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CASE BASED REVIEW

Prostate involvement in granulomatosis with polyangiitis

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Abstract

To present a case of prostate involvement (PI) in granulomatosis polyangiitis (GPA) and analyse related published reports. We employed the following keywords for retrieving reports indexed by MEDLINE/PubMed and/or Scopus: "granulomatosis with polyangiitis", "Wegener granulomatosis" and "prostate involvement". Additional searches were performed through Google Scholar and HINARI. All cases that fulfilled the American College of Rheumatology criteria for GPA, standards of Chapel Hill Consensus Conference, and did not match with exclusion criteria were analysed and summarised. A 35-year-old man presented with complaints of stuffy nose, difficulty breathing through the nose, swelling and pain in the left half of the nose, low-grade fever, and discomfort. The nasal mucosal biopsy did not reveal any specific changes. During the inpatient treatment, he developed eye redness, tearing, dysuria, and decreased urinary stream. Prostate-specific antigen (PSA) was elevated (2.81 µg/L; normal values ≤ 1.4 µg/L for males below 40 years). Prostate biopsy findings were consistent with diagnosis of GPA, which was confirmed by detecting elevated anti-PR3 antibodies (4.1 IU; normal values < 1.0 IU). We analysed our case in view of the clinical course of 45 published cases of PI in GPA. PI in GPA is a rare clinical manifestation of the vasculitis. Patients with atypical clinical symptoms of GPA are at risk of delayed diagnosis. The awareness of variable clinical presentations of GPA, particularly specific affection of the prostate gland, is crucial for timely diagnosis.

Keywords Granulomatosis with polyangiitis · Prostate · Urogenital system · Urological manifestations

Introduction

Granulomatosis with polyangiitis (GPA) is a multisystemic disorder characterized by necrotizing granulomatous inflammation of small- and medium-sized vessels in various organs. The upper respiratory tract, lungs, and kidneys are frequently affected in these patients [1]. The classic diagnostic triad of symptoms includes acute necrotizing granulomatous inflammation of the upper respiratory tract and lungs, focal necrotizing arteritis of small- and medium-sized vessels, and focal segmental glomerulonephritis as the most frequent type of renal involvement in GPA [2]. Anti-neutrophil cytoplasmic antibodies (ANCA) positivity, specific biopsy findings, and the triad of organ affections point to the diagnosis of GPA.

GPA is a rare disease globally. The incidence varies from 3 to 12 cases per million inhabitants and prevalence from 22 to 157 per million [3–5]. Urological involvement (UI) is not typical for GPA and can be categorized as an uncommon manifestation. In the majority of GPA cohort studies UI was reported in less than 1% of the patients [6], though a single study reported 10% of the same [7].

Herein, we present a case of prostate involvement (PI) in GPA and overview similar published reports. We aimed to analyze clinical manifestations, course, treatment options, and outcomes of this rare manifestation of GPA.

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Case report

A 35-year-old man was admitted to ear, nose and throat (ENT) Department with chief complaints of stuffy nose, difficulty with nasal breathing, swelling and pain in the left half of the nose, discomfort, and low-grade fever. He denied any specific past medical history. The chief complaints persisted during the week prior to the admission. The left half of the face was edematic. The wing and back of the nose were painful. On examination, the mucous membrane of the nose was swollen and infiltrated; nasal passage narrowed due to the distortion of the nasal septum. A reddish-gray soft formation with fibrinous layer prone to bleeding was detected in the left nasal passage (over the nasal septum and bottom of the nose). On laboratory examination, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were elevated to 48 mm/h and 96 mg/L, respectively; there was also mild leukocytosis (14.5×10^9/L). Other laboratory tests were unremarkable. Urinalysis pointed proteinuria (0.132 g/L) and leukocyturia (45–55 white blood cells per high power field). Nasal mucosal biopsy did not reveal any specific changes: there was necrotizing granulation tissue with up to 1/4 of the thickness of the sample in the superficial parts. Neither malignant growth nor signs of vasculitis were detected in the studied material. During the 10-day hospital treatment, the patient developed complaints of eye redness, tearing, dysuria, and decreased urinary stream. Ophthalmological and urological consultations were arranged, yielding the following clinical diagnosis: chronic hypertrophic rhinitis, migratory granuloma, bacterial conjunctivitis, acute prostatitis. Subsequently, the patient received combined treatment with 10 mg diphenhydramine intravenously, cetirizine hydrochloride 10 mg orally, levofloxacin 500 mg/100 mL intravenous infusion, ceftazidime 1000 mg intramuscularly, amikacin 500 mg intravenously, and dexamethasone 4 mg intravenously. Since there was no sign of improvement, levels of serum total and free prostate-specific antigen (PSA) were measured. Total PSA was 2.81 µg/L (normal values for males up to 40 years ≤ 1.4 µg/L) and free PSA was low at 0.065 µg/L (< 10% of the total PSA; normal values > 15%). A decision was made to perform prostate biopsy. The histological analysis revealed features of necrotizing granulomatous inflammation resembling GPA (Fig. 1).

Clinical diagnosis of GPA was confirmed by positive anti-PR3 antibodies test (4.1 IU; normal values < 1.0 IU) and the patient was referred to rheumatology department.

At the next hospital admission, the patients' general condition worsened. He was admitted with fever (38.5–39 °C). Previous complaints persisted and coughing with small amount of sputum, arthralgia, numbness of the limbs, and general weakness developed. Physical examination revealed pallor skin, puffy face, rash in the oral cavity, signs of breathing difficulty, wheezing, enlarged liver (+ 2 cm). Laboratory parameters also deteriorated: ESR (64 mm/h), CRP (173.63 mg/L), slightly decreased hemoglobin (Hb) (125 g/L). Urinalysis detected slight proteinuria (0.099 g/L), hematuria (40–50 red blood cells per high power field), leukocyturia (30–40 white blood cells per high power field). Chest radiography showed multiple nodular opacities with relatively clear outlines. Glucocorticoid therapy was initiated with intravenous methylprednisolone (250 mg/day) for 4 days, thereafter slowly tapered, and intravenous cyclophosphamide pulse therapy arranged (400 mg/week).

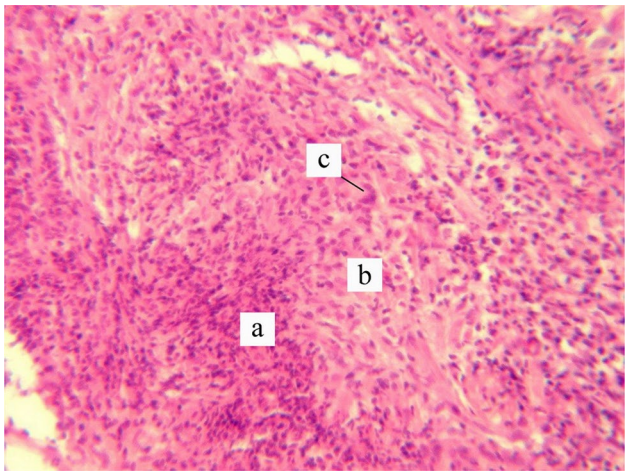

Fig. 1 Microphotograph of the patient's prostate biopsy specimen. There is infiltration of neutrophils with nuclear fragments among them due to necrosis (a); locus of necrosis is surrounded by macrophages (b) with scattered neutrophils among them and Langhans giant multinucleated giant cells (c). Hematoxylin and eosin staining × 200 magnification

After 2 weeks of treatment, a marked improvement was noted. The severity of nasal congestion decreased, urological symptoms, arthralgia disappeared, and wheezing subsided. The body temperature decreased to 37.1–37.4 °C. ESR decreased to 27 mm/h. Proteinuria, leukocyturia, and hematuria resolved. The patient was discharged on methylprednisolone 32 mg/day orally for 2 weeks, tapered gradually by decreasing 2 mg every 2 weeks, and on cyclophosphamide 50 mg/day orally.

During the 4-month follow-up, neither relapse nor occurrence of new symptoms was noted. At his last follow-up admission to hospital mild nasal congestion was noted. However, there were no signs of urological symptoms or arthralgia. The body temperature was 37.0 °C (36.8–37.2 °C during the follow-up period). ESR and CRP have not decreased to the normal values (22 mm/h and 102.54 mg/L, respectively). Urinalysis was without abnormalities. Chest radiography

showed moderate resolution of multiple nodular opacities. There were no signs any viral or other opportunistic infection due to the immune suppression. It was decided to continue maintenance therapy with 16 mg/day methylprednisolone and 50 mg/day cyclophosphamide orally by monitoring blood pressure, blood glucose, vitamin D, and Ca^{2+} levels.

Search strategy

The retrieval of relevant literature items was performed in line with recommendations on comprehensive and systematic searches through bibliographic databases [8]. We employed searches through MEDLINE/PubMed, Scopus, Google Scholar, and HINARI. Preference was given to the English-language sources. The following combination of keywords was used to retrieve relevant case reports: "granulomatosis with polyangiitis", "Wegener granulomatosis", and "prostate involvement". Although the term Wegener granulomatosis is obsolete, it was used to retrieve articles published before 2011. No time limit was set. The analysis of the retrieved articles was done on December 27, 2018. We processed only case reports fulfilling the ACR criteria for GPA [9] and standards of Chapel Hill Consensus Conference (CHCC) [10]. Unpublished descriptions in the form of congress abstracts were excluded. All cases were summarized based on their clinical course, laboratory values, morphologic features, treatment options, and outcomes.

Results

We analysed 46 cases of PI in GPA, including our own case. The previous literature review, which was published in 1994, covered 26 reports on males with PI in GPA [11]. After 1994, 19 cases were additionally reported. All these cases described male patients aged 27–82 years (50.6 ± 12.4 years) [2, 7, 11–30]. Clinical features are presented in Table 1.

Prostate involvement can develop at any stage of the vasculitis. It was the initial clinical manifestation of GPA in 12 patients (26.1%). The time between PI and diagnosis of GPA in that group was 1.5 ± 2.1 month. Clinical signs of PI varied widely. Of 46 patients, 15 (32.6%) presented with dysuria, 14 (30.4%) with chronic urinary retention, 14 (30.4%) with hematuria, 9 (19.6%) with acute urinary retention, and 5 (10.9%) with pain syndrome. PI signs were accompanied with urinary tract infection in 3 cases (6.5%), and 6 (13.0%) patients were asymptomatic. Twenty-three (50%) patients had two or more symptoms.

Of all extra-prostatic manifestations, ENT disorders were the most frequent. These disorders were observed in 39 cases (84.8%), with involvement of the nose in 26 (56.5%), ears in 9 (19.6%), vocal cords in 2 (4.4%), larynx in 1 (2.2%), and pharynx in 1 (2.2%) patient. The lungs were affected in 33 cases (71.7%), kidneys in 10 (21.7%), joints in 11 (23.9%), skin in 6 (13.0%), eyes in 6 (13.0%), heart in 3 (6.5%), nervous system in 5 (10.9%), large bowel in 2 (4.4%), parotid gland in 2 (4.4%) cases. In only one case, orchitis along with penis and urethra involvement were diagnosed.

The main laboratory findings are summarized in Table 2. As for ANCA among this group of patients the distribution was following: 1 patient was ANCA negative, 17—cANCA positive, 2—pANCA positive, 1—positive for both cANCA and pANCA, and 1 ANCA positivity (without specification). In the rest (24) no related data was recorded.

Therapeutic options and outcomes summarized in Table 3. The treatment of PI was rendered to 28 (60.9%) patients. Three (6.5%) patients underwent surgical intervention and therapeutic treatment was supplemented with surgery in 12 (26.1%) cases. One patient did not receive any treatment and information on treatment strategy of 2 patients was missing. Cytostatics were prescribed with or without glucocorticoids as initial therapy in 30 patients (65.2%). Other patients (14) received alternative treatment (antibiotics, glucocorticoids only, chemotherapy, alpha-blockers, surgical treatment only). All those patients who did not receive treatment with immunosuppressive drugs deceased during a short follow-up or developed severe complications. The patients on cytostatics undergoing maintenance therapy experienced relapse of GPA less frequently (4/13; 30.8%) than those free of cytostatics (8/14; 57.1%). The treatment outcomes were as follows: 17 (36.9%) patients achieved complete response, 15 (32.6%) had residual signs and/or complications, and 11 (25%) deceased during the follow-up.

Discussion

In 1963, Barkley Beideleman noted: "Nothing is certain about the syndrome of Wegener's granulomatosis except the complete lack of certainty" [31]. In our times we confidently classify GPA as antineutrophil cytoplasmic antibodies (ANCA)-associated vasculitis (AAV). The basis of its clinical manifestations is proliferative–destructive angiitis with primary affection of the microvasculature and perivascular granulomas prone to necrosis [1]. Although histopathological features of GPA are highly specific, clinical findings vary widely and span beyond the classic triad of symptoms.

Based on our analysis, frequency of reported cases of PI in GPA is increasing because of the improved diagnostics and awareness of atypical manifestations of GPA. A key question is, however, whether PI is specific for GPA and its severe course. Patients with PI can be categorized as those with systemic manifestations of vasculitis. Although multiple organ damages are characteristic for the latter, it is not recurrent and refractory to therapies (both are characteristics

Table 1 Clinical features of patient with GPA and prostatic involvement

Author/case	Age	PI as a first symptom of GPA	Manifestation of PI	Other organs involvement
Bansal [12]	64	No	Dysuria, acute urinary retention	Joints, hemoptysis, vocal cords
Bray [13]	N/A	N/A	N/A	Ears
	N/A	N/A	N/A	Lungs
	N/A	N/A	N/A	Lungs
	N/A	N/A	N/A	Ears, skin
	46	No	Painless gross hematuria	Nose, ear
	55	No	Decreased urinary stream, dysuria	Nose, lungs
	49	No	Dysuria, decreased urinary stream	Joints, heart (pericarditis), lungs
Brunner [14]	51	Yes	Gross hematuria and mild dysuria	Ear, nose, joints, CNS
Chan [15]	48	Yes	Hematuria, dysuria, urinary retention	Lungs, skin, joints, kidney
Davenport [16]	73	Yes	Penile discharge, urinary retention	Lungs, urethra
Dufour [17]	51	No	Acute urinary retention	Ear, nose, heart (pericarditis), lungs, large bowel
	65	No	Dysuria, gross hematuria	Ear, nose, lungs, purpura, kidney
	55	Yes	Dysuria, gross hematuria	Ear, nose, joints
	46	No	Gross hematuria, recurrent urinary tract infections	Ear, nose, joints, skin, lungs, kidney, CNS, heart
Gaber [18]	28	No	Dysuria, perineal pain, urinary retention	Nose, lungs, peripheral nerves
Gunnarsson [19]	52	No	Urinary tract obstruction	Nose
Heldmann [20]	46	Yes	Gross hematuria, perineal pain	Nose, joints(arthralgia, arthritis)
Huong [7]	44	N/A	Acute urinary retention	Nose, larynx, parotid gland, optical nerve
	37	Yes	Dysuria, pelvic pain, gross hematuria Acute urinary retention	Nose, parotid gland, lungs, CNS, hyperplastic gingivitis
	61	N/A	Acute urinary retention	Nose, lungs, kidney, joints
Khattak [21]	48	No	Urethralgia, dysuria, poor urinary flow	Nose, large bowel
Middleton [11]	65	Yes	Obstructive uropathy, severe LBP	Lungs, kidney
Murthy [22]	37	Yes	Dysuria	Lungs
Navarro [23]	63	No	Hematuria, frequency, nocturia and poor urinary flow	Kidney, lungs, eye
Sozer [24]	53	No	Nocturia, slowing urination	Nose
Stillwell [25]	51	No	Gross hematuria, dysuria	Mediastinum, lungs
	71	No	Chronic moderate obstructive voiding	Lungs, penis
Suryaprakash [26]	45	No	Poor urinary stream, dysuria, acute urinary retention	Nose, lungs
Takeuchi [27]	65	Yes	Urinary retardation, dysuria, gross hematuria	Lungs
Tsiodras [2]	41	No	Pyuria and hematuria	Skin, eyes, lungs
Tung [28]	52	No	Acute urinary retention	Ear, nose, lungs, kidney
	40	No	End-stream hematuria	Nose, lungs
Vaught [29]	55	Yes	Decreased force of stream, frequency, nocturia	Nose, lungs
Yalowitz [30]	27	No	Gross hematuria	Lungs, joints, nose, skin, eyes
	34	No	None	Joints, nose, skin, kidney
	50	No	None	Orchitis, lungs,
	38	No	Non-specific prostatitis	Lungs, nose, eyes
	63	Yes	Acute urinary retention	Eyes, pharynx, vocal cords, lungs
	47	No	None	N/A
	29	No	None	N/A
	58	No	None	Lungs, nose, joints, skin, kidney
	82	Yes	Acute urinary retention	Lungs
	60	No	None	Nose, lungs
	45	No	Prostatic obstruction, secondary infection	Nose, lungs

N/A not available information

Table 2 Laboratory findings in the patients with GPA and prostatic involvement

	Blood analysis														
	ESR			CRP			Cr			PR3/ANCA			PSA		
	Sl. el.	High	N/A	N	High	N/A	N	High	N/A	Pos.	Neg.	N/A	Pos.	Neg.	N/A
No/total no	2/46	17/46	27/46	1/46	12/46	33/46	12/46	6/46	28/46	21/46	1	24/46	5/46	6/46	35/46
%	4.3	37.0	58.7	2.2	26.1	71.7	26.1	13.0	60.9	45.6	2.2	52.2	10.9	13.0	76.1

Author/case	Urinalysis abnormalities
Bansal [12]	Numerous WBC and RBC
Bray [13]	N/A
	N/A
	N/A
	3+ proteinuria, 50–100 RBC, 50–100 WBC
	Hematuria, leukocyturia, proteinuria
	RBC too numerous to count, 26 WBC, proteinuria 30 mg/dL
Brunner [14]	250 RBC, 75 WBC, few hyaline and cellular casts
Chan [15]	Pyuria
Davenport [16]	N/A
Dufour [17]	Normal
	Gross hematuria, protein 0.6 g/day
	Gross hematuria
	Gross hematuria, protein 1.04 g/day
Gaber [18]	Normal
Gunnarsson [10]	30 WBC, 4 RBC, protein 0.63 g/day
Heldmann [26]	> 500 WBC, muddy urine, 10–20 RBC
Huong [7]	N/A
	Leukocyturia, hematuria
	N/A
Khattak [21]	No cells or casts, protein level was < 1 g/day
Middleton [11]	N/A
Murthy [22]	Microscopic hematuria and a sterile pyuria
Navarro [23]	Recurrent hematuria, some leukocytes in urinary dipstick
Sozer [24]	N/A
Stillwell [25]	Trace of protein, 10–30 RBC, 50–100 WBC
	1+ to 2+ proteinuria, 50–100 RBC, 50–100 WBC
Suryaprakash [26]	Traces of albumin and 8–10 pus cells
Takeuchi [27]	30–40 WBC and 5–9 RBC. Urine cytology is class IIIa
Tsiodras [2]	Pyuria, hematuria
Tung [28]	Normal
	N/A
Vaught [29]	Sterile pyuria, 3–5 WBC, 3–5 RBC

Table 2 (continued)

Author/case	Urinalysis abnormalities
Yalowitz [30]	Slight trace to 3 plus albumin, many finely and coarsely granular casts and many RBC
	A few RBC, WBC and casts
	Normal
	1+ albumin, occasional casts
	2+ proteinuria, many WBC; urine culture+
	N/A
	N/A
	1+ albumin, 6–8 WBC, innumerous RBC, many granular casts
	1+ albumin, "loaded" RBC, 15–20 WBC
	2+ albumin, 50–100 RBC
	Grade 1–2 proteinuria, grade 1 erythrocyturia, grade 3–4 leukocyturia, culture: proteus

N/A not available information, *RBC* red blood cell, *Sl. el.* slight elevated (not above 15 mm/h), *WBC* white blood cells

of the limited form known as "grumbling disease") [32, 33]. There were no differences by comparing various organ systems involvement between systemic form of GPA without PI [4] and selected cases of GPA with PI. ENT involvement rate among review cases (84.8%) is comparable with literature data 70–100% [4], same also with lungs involvement: 71.7% in our study and 50–90% in others [4]. However, the kidneys are affected less frequently in patients with GPA and PI (22%) than in those without PI (40–100%) [4, 7, 34].

Laboratory indices in patients with PI in GPA are no different from those characteristics for GPA (CRP and ESR are increased, cANCA and/or pANCA are positive in 95.2% (21/22) of patients). However, PSA test is crucial for comprehensively evaluating PI. Since the average age of patients included in our analysis is above 50, the increase of PSA, especially in combination with radiological signs of lung injury (nodules), can be mistakenly interpreted as prostate cancer with metastases.

The ACR Classification Criteria of GPA included ANCA positivity as a diagnostic criterion. Experimental studies also suggested that ANCA play a major role in the disease progression [35].

According to the review data cANCA is more common than pANCA positivity by the patients with GPA and PI. In 1 case ANCA positivity was declared without specification and in another one there were positive both types of ANCA, therefore, they were excluded from the count. Due to the performed analysis we got the following results: (17/19 [89.5%]) of the observed cases were cANCA positive and the rest (2/19 [10.5%]) were positive for pANCA. The latter proportions are comparable with those of a single-centre study on 364 GPA patients (cANCA and pANCA positivity in 91.7% and 7.1%, respectively) [36]. One study, however, pointed to cANCA and pANCA positivity in 39% and 45% of cases, respectively [37]. Such a discrepancy can be due to relatively small sample (38 patients) and high prevalence of females in the second study (82% of the pANCA-GPA group cases were female [37]).

Our analysis demonstrated that the most effective initial treatment for PI in GPA includes immune suppressive drugs and glucocorticosteroids. Cyclophosphamide is more preferable than other immune suppressive agents; there are only 3 published reports on azathioprine and 1 report on rituximab therapy.

To sum up, PI in GPA is rare but not casuistic. Rheumatologists and urologists should be aware of such a clinical combination to choose correct management tactics and avoid unnecessary surgical interventions. Our case highlights the complexity of manifestations in GPA that can be presented without specific features of nasal biopsy, necessitating histological examination of atypical affections.

Table 3 Peculiarities of treatments strategies and outcome

Author/case	Treatment		Outcome
	Initial therapy	Other treatment	
Bansal [12]	CYC + GC	MT: MX	CR
Bray [13]	CYC	–	Hemorrhagic cystitis
	CYC	–	Inactive sediment
	CYC + GC	–	Hemorrhagic cystitis
	None	TURP	Deceased 21 days after TURP
	None	–	Deceased 25 days after cystoscopy
	CYC + GC	–	Inactive sediment at 18 months
	TMP-SMX + GC	CYC TURP	Mild prostatic obstructive symptoms; in 13 months recurrence; after TMP-SMX + GC + CYC = CR
Brunner [14]	CYC + GC	MT: AZA	CR
Chan [15]	CYC + GC	A/b, TURP	Patient is dialysis dependent
Davenport [16]	Prostatectomy	–	Without response
Dufour [17]	CYC + GC = PR (persistent dysuria)	TURP, oral CYC = CR MT: AZA	No GPA relapse; recurrent urinary tract infections; recent diagnosis of prostatic carcinoma
	CYC + GC	MT: MMF	Urogenital relapse (prostatitis with acute urinary retention under MMF) treated with TURP
	CYC + GC	MT: MTX + GC	CR
	CYC + GC	–	2 relapses of GPA with prostatitis recurrences treated with (1) MMF + GC = CR, (2) CYC + GC = CR Recent relapse of GPA without urogenital manifestation treated with R
Gaber [18]	CYC + GC	MT: AZA	In 5 years, a relapse with PI CYC + GC in 3 months; MT: AZA = no relapse, but stricture in the bulbar urethra occurred
Gunnarsson [19]	CYC + GC	MT: MX + GC	CR
Heldmann [20]	CYC + GC	MT: MX + GC	Focus neuropathy of the left leg and epididymis occurred, after increase of dosage—CR
Huong [7]	GC; CYC + GC	Suprapubic cystostomy TURP	1 relapse with acute urinary retention, cured by CYC + GC; CR on low dose of GC
	CYC + GC	MT: CYC + GC Suprapubic cystostomy	Urinary incontinence, retrograde ejaculation persisted
	CYC + GC	Suprapubic cystostomy	CR
Khattak [21]	CYC + GC	TURP	1 relapse with PI, after TURP—CR
Middleton [11]	CYC	–	CR
Murthy [22]	CYC + GC	–	CR
Navarro [23]	GC + CYC + R GC + R	MT: AZA + GC and R; TURP MT: R	2 relapses of GPA treated with R After occurrence of PI: TURP and GC + R; MT with R—no relapses
Sozer [24]	Suprapubic prostatectomy		Deceased in 7 months of follow-up
Stillwell [25]	CYC	CYC (150 mg/day)	After treating with CYC in 3 years a relapse with PI; 2 years therapy with CYC—CR
	CYC + GC	MT: CYC (100 mg/day); TURP	In 5 years, a relapse with gross hematuria; in otherwise remains good health
Suryaprakash [26]	CYC + GC	–	1 relapse with subglottic stenosis, sensorineural deafness, then patient was lost to follow-up, presumed that he died
Takeuchi [27]	Alpha blocker	TURP	N/A
Tsiodras [2]	MMF + GC	A/b with no improve	CR
Tung [28]	CYC + GC	Plasmapheresis, dialysis	Improve after TUR prostatectomy
	GC + AZA	A/b; TURP	End-stream hematuria persisted
Vaught [29]	CYC + GC	–	CR

Table 3 (continued)

Author/case	Treatment		Outcome
	Initial therapy	Other treatment	
Yalowitz [30]	A/b	–	Deceased in 2 months after the second admission
	GC	A/b	Deceased in 1 year after first symptom
	Chemotherapy	–	Deceased in 3 weeks after admission
	GC + ACTH	Radiotherapy, triethylene melamine, stilbestrol, testosterone	Patient became almost blind
	GC + A/b	Supportive therapy	Deceased on the 51 day after admission
	N/A	N/A	N/A
	N/A	N/A	N/A
	GC	A/b	Deceased in 8 months after the onset of the disease
	A/b	–	Deceased on the 4th day after admission
	GC	A/b	Deceased in about 2 weeks after admission
	GC	TURP	Deceased in 3 weeks after diagnosis

A/b antibiotics, *ACTH* adrenocorticotropic hormone, *AZA* azathioprine, *CR* complete response, *CYC* cyclophosphamide, *GC* glucocorticoid, *MX* methotrexate, *MMF* mycophenolate mofetil, *MT* maintenance therapy, *N/A* not available information, *PR* partial response, *R* rituximab, *TURP* transurethral resection of prostate

Author contributions RY supervised the patient management, interpreted the obtained data, and edited manuscript. OZ manuscript writing and revision, took part in the consultations for the reported case. MB performed pathomorphological examination, interpreted the data, and revised the manuscript. BD collected data and wrote the initial version of the manuscript, took part in the consultations for the reported case. VH took part in the patient management and manuscript writing. All authors approved the final manuscript for publication.

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Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Written informed consent was obtained from the patient reported in the study.

References

1. Zerbino DD, Zimba EA (2015) Morphological pathology of vessels in granulomatosis with polyangiitis (Wegener's disease). Arkh Patol 77(5):9–13. https://doi.org/10.17116/patol20157759-13
2. Tsiodras S, Poulakou G, Leventakos K, Panopoulou H, Elezoglou A, Manoloudaki K, Panayiotides IG (2016) 'Prostate abscess' as the initial manifestation of granulomatosis with polyangiitis (Wegener's granulomatosis). Urol Int 96(2):244–246
3. Watts RA, Mahr A, Mohammad AJ, Gatenby P, Basu N, Flores-Suarez LF (2015) Classification, epidemiology and clinical subgrouping of antineutrophil cytoplasmic antibody(ANCA)-associated vasculitis. Nephrol Dial Transplant 30(1):14–22
4. Comarmond C, Cacoub P (2014) Granulomatosis with polyangiitis (Wegener): clinical aspects and treatment. Autoimmun Rev 13(11):1121–1125
5. Pearce FA, Grainge MJ, Lanyon PC, Watts RA, Hubbard RB (2017) The incidence, prevalence and mortality of granulomatosis with polyangiitis in the UK Clinical Practice Research Datalink. Rheumatology 56(4):589–596. https://doi.org/10.1093/rheumatology/kew413
6. Alba MA, Moreno-Palacios J, Beça S, Cid MC (2015) Urologic and male genital manifestations of granulomatosis with polyangiitis. Autoimmun Rev 14(10):897–902
7. Huong DL, Papo T, Piette JC, Wechsler B, Bletry O, Richard F, Godeau P (1995) Urogenital manifestations of Wegener granulomatosis. Medicine 74(3):152–161
8. Gasparyan AY, Ayvazyan L, Blackmore H et al (2011) Writing a narrative biomedical review: considerations for authors, peer reviewers, and editors. Rheumatol Int 31:1409–1417. https://doi.org/10.1007/s00296-011-1999-3
9. Leavitt RY, Fauci AS, Bloch DA, Michel BA, Hunder GG, Arend WP et al (1990) The American College of Rheumatology 1990 criteria for the classification of Wegener's granulomatosis. Arthritis Rheum 33:1101–1107
10. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F et al (2013) 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum 65:1–11
11. Middleton G, Karp D, Lee E, Cush J (1994) Wegener's granulomatosis presenting as lower back pain with prostatitis and ureteral obstruction. J Rheumatol 21(3):566–569
12. Bansal N, Duggal L, Jain N, Jain S, Sharma A, Arora N (2017) Prostate involvement in granulomatosis with polyangiitis: a rarity. Int J Rheum Dis 20(11):1841–1842
13. Bray VJ, Hasbargen JA (1991) Prostatic involvement in Wegener's granulomatosis. AJKD 17(5):578–580
14. Brunner A, Tzankov A, Akkad T, Lhotta K, Bartsch G, Mikuz G (2004) Wegener's granulomatosis presenting with gross hematuria due to prostatitis. Virchows Arch 444(1):92–94

15. Chan J, Braun M, Elzawawy H, Berho M, Kirsch J (2012) Granulomatosis with polyangiitis presenting as prostatitis: an uncommon scenario. WJNU 1(2–3):94–97
16. Davenport A, Downey SE, Goel S, Maciver AG (1996) Wegener's granulomatosis involving the urogenital tract. Br J Urol 78(3):354–357
17. Dufour JF, Le Gallou T, Cordier JF, Aumaître O, Pinède L, Aslangul E, Dubois A (2012) Urogenital manifestations in Wegener granulomatosis: a study of 11 cases and review of the literature. Medicine 91(2):67–74
18. Gaber KA, Ryley NG, MacDermott JP, Goldman JM (2005) Wegener's granulomatosis involving prostate. Urol 66(1):15
19. Gunnarsson R, Omdal R, Kjellevold KH, Ellingsen CL (2004) Wegener's granulomatosis of the prostate gland. Rheumatol Int 24(2):120–122
20. Heldmann F, Brandt J, Schoppe H, Braun J (2006) A 46-year-old-patient with granulomatous prostatitis, arthralgia and haemorrhagic rhinitis. Dtsch Med Wochenschr 131(1–2):22–25
21. Khattak AQ, Nair M, Haqqani MT, Williamson EP (1999) Wegener's granulomatosis: prostatic involvement and recurrent urinary tract infections. BJU Int 84(4):531–532
22. Murty GE, Powell PH (1991) Wegener's granulomatosis presenting as prostatitis. Br J Urol 63:107–108
23. Navarro D, Pusey C (2018) Prostate involvement in granulomatosis with polyangiitis: response to rituximab treatment. Port J Nephrol Hypertens 32(1):75–77
24. Sözer IT (1986) Wegener's granulomatosis with infiltration of the prostate. Br J Urol 58(2–4):335
25. Stillwell TJ, DeRemee RA, McDonald TJ, Weiland LH, Engen DE (1987) Prostatic involvement in Wegener's granulomatosis. J Urol 138(5):1251–1253
26. Suryaprakash V, Murthy P, Liza R, Ramreddy Ch, Srinivas N, Prayag A (2006) Wegener's granulomatosis of urinary tract presenting as bladder outlet obstruction. Indian J Urol 22:264–265
27. Takeuchi H, Kuroda I, Takizawa I, Aoyagi T, Tachibana M (2016) Granulomatosis with polyangiitis (Wegener's granulomatosis) accompanied by dysuria. Urol Case Rep 2016:3. https://doi.org/10.1155/2016/7812875
28. Tung KT, Woolf A, Falzon M (1987) Prostatic involvement in Wegener's granulomatosis. Postgrad Med J 63(735):53–54
29. Vaught WW, Wilson TM, Raife MJ, Horne DW (1989) Wegener granulomatosis: prostatic involvement and bladder outlet obstruction. Urol 34(1):43–45
30. Yalowitz PA, Greene LF, Sheps SG, Carlin MR (1966) Wegener's granulomatosis involving the prostate gland: report of a case. J Urol 96:801–804
31. Beidleman B (1963) Wegener's granulomatosis: prolonged therapy with large doses of steroids. JAMA 186(9):827–830. https://doi.org/10.1001/jama.1963.03710090027005
32. Hoffman GS, Kerr GS, Leavitt RY, Hallahan CW, Lebovics RS, Travis WD et al (1992) Wegener granulomatosis: an analysis of 158 patients. Ann Intern Med 116:488–498
33. Holle JU, Gross WL, Holl-Ulrich K, Ambrosch P, Noelle B, Both M et al (2006) Prospective long-term follow-up of patients with localised Wegener's granulomatosis: does it occur as persistent disease stage? Ann Rheum Dis 69:1934–1939
34. Sinico RA, Di Toma L, Radice A (2013) Renal involvement in anti-neutrophil cytoplasmic autoantibody associated vasculitis. Autoimmun Rev 12(4):477–482
35. Salama AD, Little MA (2012) Animal models of antineutrophil cytoplasm antibody-associated vasculitis. Curr Opin Rheumatol 24:1–7
36. Kallenberg CG (2015) Pathogenesis and treatment of ANCA-associated vasculitides. Clin Exp Rheumatol 33(4 Suppl 92):11–14
37. Ono N, Niiro H, Ueda A, Sawabe T, Nishizaka H, Furugo I, Tada Y (2015) Characteristics of MPO-ANCA-positive granulomatosis with polyangiitis: a retrospective multi-center study in Japan. Rheumatol Int 35(3):555–559