

# Haemolytic Uraemic Syndrome and Its Relation to Metastatic Prostate Adenocarcinoma: A Case Report

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## Abstract

Haemolytic Uraemic Syndrome (HUS) has been rarely related to prostate cancer. The few cases reported in the literature show a better prognosis with the implementation of oncologic treatment. Its pathogenesis is unknown and has never been described as a consequence of treatment with bicalutamide. At the presented case this association couldn't be dismissed due to its temporal relationship, so surgical castration was carried out. It is important to recognize signs and symptoms of HUS on time because an early intervention is related to a better outcome.

## Introduction

Prostate cancer is the second most frequent malignancy in men affecting more than one million patients in the USA and it is the third leading cause of death of cancer in developed countries. The diagnosis at a metastatic stage is unusual but it is commonly seen when local treatments fail to control the disease. Since 1940s androgen deprivation therapy (ADT) has been used as the mainstay of initial treatment for advanced hormone-sensitive prostate cancer [1], but since the publication of the results of clinical trial CHAARTED, it has been confirmed that some patients benefit from an early therapy with a chemo-hormonal strategy based on docetaxel and ADT [2].

Haemolytic Uraemic Syndrome (HUS) is defined as a potentially life-threatening disease belonging to the spectrum of thrombotic microangiopathies. Its signs and symptoms are characterized by neurologic abnormalities, fever and risk of bleeding, derived from endothelial dysfunction which leads to consumption thrombocytopenia, microangiopathic haemolytic anaemia, and acute renal failure. Its aetiology is normally unknown and it is associated with a fatal prognosis and high rates of mortality.

Its relation to cancer is uncommon and only a few cases of HUS as the initial presentation of a prostate cancer have been described [3].

Here we present a case of a patient who after a recent diagnosis of a metastatic prostate cancer developed a HUS.

## Case Report

A 61 years-old man was admitted to our hospital in July 2015 because of a spinal cord compression (back pain with fast progression in 24 hours to paresis in lower limbs). He was an ex-smoker and had a past medical history of beta thalassemia minor and COPD with an emphysema phenotype. He underwent a D6-D7 laminectomy with decompression of spinal cord followed by D4-D9 fixation. Histopathology of the resected bone tissue was consistent with metastasis of a prostate cancer and blood tests showed a PSA of 514.2 ng/ml [ $<4.0$  ng/ml].

Once the patient was stable he underwent prostatic biopsy, which confirmed prostate adenocarcinoma Gleason 8 (4+4). Staging evaluation was completed with a CT scan that didn't show visceral compromise and a bone scintigraphy confirmed bone metastasis in D6-D7. Androgen deprivation therapy was then started with bicalutamide 50mg PO daily.

One week later the patient presented to the emergency department with acute vomiting, nausea and high fever. On physical examination he was alert and cooperative, had a temperature of 39°C and oliguria. Laboratory tests revealed acute renal failure (serum Creatinine level of 11.1 mg/dl) and parameters suggestive of thrombotic microangiopathy (LDH  $> 5.000$  UI/L; Hb 6.9 g/dl; low platelet count of  $34 \times 10^9/L$ ; peripheral blood smear with schistocytes). With a presumed diagnosis of Haemolytic Uremic Syndrome, daily plasma exchange was started. However, a poor hematologic response was obtained and renal impairment persisted, so the patient required haemodialysis and Eculizumab as a target therapy for HUS.

Regarding the aetiology of HUS, the main hypothesis was that it was due to a paraneoplastic syndrome, not being able to exclude its relationship with the antiandrogenic hormonal treatment with bicalutamide that was initiated just a few days before, so we decided to accomplish castration with surgery, undergoing bilateral orchiectomy.

Afterwards, treatment of the spinal cord compression was completed with consolidation radiotherapy on D5-D10 for 10 sessions of 3Gy each until a total dose of 30 Gy.

Once renal function and anaemia were normalized (Creatinine level 0.75 mg/dl and Hb 10.9 g/dl) without a trace of schistocytes in peripheral blood smear and having experienced a substantial clinical recovery, he was discharged. Already in an outpatient setting we decided to begin chemotherapy based on docetaxel 75mg/m<sup>2</sup> every 3 weeks. The patient completed 6 sessions with good tolerance and evolution, achieving a PSA level of 3.4 ng/ml.

## Discussion

Initial treatment of hormone-sensitive prostate cancer consists of androgen deprivation through a pharmacological or surgical

castration, being preferred generally the first option using LHRH analogous and antiandrogens due to its aesthetic and psychological implications. However, if it is not possible to decrease testosterone levels to <50 ng/dl with the available drugs nowadays, or if bicalutamide can not be used, as it happened in our case, it is possible to use a surgical strategy undergoing a bilateral orchiectomy.

Since the recent publication of the clinical trial CHAARTED, the use of docetaxel in the first 3 months of ADT has demonstrated better results than the ADT alone in terms of overall survival (57.6 vs 44 months), progression free survival and biochemical response, above all among patients with high burden disease, not having achieved yet median survival in the subgroup of patients with low burden disease. These results happen to confirm the ones at the clinical trial STAMPEDE, presented at the last ASCO 2015 [4].

No relationship has been found described in the literature between bicalutamide and the development of HUS, which led us to think about the possibility of a paraneoplastic syndrome as the cause of the HUS in the above presented case, but because of the severity of the situation and the temporal association with the use of bicalutamide, none could be dismissed. Surgical castration was chosen because it gets a quickly drop of testosterone levels compared to pharmacological therapy. Until now almost 20 cases have been found reported in the literature that show an association of HUS and prostate cancer, the majority of them describing metastatic disease with high levels of PSA, having a better prognosis and response to haemodialysis, plasmapheresis and oncologic treatment. It has also been described the association of HUS to other malignancies, more frequently adenocarcinomas, although in oncology the most commonly presentation is secondary to chemotherapy (especially mitomycin and gemcitabine) [5,6].

Eculizumab is a humanized monoclonal antibody that blocks the complement cascade binding with high affinity to the human C5 complement protein. It has shown its efficacy in the treatment of

atypical HUS in two phase 2 studies, demonstrating improvement of renal function and haematological parameters, being possible the discontinuation of plasmapheresis in the majority of patients treated with this drug [7]. However, its high price and potential severe secondary effects restricts its use.

Our case reflects similar characteristics to the ones described in previously reported cases in the literature: metastatic prostate cancer with high levels of PSA which presents a good evolution of HUS after establishment of pertinent therapy. Nevertheless, it is important to recognise symptoms on time because an early intervention is related to better prognosis [8].

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