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Oncology

Successful recovery from multiple organ failure associated with bicalutamide and leuprorelin acetate for prostate cancer

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ABSTRACT

I report a case of multiple organ failure (acute kidney injury, interstitial pneumonitis and liver dysfunction) associated with combined androgen blockade(CAB) with bicalutamide and leuprorelin acetate for prostate cancer that was successfully managed by prompt hemodialysis and withdrawal of medications. Finally, patient received orchiectomy for the treatment of prostate cancer, and the histology of renal biopsy revealed drug-induced tubulointerstitial nephritis. Although the condition is extremely rare, urologists should be aware of CAB-induced organ failures such as those of the lung, kidney and liver. It should also be noted that urologists should not initially prescribe long-acting Gn-RH.

Introduction

Combined androgen blockade (CAB) with bicalutamide and leuprorelin acetate is one of the standard treatments for prostate cancer. Although several cases associated with interstitial pneumonitis and/or liver dysfunction induced by antiandrogen and/or gonadotropin-releasing hormone agonists (GnRH) have been reported,[1–4] multiple organ failure including acute kidney injury is extremely rare. Herein I report a case of multiple organ failure induced by CAB for prostate cancer.

Case report

A 79-year-old man complained of a 1-month history of urinary retention with 420 cc of residual urine, a prostate volume of 57.5 cc, PSA of 97.62 ng/ml, normal digital rectal examination and transrectal ultrasonography results on 2015.08.25 as shown in Fig. 1. On 2015.09.05 the patient was admitted to the hospital, underwent a 12-core prostate biopsy and was diagnosed as having prostate cancer with a Gleason score of 4 + 5 from all of the regions. He had multiple bone metastases on bone scan and was diagnosed as cT4N0M1. He was treated with an indwelling urinary catheter and CAB with bicalutamide and leuprorelin acetate. Laboratory data at admission were Cr 1.46, BUN 21.2, and eGFR 36.6. On 2015.09.20 liver dysfunction with GOT 89 and GPT 147, and renal dysfunction with Cr 3.09, BUN 45,7, and eGFR 15.7 were found. He was treated with intravenous drip infusion with 1000 cc of 5% glucose and 40 cc of stronger neo-Minophagen C as liver treatment. Urinary protein was 3.15 g/g Cr, and therefore I suspected rapidly progressive glomerulonephritis including ANCA-related glomerulonephritis. However, blood tests related to nephritis were all within normal levels. On 2015.10.15, real function was worse with Cr 5.57, BUN 100.2, and eGFR 7.5. In addition, he developed breathing difficulties (pO2 55, pCO2 33, and spO2 89), edema in general and hypertension (200/115 mmHg). Lung auscultation revealed bilateral fine crackles. Chest x-ray showed bilateral, diffuse reticulonodular shadowing, which was confirmed by a chest computed tomography scan (CT) as shown in Fig. 2. He was diagnosed as having CAB-induced multiple organ failure and treated with prompt hemodialysis and withdrawal of all of the medications. By 2015,11,24, his condition, including blood test results, had improved to Cr 1.48, BUN 31.0 and eGFR 35.0. He was then taken off hemodialysis, and chest CT showed marked improvement. On 2016.02.04 he underwent an orchiectomy and PSA decreased to 0.338 ng/ml, and urinary catheter was removed. On 2016.04.06, he underwent renal biopsy and the histological result was drug-induced tubulointerstitial nephritis as shown in Fig. 3.

Discussion

The most common side effects of nonsteroidal antiandrogens are breast changes, sexual dysfunction, reproductive change, gastrointestinal troubles, hot flashes, psychological problems, anemia, skin changes, and liver toxicity. Bicalutamide, one of the nonsteroidal antiandrogens, may rarely cause liver changes such as elevated transaminases and jaundice. In the EPC study of 4052 prostate cancer patients

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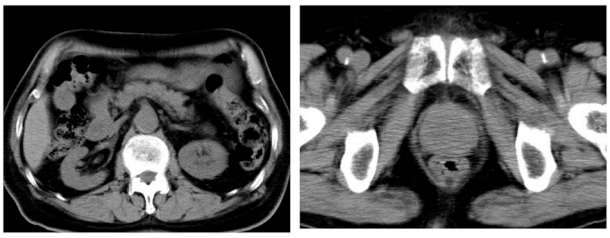

Fig. 1. In 2015.9.16, Abdominal CT scan shows mild prostate hypertrophy and normal kidneys.

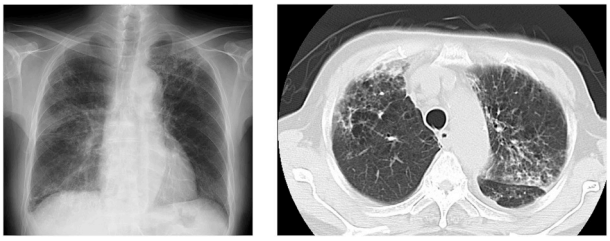

Fig. 2. In 2015.11.5 Chest X-ray shows diffuse bilateral reticulonodular infiltration and chest CT scan shows multifocal ground glass and air-space opacities bilaterally.

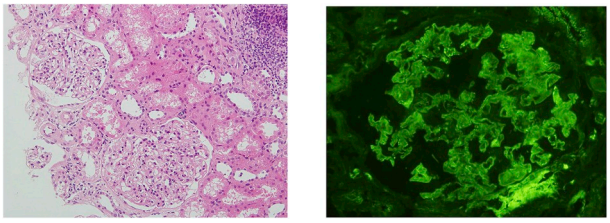

Fig. 3. Histology of renal biopsy reveals that atrophy of renal tubules and interstitial fibrosis demonstrating on the recovery from drug-induced tubulointerstitial nephritis. The immuno-fluorescence staining shows no significant appearance.

who received bicalutamide as a monotherapy, the incidence of abnormal liver function test was 3–4% for bicalutamide and 1.9% for standard care at 3-year median follow-up(2). The drug was discontinued due to liver changes in approximately 0.3–1% of patients treated with it for prostate cancer in clinical trials.[1–3] Out of millions of patient exposure, two of which were fatal were reported in the medical literature as of 2016.[3] The clinical studies that reported elevated liver enzyme levels and hepatotoxicity with bicalutamide have all specifically pertained to men of advanced age with prostate cancer.[3] It is notable that older age, for a variety of reasons, appears to be an important risk factor for drug-induced hepatotoxicity. Several case reports of lung toxicity like interstitial pneumonitis (which can progress to pulmonary fibrosis) in association with androgen deprivation treatment have been published in the medical literature.[1] In a very large cohort of prostate cancer patients, the incidence of interstitial pneumonitis with nonsteroidal antiandrogen was 0.77% for nilutamide, but only 0.04% for flutamide and 0.001% for bicalutamide.[1]

The most common side effects of GnRH are hot flashes, sweating, acne, itching, scaly skin, mood changes, headache, and general pain. However, some serious side effects have been reported, including gastrointestinal troubles, joint/muscle aches or pain, insomnia, sexual dysfunction, psychological toxicity, and lung, liver and kidney toxicities. Three case reports link leuprorelin use with interstitial pneumonitis, and there are isolated but consistent reports of other antiandrogens used for prostate cancer inducing interstitial pneumonitis.[4] Although only one case report of flutamide-related acute kidney injury has been reported, Lapi et al.[5] reported that, in a cohort of patients newly diagnosed non-metastatic prostate cancer, the use of GnRH was significantly associated with an increased the risk of acute kidney injury. Their overall incidence rate of acute kidney injury is greater than what has been estimated in the general population (5.5 vs 1.8 per 1000 person-years), which is expected in a cohort of men with prostate cancer.

Fortunately, the lung toxicity in the present case was limited and the patient recovered in 1 month without steroid. The acute kidney injury was treated with prompt hemodialysis and renal function was also recovered successfully in 1 month.

Although the condition is extremely rare, urologists should be aware of CAB induced organ failures such as those of the lung, kidney and liver. It should also be noted that urologists should not initially prescribe long acting GnRH.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.eucr.2019.101108.

References

1. Bennett CL, Raisch DW, Sartor O. Pneumonitis associated with nonsteroidal antiandrogens; presumptive evidence of a class effect. *Ann Intern Med.* 2002;137:625–628.
2. Wellington K, Keam SJ. Bicalutamide 150 mg: a review of its use in the treatment of locally advanced prostate cancer. *Drugs.* 2006;66:837–850.
3. Hussain S, Haidar A, Bloom RE, Zayounal N, Piper MH, Jafri SM. Bicalutamide-induced hepatotoxicy: a rare adverse effect. *Am J Case Reports.* 2014;15:266–270.
4. Tan HE, Lake F. Interstitial pneumonitis secondary to leuprorelin acetate for prostate cancer. *Respirol Case Rep.* 2016;31, e00146.
5. Lapi F, Azoulay L, Niazi MT, Yin H, Benayoun S, Suissa S. Androgen deprivation therapy and risk of acute kidney injury in patients with prostate cancer. *J Am Med Assoc.* 2013;310:289–296.