Acute renal failure as the presenting sign of disseminated intravascular coagulation in a patient with metastatic prostate cancer

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Abstract: Disseminated intravascular coagulation (DIC) is the most frequent coagulation disorder in patients with prostate cancer. However, renal involvement in DIC associated with prostate cancer has rarely been documented. Herein, we present a case of metastatic prostate cancer presenting with acute renal failure (RF) triggered by DIC. An 80 year old man with metastatic prostate cancer was treated with antihormone therapy at an outpatient clinic. He was admitted to our hospital because of severe dyspnea and progressive RF. A hemorrhagic tendency was not clinically evident. Laboratory tests exhibited a significant coagulation disorder, suggestive of DIC. Despite treatment, his RF and dyspnea worsened, and he eventually passed away. An autopsy study revealed hypertensive nephrosclerosis superimposed by fibrin rich thrombi formation involving glomerular capillaries and arterioles characteristic of DIC. Additionally, focal segmental glomerulosclerosis was identified, which was presumably secondary to the glomerular endothelial and/or podocyte injury augmented by DIC. Those findings showed that glomerular injury, which was induced and subsequently exacerbated by DIC associated with prostate cancer, highly contributed to the progression of RF in our case. A differential diagnosis of DIC should be considered when a patient with prostate cancer presents with renal dysfunction.

Keywords: disseminated intravascular coagulation, prostate cancer, renal pathology

Introduction

Disseminated intravascular coagulation (DIC) is the most frequent coagulation disorder in patients with prostate cancer. DIC occasionally occurs as a presenting sign of metastatic prostate cancer. Clinical symptoms of DIC associated with prostate cancer range from a subclinical marker of disease to overt bleeding after trauma or surgical procedures.

Despite its frequent occurrence, little is known about the clinical presentation of DIC in prostate cancer. Specifically, renal involvement in DIC as a presenting sign has not been reported in the literature. In the present article, we describe an autopsy case of metastatic prostate cancer presenting with progressive renal dysfunction, which was augmented by DIC. We have described this case with emphasis on the renal histopathology characteristic of DIC, and include a brief review of the literature. This unusual case presentation demonstrates that DIC should be considered when prostate cancer patients present with renal dysfunction due to unknown etiology and therefore a comprehensive work up for DIC should be performed even in the absence of apparent hemorrhagic tendency.

Case presentation

An 80-year-old Japanese man was found to have increased serum prostate specific antigen levels of 231.5 ng/mL (normal: <1.0 ng/mL) on a routine medical checkup. He had...
a long-standing history of hypertension and underwent a needle biopsy of the prostate gland that showed Gleason 4 + 5 = 9 adenocarcinoma. A computed tomography scan revealed that the tumor had invaded the bladder, and multiple metastatic lesions were found in the lumbar regions. He was started on a luteinizing hormone releasing hormone agonist (leuprolide) and androgen antagonist (flutamide), and was followed at an outpatient clinic. His serum creatinine levels were within a normal range (0.8–1.4 mg/dL) at this time.

The patient’s prostate specific antigen level increased to 1530 ng/mL 4 months later. A computed tomography scan revealed an increasing number of metastatic lesions in the lumbar bones. At this time, he complained of dyspnea that was probably due to pulmonary edema. His serum creatinine was 2.1 mg/dL. After 1 month, his dyspnea worsened as the renal failure progressed with a creatinine level of 2.89 mg/dL. A urine test showed strong presence of protein (++++) and occult blood (++) His serum total protein was 5.8 g/dL (normal: 6.0–8.3 g/dL), and his albumin was 2.3 g/dL (normal: 3.5–5.5 g/dL). He was admitted to the intensive care unit for further investigation and treatment.

Laboratory evaluation performed on the first day of intensive care unit admission revealed the following results: hemoglobin level, 10.2 g/dL; platelet count, 60 × 10^3/µL (normal: 150–400 × 10^3/µL); and total leukocyte count, 18.2 × 10^3/mm^3 (normal: 4.0–11 × 10^3/mm^3). His prothrombin time was 16.3 seconds (normal: 11.5–15.5 seconds), and his prothrombin time and international normalized ratio was 1.8 (normal: 1–1.25). The activated partial prothrombin time was 38.5 seconds (normal: 25.2–36 seconds); the serum fibrinogen level, 168 mg/dL (normal: 170–410 mg/dL); and D-dimer level, 28.8 µg/mL (normal: <1.0 µg/mL). His fibrin degradation product level was 93.9 µg/mL (normal: <10 µg/mL).

Although a bleeding tendency was not clinically evident, he was diagnosed with DIC based on the laboratory data. Treatment with antithrombin-III and blood transfusion was initiated. On the second day at the intensive care unit, he had oliguria associated with a serum creatinine level of 5.19 mg/dL, for which hemodialysis was started. His serum total protein was 5.1 g/dL, and his albumin level was 1.9 g/dL. The dyspnea progressively worsened despite treatment. His serum creatinine ranged from 4.5–5.0 mg/dL. Chest X-ray revealed pulmonary infiltrates in both lungs, which was suggestive of alveolar hemorrhage. On day 14, he experienced cardiac arrest and expired. An autopsy was performed after obtaining permission from family members which was suggestive of alveolar hemorrhage. On day 14, Chest X-ray revealed pulmonary infiltrates in both lungs, which was suggestive of alveolar hemorrhage. On day 14, his dyspnea progressively worsened despite treatment. His serum creatinine ranged from 4.5–5.0 mg/dL. Chest X-ray revealed pulmonary infiltrates in both lungs, which was suggestive of alveolar hemorrhage. On day 14, he experienced cardiac arrest and expired. An autopsy was conducted after obtaining permission from family members to elucidate the mechanisms of renal failure (RF).

**Discussion**

DIC has been one of the most common complications of prostate cancer since the first report in 1953. Clinical signs of DIC are noted in only 0.4%–1.65% of patients with prostate cancer, including a bleeding tendency. In these patients, DIC can be triggered by surgical procedures like prostate biopsy causing hemorrhage in multiple sites, such as the skin, genitourinary organs, gastrointestinal tracts and
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and medium sized vessels. In cancer patients, tumor cells removal of fibrin results in thrombotic occlusion of small The combination of increased formation and impaired anticoagulation mechanism, and inadequate fibrinolysis. an increased generation of thrombi, impaired physiological occurrence of systemic fibrin formation resulting from the coagulation pathway. 

In our case, the patient had prostate cancer with a Gleason high grade disease (Gleason scores of eight, nine, or ten). Another remarkable renal finding in our case was FSGS. FSGS is a pattern of glomerular injury that occurs as a primary form or as secondary to many conditions. The cause of primary FSGS is usually unknown, and patients often present with significant nephrotic syndrome, which was not identified in our case. In contrast, secondary forms of FSGS may be associated with a variety of conditions, including chronic hypertension, pyelonephritis, morbid obesity, and renal transplantation. A possible mechanism of secondary FSGS is a reduced number of nephrons, which increases glomerular pressure within remnant glomeruli and results in glomerular podocyte and/or endothelial injury. In our case, the patient appeared to have a reduced number of nephrons.
due to hypertensive nephrosclerosis before the onset of DIC. We therefore speculate that the occurrence of DIC to the kidney with reduced nephrons may have augmented podocyte and/or endothelial injury of glomeruli, resulting in FSGS.

In summary, we have reported an autopsied patient who died of DIC associated with metastatic prostate cancer. This case was unique because acute RF was the initial presenting sign of DIC. We described clinicopathological aspects of DIC in prostate cancer and renal pathology of DIC along with a brief review of the literature. We propose that a differential diagnosis of DIC should be considered when a patient with prostate cancer presents with renal dysfunction and that complete physical and laboratory tests, including coagulation study, should be performed to detect a cause of renal dysfunction even in the absence of hemorrhagic tendency.

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Disclosure
The authors report no conflicts of interest in this work.

References
Renal failure in DIC associated with prostate cancer