

Non-interventional management of obstructive acute renal-failure in hormone-naïve prostate cancer

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AGARWAL MM, SINGH SK, ACHARYA NC, METE UK, MANDAL AK. Non-interventional management of obstructive acute renal-failure in hormone-naïve prostate cancer. *The Canadian Journal of Urology*. 2007;14(3):3580-3582.

Advanced carcinoma prostate (CaP) commonly presents as bilateral ureteric obstruction. The management often requires androgen ablation along with temporary urinary diversion (percutaneous nephrostomy or ureteric catheterization) which is not infrequently associated with complications. Two

patients of hormone-naïve CaP presented to our emergency department with oliguric renal failure due to bilateral ureteric obstruction and were treated with dialysis, ketoconazole (for androgen ablation) and corticosteroids; urinary diversion was not feasible in either at the time of presentation. Brisk diuresis occurred within 48 hours obviating the need of urinary diversion. Follow-up of these cases is presented and justification of this approach is discussed.

Key Words: prostate cancer, ketoconazole, oliguria orchidectomy

Introduction

Prostate cancer (CaP) is the leading cancer diagnosis and the second most common cause of cancer-related mortality in the United States, amounting to approximately 19.4 per hundred thousands (1997).¹ Although, screening with prostate-specific antigen has led to a shift of stage at diagnosis from advanced to early (especially in the developed countries) over last 2

decades, advanced CaP continues to be an important cause of morbidity and mortality in men more than 50 years of age, especially in countries where screening is not practicable.² It presents as urinary retention, ureteric obstruction,³ bone-pain, spinal cord compression⁴ and hematological dysfunction (disseminated intravascular coagulation and anemia).⁵

Most hormone-naïve CaP are hormone sensitive and responsive, and androgen ablation (orchiectomy, luteinizing hormone-releasing hormone agonists, estrogens and antiandrogens) confers a clinical response rate of 60%-70% which typically last for a median of 18-24 months.² Ureteric obstruction also responds to these hormone manipulations with a reported improved drainage rate of 55%-85%;⁶

Accepted for publication March 2007

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however, presence of bilateral ureteric obstruction with renal failure may compel the urologist to resort to urinary diversion (percutaneous nephrostomy or ureteric stenting) which is not without complications. Non-interventional management of these cases is scarcely reported and we present two such cases.

Case reports

Case 1

A 60-year old male presented with anuria of 3 days duration, 2 months following transurethral resection of prostate (TURP) done elsewhere for refractory urinary retention. The histopathological examination of TURP chips showed adenocarcinoma prostate, Gleason score 10. At presentation, he had fluid overload and respiratory distress. Investigations revealed blood urea nitrogen 54.59 mg/dl (19.49 mmol/L), serum creatinine 13.6 mg/dL (1202.3 µmol/L), severe metabolic acidosis (pH 7.10, bicarbonate 8 meq/L) and hyperkalemia (serum K⁺ = 6.8 meq/L); serum PSA was 79.8 ng/ml. Digital rectal examination revealed grade III hard nodular prostate and ultrasound of the abdomen showed bilateral mild hydroureteronephrosis (calyceal separation 5 mm-6 mm). Initial management included antikalaemic measures and hemodialysis (two sessions), and he was started on ketoconazole (400 mg t.i.d.) along with dexamethasone 8 mg q.i.d. Percutaneous nephrostomy was not feasible due to minimal hydronephrosis. He went into a state of post-obstructive diuresis after 48 hours and his serum creatinine normalized over 1 week. Tc99m-MDP bone-scan at this time revealed wide-spread metastases subsequent to which he underwent bilateral orchidectomy under local anesthesia. Ketoconazole was stopped after orchidectomy and steroid after 1 month. After short lasting initial response, he developed hormone refractory status within 6 months and died of widespread metastases.

Case 2

A 79-year old male presented with anuria of 4 days duration and altered sensorium for 1 day. He had a history of lower urinary tract symptoms for 4 years. Investigations done elsewhere (ultrasound and computed tomography) showed bilateral moderate hydroureteronephrosis and bulky retroperitoneal lymphadenopathy. On evaluation at our center, the patient was in fluid overload and respiratory distress. Investigations revealed blood urea nitrogen of 55.99 mg/dL (19.99 mmol/L), serum creatinine 8.0 mg/dL (707.2 µmol/L), serum K⁺ 6.4 meq/L, PSA 100 ng/ml

and severe metabolic acidosis. Digital rectal examination revealed grade III hard nodular prostate. Initial management was similar to the previous patient (hemodialysis, ketoconazole and corticosteroids) and PCN was not performed initially due to deranged coagulation profile and mental irritability (encephalopathy). He showed post-obstructive diuresis and drop in serum creatinine to 1.2 mg/dL (106.1 µmol/L) was observed within 7 days. Afterwards, prostate biopsy revealed adenocarcinoma prostate (Gleason score 10) and he underwent bilateral orchidectomy. At 2 years of follow-up, his renal functions have remained stable, but he has required secondary hormonal (bicalutamide, fofestrol) and other medical manipulations (thalidomide) due to development of hormone refractory status.

Discussion

The manifestations of hormone-naïve advanced carcinoma prostate such as bone pain, spinal cord compression, infravesical obstruction and hematological dysfunction are treated preferably by hormonal manipulation.⁷ Ureteric obstruction is an important complication which is associated with a significant morbidity, and often reported as indicative of poor prognosis.⁸ The incidence varies from 2%-51% depending on the population studied and inclusion-exclusion diagnostic criteria, and 36% of these are bilateral.⁹ It is caused by direct spread to the trigone and intramural ureter, lymph-node metastases compressing the ureters, and rarely intraluminal metastases.⁹ Unilateral obstruction in presence of normal renal function may be treated with androgen ablation alone as the reported response rate in the form of improved renal drainage is high (up to 85% at 4 weeks).⁶ However, bilateral obstruction in the presence of oliguric renal failure has conventionally been treated with temporary urinary diversion (percutaneous nephrostomy and ureteral stenting) in addition to hormone ablation and renal replacement therapy. Although, ultrasound or fluoroscopy guided percutaneous nephrostomy is considered to be safe, the complication rate is significant at 11%-45% depending on various patient-related, interventionist's expertise related as well as set-up related factors. The complications include hematuria, contrast extravasation, fever, sepsis, perirenal hematoma and catheter detachment. In the setting of injury to major renal vessels even nephrectomy may be needed to be resorted to.¹⁰ It has also been noted that the elderly population are prone to develop non-dilated obstructive uropathy

where percutaneous nephrostomy can be technically difficult.¹¹ Retrograde ureteral stenting also can be difficult or impossible especially when there is subtrigonal infiltration. Moreover, indwelling ureteric stents are associated with complications e.g. migration, encrustation, infection, patient-discomfort, vesicoureteric reflux and ineffective drainage.¹²

Hamdy and Williams¹³ reported efficacy of 90% (10/11) of dexamethasone for relief of ureteric obstruction in advanced CaP patients (both hormone-naïve and hormone resistant) and found that the response was sustained after steroid withdrawal only in the former group. Lichtenberg et al,⁶ in their retrospective study on management of bilateral ureteric obstruction, reported a better survival of patients treated with androgen ablation alone (median 26 months) versus those with androgen ablation along with urinary diversion (median 13 months; $p = 0.00002$). They also found that orchiectomy was more efficacious than estrogens ($p < 0.05$). This is plausible as orchidectomy (and also ketoconazole) leads to castrate levels of testosterone in 4-8 hours whereas it takes LHRH agonists and estrogens 3-8 weeks for the same effect.² We initially used ketoconazole to avoid morbidity of surgical procedure in acute phase and found it to be effective. Ketoconazole is considered to be safe in acute renal failure by virtue of hepatic metabolism. Bilateral orchidectomy was carried out in both of our cases once the condition improved. Efficacy of corticosteroids has been reported for management of ureteric obstruction in various locally advanced pelvic malignancies other than prostate cancer also.

Conclusion

Select patients of hormone-naïve CaP presenting with bilateral ureteric obstruction and oliguric renal failure may be managed with essential dialytic support along with androgen ablation and steroids avoiding the need of urinary diversion. The definition of 'select' group remains to be defined but patients with coagulopathy, mental irritability (encephalopathy), and minimal upper tract dilation certainly constitute some such circumstances. In addition, facilities of the urologist and necessary equipment for PCN and stenting are largely not available in rural and suburban setting of a typical developing country like India. In absence of an effective medical insurance system, financial constraint on the part of the patient further complicates the issue and causes a delay in institution of appropriate therapy. Furthermore, tertiary referral centers are always overworked and

there is significant delay (at times for days) before an appointment for PCN or stenting may be made. Keeping all these constraints and reported efficacy of the above-described non-interventional approach in mind, many such patients may be managed or at least started on medication by physicians at primary care level before referral to specialist uro-nephrology centers as well as within the tertiary centers while the patient is awaiting the appointment for diversion. This will take care of a significant burden of urinary diversion at these centers and help in better patient management. □

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