



Oncology

Trousseau's syndrome manifesting as multiple cerebral infarctions caused by bladder cancer

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ABSTRACT

Cerebral infarction in patients with cancer is often called Trousseau's syndrome, which is a cancer-associated hypercoagulable state that causes thrombosis; however, the syndrome is rarely caused by bladder cancer. We report a case of Trousseau's syndrome manifesting as multiple cerebral infarctions caused by advanced bladder cancer in a 46-year-old male patient. The patient died due to the infarctions in the hospital. The prognosis of patients with Trousseau's syndrome caused by advanced cancer is poor. According to changing urological clinical settings, considering the risk of Trousseau's syndrome has become crucial for urologists treating patients with advanced cancer.

Introduction

Cerebral infarction (CI) that develops in patients with cancer is often called Trousseau's syndrome, which is a cancer-associated hypercoagulable state that causes venous or arterial thrombosis, and is well known among neurologists and cardiologists.^{1,2} Owing to the absence of a standard definition, Trousseau's syndrome could broadly include all types of cancer-associated thromboses (CAT). In a narrow definition, it would include only severe thromboses, such as symptomatic CI.^{1,2} Adenocarcinoma and mucinous carcinoma in the lung, pancreas, breast, ovary, stomach, or prostate are known as the causative cancer of this syndrome; however, the syndrome being caused by bladder cancer has rarely been reported in the literature.^{3,4} Here, we report the case of a male patient in whom Trousseau's syndrome manifested as crucial multiple CIs caused by bladder cancer following *trans*-urethral resection (TUR) in the hospital.

Case presentation

A 46-year-old male presented with gross hematuria to our department. Based on cystoscopy, urine cytology, and computed tomography results, he was diagnosed with advanced bladder cancer with right-side hydronephrosis and multiple lymph node enlargements (Fig. 1). He was a smoker and was undergoing medication for hypertension and diabetes mellitus (DM). The serum fibrin degradation product (FDP) and D-

dimer levels were not measured, because we did not routinely measure them pre-operation; however, results of blood laboratory examination were almost within normal range, except for the serum creatinine level at 1.76 mg/dL. Electrocardiogram and echocardiography revealed no arrhythmia or heart failure. TUR, which was an incomplete resection, was performed uneventfully under general anesthesia, and the patient survived until the following night after the operation as usual. The patient's course in the hospital was uneventful until early on the second morning after the operation. He suddenly presented with paralysis and disturbance of consciousness. Multiple CIs were revealed using magnetic resonance imaging (MRI) (Fig. 2). At the time, results of blood laboratory examination were as follows: platelets 15.9×10^4 counts/ μ L, creatinine 2.93 mg/dL, activated partial thromboplastin time (APTT) 79.8%, international normalized ratio of prothrombin time (PT-INR) 1.10, FDP 76.4 (normal value, < 5) μ g/mL, and D-dimer 21.6 (normal value, < 1) μ g/mL. A neurologist examined the patient and determined that the CIs were Trousseau's syndrome, and worsened renal failure suggested the presence of renal thrombosis. Although anticoagulant therapy was considered, it was forgone because the CIs were considerably extensive for recovery and the concern about bleeding from either the remaining bladder cancer or CI lesions existed. Following palliative treatment for 3 weeks in the hospital, the patient presented with coma, suggesting the development of a second episode of CI, and he died. Histopathological findings revealed high-grade urothelial carcinoma (Fig. 3).

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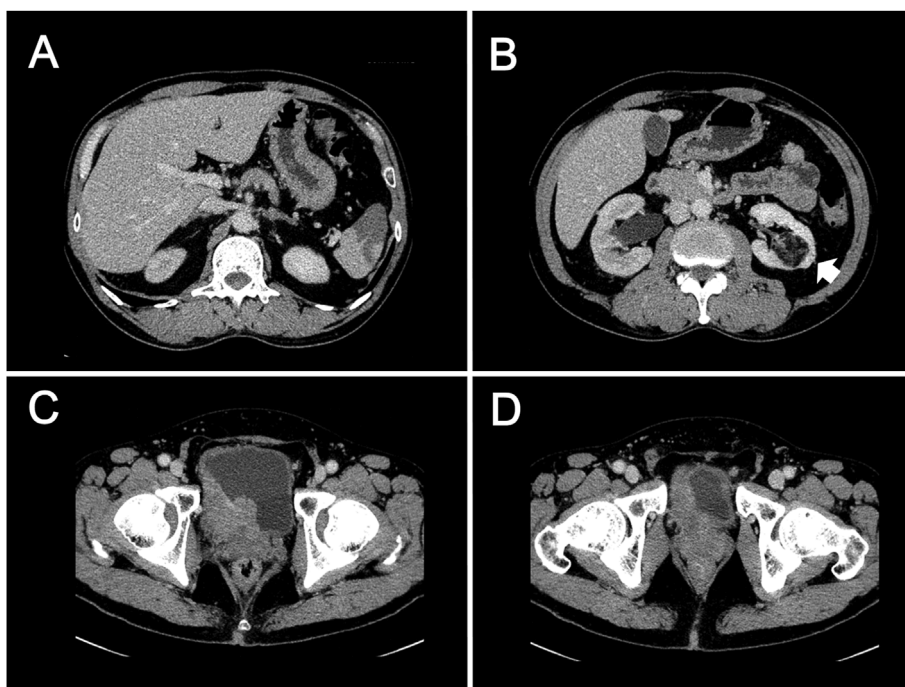


Fig. 1. Abdominal computed tomography. Computed tomography revealed an asymptomatic splenic infarction (A), right-side hydronephrosis and an angiomyolipoma in the left kidney (white arrow) (B), large invasive bladder cancer suggesting prostate invasion with bilateral extra-iliac lymph node enlargements (C, D).

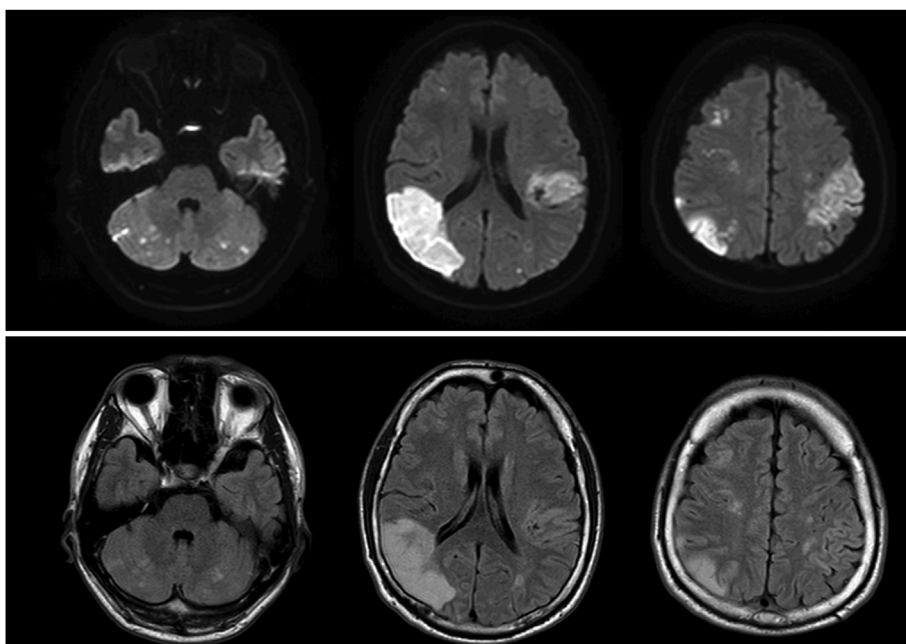


Fig. 2. Magnetic resonance imaging (MRI) of the brain. Diffusion-weighted images (DWI) (upper). Fluid-attenuated inversion recovery images (FLAIR) (lower). Non-segmental multiple cerebral infarctions of various sizes are revealed in the cerebellum, cerebral cortex, and the cerebral white matter. Because these infarctions appeared as high-density areas using DWI and as iso- or high-density areas using FLAIR, these were ultra-acute infarctions.

Discussion

Trousseau's syndrome is a paraneoplastic syndrome, and CI due to Trousseau's syndrome is one of important causes of mortality in patients with cancer. It has been suggested that approximately 15% of patients with cancer had a concomitant cerebrovascular disease that included CI but not only CI.^{2,5} Because CAT including CI due to Trousseau's syndrome in patients with urological cancer has mainly been reported as clinical case reports, the incidence of such thromboses caused by urological cancer would be low. However, risk factors for CAT, such as older age, presence of a comorbidity, prolonged immobility, prior history of thrombosis, advanced cancer, and history of chemotherapy or hormonal agents, are increasing among patients with urological cancer

in clinical practice corresponding to the extension of their prognosis or average life span.^{1,2,5} Therefore, considering CAT as Trousseau's syndrome has become more crucial for urologists. Our present case included characteristics, such as the presence of hypertension and DM, receiving bed rest for a night following the surgery, asymptomatic splenic thrombosis, and advanced bladder cancer. To our best knowledge, this case was the fourth reported case of CI as Trousseau's syndrome caused by bladder cancer, but it was the second reported case of severe CI caused by bladder cancer that was sufficient to directly lead to death.^{3,4} The characteristics of CI as Trousseau's syndrome observed using MRI include lesions that are multiple, disseminated, bilateral, and of various sizes, located across the governing region of different cerebral arteries, and often with cerebellar infarction.² The CIs of our

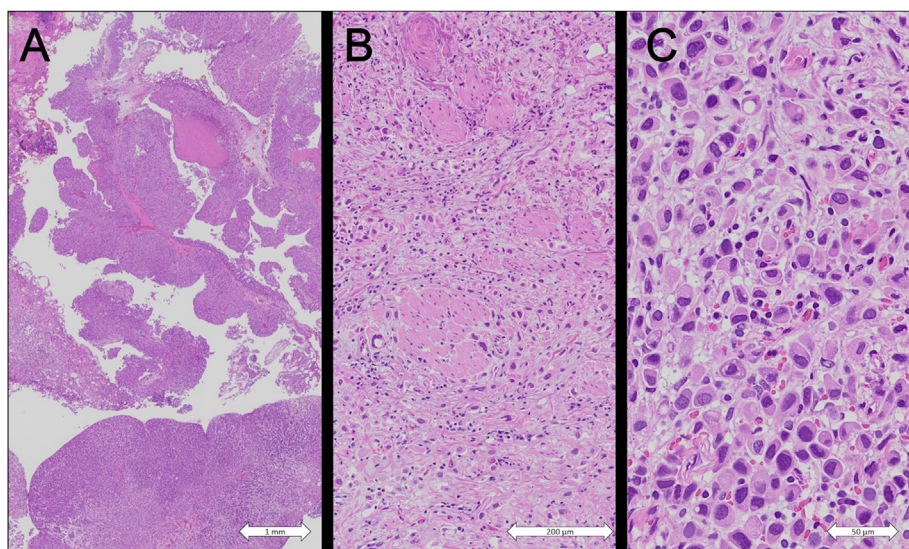


Fig. 3. Histopathological findings. Hematoxylin and eosin staining. Bladder cancer resected via *trans*-urethral resection (A). Exhibition of muscle-invasion (B) and lymphoma-like high-grade urothelial carcinoma (C).

present case matched these characteristics. Currently, there is no specific biochemical marker for CAT diagnosis. According to the diagnostic criteria for disseminated intravascular coagulation (DIC), serum platelet, APTT, PT-INR, FDP, and D-dimer levels are used as general markers of thrombosis, and an increase in serum D-dimer level would reflect the CAT more sensitively than the other markers in pre-DIC state.^{1,2,5}

Heparin is recommended as the standard treatment for acute CAT.^{1,2,5} However, the benefits of anticoagulant therapy should be weighed against the risks—particularly, the bleeding risk. When our present case developed CI, we decided against heparin use because there was a concern of bleeding from both extensive CIs and remaining bladder cancer. Because patients with CAT exhibit a higher incidence of recurrent CAT, the importance of long-term anticoagulant therapy for CAT has been emphasized; however, the prognosis of patients who developed CAT is poor unless causative cancer can be effectively controlled.^{1,2,5}

Conclusion

Trousseau's syndrome is a paraneoplastic syndrome, and the prognosis of patients in whom it is caused by advanced cancer is poor. Because the incidence of the syndrome could possibly increase in the urological clinical setting, urologists treating patients with cancer should consider the risk of CAT as Trousseau's syndrome.

Consent

Verbal informed consent was obtained from the patient for the publication of this case report.

Declarations of interest

None.

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Abbreviations

APTT	activated partial thromboplastin time
CAT	cancer-associated thrombosis
CI	cerebral infarction
CT	computed tomography
DM	diabetes mellitus
FDP	fibrin degradation products
MRI	magnetic resonance imaging
PT-INR	international normalized ratio of prothrombin time
TUR	<i>trans</i> -urethral resection

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.eucr.2019.100884>.

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