was 41 g/L at 6 postoperative months. The immunofluorescence and electron microscopy found the decrease of staining of IgG and C3, and absorption of immune-complex by the glomerular basement membrane

(**Figure 1E and 1F**). No relapse of nephrotic syndrome or prostate cancer (PSA 0.01 ng/ml) was observed during nearly 3 years of follow-up.

### Discussion

Membranous nephropathies manifesting nephrotic syndrome is the most common nephropathy associated with neoplasm, it was estimated to be a paraneoplastic glomerulopathy [2]. However, the associations between nephrotic syndrome and prostate cancer are less reported. The first report about the association between nephrotic syndrome and prostate cancer was in 1986 (**Table 1**) [3]. Afterwards, Leeaphorn et al reviewed 13 cases of nephrotic syndrome due to membranous nephropathy concomitant with prostate cancer [1]. Because the prognosis of nephrotic syndrome and the pathological change after treatment of prostate cancer were not reported, the causal relationship between them was not identified. Matsuura described a patient had a complete remission of nephrotic syndrome after treatment of prostate cancer [4]. But Porush thought that the case might be coincidental because of no tangible pathological evidence [5].

In our case, nephrotic syndrome developed with the diagnosis of prostate cancer and achieved clinical remission after radical prostatectomy. Moreover, subepithelial IgG and C3

were observed along the glomerular capillary loops and decreased after operation. It might be prostate cancer related immune deposits. We tried to identify tumor antigens and antitumor antibodies within immune deposits in renal tissue. PSA was not detected by doing immunoperoxidase in renal biopsy. Those immune deposits could be other prostate cancer related immune-complexes which disrupts the glomerular filtration barrier, manifesting as nephrotic syndrome. After radical prostatectomy, the relevant immune-complex deposition or immune attack on the glomerular basement membrane ceases, resulting in the complete remission of nephrotic syndrome. The decrease of staining of IgG and C3, and absorption of immune-complex by the glomerular basement membrane supports the hypothesis. This could also explain the complete remission of membranous nephropathy after treatment of prostate cancer in Matsuura's and Porush's case, and also the negative found of PSA in kidney biopsy [4].

In conclusion, although case size was limited, the observation of clinical remission after radical prostatectomy and pathological findings before and after operation in our study indicates that there is a relationship between prostatic cancer and nephrotic syndrome. Our case suggests that an underlying malignancy, including prostate cancer, should be considered in the diagnosis of membranous nephropathy. The examination and screening should be considered.

### Disclosure of conflict of interest

None.

**Address correspondence to:** Dr. Weigang Yan, Department of Urology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Shuaifuyuan 1#, Beijing 100730, P. R. China. Tel: 0086 13521624987; Fax: 0086 10-69156002; E-mail: yanweigangpumch@sina.com

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