



## Case Report

# Rapid resolution of prostate cancer-related hemolytic uremic syndrome without plasma exchange – a case report



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## Introduction

Thrombotic microangiopathy is a broad term that encompasses a range of conditions from immune-mediated thrombotic thrombocytopenic purpura (TTP) to complement-mediated atypical hemolytic uremic syndrome (aHUS).<sup>1</sup> The typical presentation involves microangiopathic hemolytic anemia (MAHA), consumptive thrombocytopenia and acute renal failure, with varying degrees of fever and neurological dysfunction.<sup>1,2</sup> Patients with cancer are at an increased risk of thrombotic microangiopathy, however, it is a rare phenomenon and the underlying pathophysiology remains unclear.<sup>2</sup> A pronounced association has been reported between prostate cancer and MAHA/TTP-like illness.<sup>1,3</sup> For purposes of this report, we will refer to MAHA/TTP-like illness as cancer-related hemolytic uremic syndrome (CR-HUS).

Gastric, breast and lung are other examples of cancers commonly associated with CR-HUS, with up to 91.8% of patients having metastatic disease.<sup>1</sup> In the setting of prostatic cancer, in addition to treating the underlying malignancy, most cases are also treated with plasma exchange, without clear evidence supporting its benefit.<sup>1,4–8</sup> We report the case of a patient with metastatic prostate cancer and CR-HUS, whose signs and symptoms resolved without the need for plasma infusions or plasma exchange.

## Case summary

A 51-year-old gentleman presented to the hospital with oliguria, nausea, vomiting and severe back pain. He had a prior history of borderline hypertension, but his blood pressure was mildly elevated at the time of admission. He

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was on no prescription medications at home. He denied any non-steroidal anti-inflammatory drug use. He had no complaints of diarrhea. Laboratory work showed anemia (hemoglobin 10.1 g/dL), thrombocytopenia (platelet count  $37 \times 10^9/L$ ), elevated blood urea nitrogen (BUN) (198 mg/dL), elevated creatinine (15.6 mg/dL), hyperkalemia (potassium 6.1 mEq/L), low haptoglobin (20 mg/dL) and elevated lactate dehydrogenase (2436 U/L). Total bilirubin, fibrinogen, d-dimer, plasma prothrombin time and activated partial thromboplastin time were within normal limits. A peripheral blood smear demonstrated thrombocytopenia with 2–3 schistocytes per high power field. Imaging studies at the time of admission revealed no evidence of hydronephrosis, but did show several osteosclerotic lesions in the spine. A digital rectal exam demonstrated an enlarged, nodular left lobe of the prostate gland. The subsequent prostate-specific antigen (PSA) level was 151 ng/mL.

A diagnosis of metastatic prostate cancer was made and the patient was started on oral bicalutamide at 50 mg/day and a four-day course of intravenous dexamethasone at 40 mg/day. He underwent daily hemodialysis for four days. The patient's serum creatinine peaked at 16.5 mg/dL before trending down to 3.1 mg/dL on the sixth day, while his urinary output continued to increase. No further sessions of hemodialysis were required. His back pain also resolved rapidly. He was subsequently transitioned to leuprolide therapy and received six cycles of docetaxel, with normalization of his PSA. Six months after the initial diagnosis, his renal function remained within normal limits without any biochemical evidence of ongoing microangiopathy.

In retrospect, the patient had an episode of acute kidney injury (peak serum creatinine of 4.4 mg/dL) approximately eighteen months prior to the present encounter. This episode spontaneously resolved without any identifiable cause in the workup. A PSA level measured 12 months prior to the present encounter was 65 ng/mL, but had not been addressed. Therefore it is possible that the prior episode of acute kidney injury may have also been a similar phenomenon of CR-HUS.

## Discussion

Thrombotic microangiopathy is a disease of potentially devastating and even life-threatening consequences. A mortality rate as high as 41.6% has been reported.<sup>1</sup> While TTP is usually treated with plasma exchange, aHUS has not been shown to benefit from such exchange and is better treated with eculizumab.<sup>1</sup> The pathophysiology of CR-HUS is not well understood, and its rarity hampers ascertaining the exact pathologic mechanisms underlying the disease.<sup>1,3</sup> In light of the potential serious consequences of the disease, most clinicians employ plasma exchange therapy despite lack of high-quality evidence indicating benefit with such an approach.<sup>1,4-8</sup>

Lechner et al.,<sup>1</sup> conducted a search of all cases of CR-HUS reported in the literature from 1979 to 2012. A total of 168 cases of microangiopathy were identified, of which 154 were related to solid tumors. The vast majority of cases comprised of MAHA without significant renal dysfunction. The exception was prostate cancer, where 17 out

of the 23 reported cases showed signs similar to aHUS. After a review of all these cases, the authors concluded that plasma exchange and fresh frozen plasma infusions were rarely effective in CR-HUS, with the possible exception of prostate cancer. However, they acknowledged that the benefit of plasma exchange was unclear, as it was given concurrently with hormonal treatment. Almost all cases of prostatic cancer showed evidence of metastatic disease.<sup>1</sup> The same scenario was observed in other case reports, in which patients presented with evidence of widespread metastatic disease.<sup>2,4-7</sup>

Our case involves mostly findings similar to aHUS, including intravascular hemolysis with evidence of schistocytosis, thrombocytopenia and severe acute renal failure. These were treated without plasma exchange or fresh frozen plasma infusions, thereby proving the concept that these treatments may not be necessary in treating CR-HUS in the case of prostate cancer, as long as treatment for the underlying malignancy is initiated promptly. The report by Kanavaran et al.,<sup>2</sup> is in line with our opinion, wherein prostate cancer associated with TTP-like illness was treated with endocrine therapy alone. However, in that case there was no associated renal dysfunction and recovery of blood counts could be attributed to treatment of prostate cancer involving the bone marrow.<sup>2</sup> Detailed studies and case reviews have shown that there is no benefit of plasma exchange in CR-HUS.<sup>9,10</sup> Patients with cancer exhibiting TTP-like illness have been found to have normal levels of ADAMTS13 (a von Willebrand Factor cleaving protease),<sup>11</sup> which provides a reasonable explanation why plasma exchange is not beneficial, and hence, not necessary for treating patients with CR-HUS. Our case also highlights the excellent recovery from CR-HUS in prostate cancer if anti-cancer treatment is initiated promptly without the need for plasma exchange, which should be the focus of therapeutic approach when CR-HUS is first suspected.<sup>10</sup> Another series reported four cases of CR-HUS in patients with prostate cancer, two of whom were treated without plasma exchange.<sup>7</sup> Of these two patients, one made a complete recovery from CR-HUS, while the other remained dialysis dependent.

Reports have also indicated recurrent cases of CR-HUS<sup>5,12</sup> and though impossible to prove, it is conceivable that our patient's presentation with acute kidney injury several months before this admission was an initial, milder case of CR-HUS that surprisingly resolved spontaneously. The current presentation may simply be a more severe recurrence.

To conclude, our case report highlights that plasma exchange or fresh frozen plasma infusion is not a necessary part of the CR-HUS treatment. In the appropriate clinical context, suspicion of CR-HUS should elicit a prompt workup to avoid unnecessary and inappropriate plasma exchange, and to avoid delays in anti-cancer therapy, as the primary strategy should be aimed at treating the underlying malignancy.<sup>10,13</sup> Prostate cancer patients with CR-HUS may have a better prognosis than otherwise expected with CR-HUS. Although the exact reason for this observation is not yet clear, it is a potential topic of future research interest that can provide insight into the pathologic mechanisms and pathophysiology of this rare entity.

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### Contributor's statement

SZA took care of the patient and wrote the first draft of the manuscript. SZA, MFZ and MAM completed the second draft of the manuscript. All authors revised the manuscript for intellectual content and approved the final version of the manuscript being submitted.

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### Statement

The manuscript has been read and approved by all the authors. The requirements for authorship as stated have been met.

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### Conflicts of interest

The authors declare no conflicts of interest.

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None to declare.

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