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Original Research Article

Pattern of Bilateral Orchidectomy for Advanced Cancer of the Prostate- A 10-Year Review

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Abstract: Bilateral orchidectomy has been one of the methods of androgen deprivation therapy. Others are Luteinizing hormone releasing hormone (LHRH) agonist and antagonist and oestrogen compounds. It is cost-effective, simple, permanent and with fewer side effects as compared to other methods. We retrospectively studied case notes of patients diagnosed of prostate cancer in a 10-year period between January 2006 and December 2015 and came up with the result that out of 404 patients diagnosed, 173 representing 42.8% underwent bilateral orchidectomy. We also noted that, there have been an increase in the number of cases diagnosed in the last 4 years and a corresponding increase in the number of this surgery in the same period of time. This may as well be a result of health awareness campaigns and increased use of prostate specific antigen (PSA) testing in men in recent years.

Keywords: Bilateral orchidectomy, advanced prostate cancer, androgen deprivation therapy.

INTRODUCTION

Cancer of the prostate is an exclusive name for adenocarcinoma of the prostate occurring commonly in elderly men and majority of them being diagnosed in their 7th decade of life [1]. Diagnosis of cancer of the prostate (Cap) starts with suspicious symptoms in the history, a focused physical examination mostly targeting abnormal findings on rectal examination of the prostate, biochemical assay of a raised prostate specific antigen(PSA>10ng/ml). All of these will direct further investigative modalities namely a transrectal ultrasound scan of the prostate and a biopsy for histology. Imaging studies especially in this group of patients is central to localizing targets of tumour spread. Advanced prostate cancer refers to tumour originating in the prostate with confirmed extension outside the gland. It could be classified into locally advanced and metastatic Cap based on the information from the history, physical examination, biochemical and imaging studies. Locally advanced Cap may cause local symptoms due to bladder outlet obstruction presenting as lower urinary tract symptoms (LUTS). By extension or infiltration to the adjacent structures, it may cause haematuria where cancer cells infiltrate the bladder or prostatic urethra bleed sloughing. and by It can cause tenesmus/constipation as it encroaches into the rectum, haematospermia and erectile dysfunction as tumour infiltrates the seminal vesicles and the neurovascular bundles respectively. Metastatic Cap on the other hand may also cause disabling symptoms including bone pain, weight loss, pathological fracture, paraparesis, paraplegia and recurrent anaemia.

Treatment of advanced Cap precludes cure, with palliative measure as the anchor of care. Charles Huggins in 1941 established the use of androgens in stimulating prostate cancer growth [2]. This knowledge formed the basis for androgen deprivation therapy (ADT) in the treatment of advanced prostate cancer with tremendous hope and success although short-lived with emergence of castration resistance. ADT is regarded as the gold standard for treating advanced Cap [3], comprising surgical orchidectomy, medical orchidectomy and estrogen therapy.

In this study, we focused on the pattern of bilateral orchidectomy for advanced Cap and report that for the preceding four (4) years, there have been an increase in the percentage of patients (81.4%) diagnosed and a corresponding increase in percentage of patients (49.7%) undergoing this operation. The reason for this may not be far fetched. Bilateral orchidectomy is a simple, permanent, cost-effective modality of treatment with fewer side effects, although, psychological disturbance of an "empty scrotum" may be a strong factor bothering on the quality of life of these patients. Other treatment modalities such as LHRH agonist/antagonists, oestrogen compounds together with pure and steroidal ant-androgens are also in use with varying proportions of unwanted side effects.

MATERIALS AND METHOD

We retrospectively looked at information and health management records of our hospital for data on patients who presented between January 2006 and December 2015 in which a diagnosis of Cap was made. A search was also made in the theatre for cases of bilateral orchidectomy done for this same period. Relevant data for this article were collated and entered into the statistical package for the social sciences (SPSS) version 20.0 software and analyzed for discussion.

RESULTS

Four Hundred and Four (404) cases of the Cap were diagnosed within this period and of this number, one hundred and seventy three (173) underwent bilateral orchidectomy representing 42.8% of the study population. The mean age was 67.67 years (\pm 9.272) ranging from 45 to 96 years. The last four years saw an increased number of patients diagnosed with Cap 329(81.4%) and the number of surgery also increased in the same period 86(49.7%). Majority of the patients diagnosed and also operated upon were in their 7th decade of life (Table 4).

Year	Frequency	Valid Percent	Cumulative percent
2006	9	2.23	2.23
2007	10	2.48	4.71
2008	3	0.74	5.45
2009	1	0.25	5.70
2010	44	10.89	16.59
2011	8	1.98	18.57
2012	91	22.52	41.09
2013	88	21.78	62.87
2014	74	18.32	81.19
2015	76	18.81	100.0
Total	404	100.0	

Table-1: Cases diagnosed per year

Table-2: Frequency of bilateral orchidectomy per year

Year	Frequency	Valid Percent	Cumulative percent
2006	9	5.2	5.2
2007	10	5.8	11.0
2008	9	5.2	16.2
2009	19	11.0	27.2
2010	22	12.7	39.9
2011	18	10.4	50.3
2012	24	13.9	64.2
2013	26	15.0	79.2
2014	15	8.7	87.9
2015	21	12.1	100
Total	173	100.0	

Table-3: Frequency of diagnosis/bilateral orchidectomy

Diagnosis	Bilateral orchitecomy	Percentage
404	173	42.8

Table-4. Age/Trequency of Burgery						
Age (in decades)	Frequency	Valid percent	Cumulative percent			
5 th	10	5.9	5.9			
6 th	31	18.2	24.1			
7 th	67	39.4	63.5			
8 th	49	28.8	92.3			
9 th	12	7.1	99.4			
10^{th}	1	0.6	100.0			
Total	173	100.0				

Table-4: Age/Frequency of Surgery

DISCUSSION

Treatment of advanced prostate cancer has evolved over the years with additions of newer therapeutic agents. Traditionally, bilateral orchidectomy and estrogen therapy had been the only means of androgen (testosterone) suppression. This has expanded to include the use of anti-androgens, LHRH agonists and recently LHRH antagonist. Despite these attempts and efforts, long term survival is still poor. However, these treatment modalities are not aimed at cure but palliative to give the terminally-ill patients some quality of life. Combined androgen blockade (CAB) has also been practiced aimed at eliminating, in addition, the adrenal androgens, but the picture is quite the same with additional side effect coupled with continuous debate and uncertainties regarding the safety, efficacy and long term use of this treatment [4].

Among the monotherapies for advanced Cap, bilateral orchidectomy seems to be the simplest, easiest, cheapest and most complaint option of treatment. Side effects, just like LHRH agonists are hot flashes, loss of libido, erectile dysfunction, lack of drive and emotional and psychological distress due to loss of testicles in orchidectomized patients. Anti-androgens especially in the non-steroidal class, patients usually retain libido and potency because of stabilized serum levels of testosterone, but cost may preclude compliance. There is a progestational side effect with steroidal antiandrogen and loss of libido/impotence is worrisome. With these in mind, a newly diagnosed prostate cancer patient is counseled on these three modalities of treatment and considering the prevailing economical impact, the last 4 years have recorded a surge in the number of patients undergoing bilateral orchidectomy in our facility. The number of orchidectomies are more than the number of patients diagnosed in some of the years (Table 1 and 2), this is because after clinical decision is taken, patients are counseled for surgery and allowed a time to consent for operation with anti androgen as initial treatment. This actually leads to a spill-over into another year. The last 4 years also witnessed an increase in prostate cancer diagnosis apparently due to efforts deployed in mounting health care awareness campaigns and the use of PSA testing in men of this age group. Bilateral orchidectomy with its advantages is gaining popularity in the treatment of advanced Cap. Most authors worry about the emotional and psychological impacts of an "empty scrotum" which was not noted in our records howbeit retrospective. Those who are concerned about this choose sub-capsular orchidectomy with sizeable tissues in the scrotum. McDonald and Calams (1958, 1959) pointed out that the presence of Leydig cells in the tunica albuginea and the epididymis which are left sub-capsular orchidectomy insitu in are morphologically similar to those found in the testis and are capable of secreting testosterone [5]. However Chapman JP in his study did not report any significant difference in serum testosterone among patients who

had total orchidectomy and those after sub-capsular orchidectomy [6]. Another author made similar observation [7]. We capitalized on the advantage of quick, rapid effectiveness and achievement of castrate level of testosterone within 3 to 12 hours after surgery in majority of our patients who presented late [8]. In contrast, medical orchidectomy with LHRH agonist achieves this fit in 3-4 weeks after the first injection with an added disadvantage of cost and tumour flare with worsening symptoms if anti-androgen is not started prior to or added to the treatment regimen [9].

In this study, maximum androgen blockade (MAB) was practiced with addition of a non steroidal anti-androgen (Flutamide or Bicalutamide) after surgery. The aim was to abolish the effect of adrenal androgen said to provide precursors which are converted into more potent steroids in the prostate gland [10]. Studies have shown no added benefit of MAB when compared with orchidectomy alone leaving us with a drive to prospectively confirm or refute this [11, 12]. MAB enhances anti-tumour effects and has been shown to reduce the size of normal prostates and seminal vesicles in animal models [13]. This however may cause a rapid relief of symptomatology but may not ultimately confer survival benefits which is also affected by other factors such as age, tumour stage, health and performance status of the patients. Other large control trials together had reported a survival advantage of MAB [14, 15]. Controversies still loom on this topic as recent meta-analyses can not exactly resolve the argument surrounding the ultimate survival benefits of combined androgen blockage [16, 17].

Irrespective of the treatment modality adopted in advanced prostate cancer, palliation of symptoms is the role and all patients eventually progress to a state of androgen insensitivity. At this stage, no treatment can prolong survival [18]. Median progression-free survival has been reported by Lam et al as 18 to 34 months [19]. When castrate resistance state is reached which is defined as symptom progression despite castrate level of testosterone (<50ng/ml), the need for other manipulative therapies arise. ADT with chemotherapy has been in use. Wang et al who worked with locallyprostate cancer patients advanced receiving chemotherapy reported an initial objective response rate and longer median survival (60 VS 30 months P = 0.04) than patients treated with monotherapy alone [20]. He did not however demonstrate any advantage in metastatic prostate cancer patients who also were treated with chemotherapy. Frustrating as it may look like, newer chemotherapeutic agents are being investigated and synthesized in an effort to improve survival as the end point.

CONCLUSION

Treatment of advanced prostate cancer has revolved around bilateral orchidectomy due to its rapid suppression of endocrine testicular function with minimal side effects. It has been regarded as the gold standard of treatment. In recent times, this treatment modality has been accepted and embraced by this group of patients who visit our facility for care.

REFERENCES

- 1. Bechis SK, Carroll PR, Cooperberg MR. Impact of age at diagnosis on prostate cancer treatment and survival. Journal of Clinical Oncology. 2010 Dec 6;29(2):235-41.
- Huggins C, Stevens RE, Hodges C. The effect of castration on advanced carcinoma of the prostate gland: studies on prostatic cancer. Arch Surg. 1941;43:209-23.
- 3. Rud O, Peter J, Kheyri R, Gilfrich C, Ahmed AM, Boeckmann W, Fabricius PG, May M. Subcapsular orchiectomy in the primary therapy of patients with bone metastasis in advanced prostate cancer: an anachronistic intervention?. Advances in urology. 2011 Sep 14;2012.
- Eisenberger MA, Blumenstein BA, Crawford ED, Miller G, McLeod DG, Loehrer PJ, Wilding G, Sears K, Culkin DJ, Thompson Jr IM, Bueschen AJ. Bilateral orchiectomy with or without flutamide for metastatic prostate cancer. New England Journal of Medicine. 1998 Oct 8;339(15):1036-42.
- McDonald JH and Calams JA (1958) Journal of Urology 79, 850-858.(1959) Journal of Urology 82, 142-147.
- 6. Chapman JE. Comparison of testosterone and LH values in subcapsular vs total orchiectomy patients. Urology. 1987 Jul 1;30(1):27-8.
- Hering FL, Dall'ogollo MF, Caponero R, Rodrigues PR, Nesrallah IJ, Srougi M. Total Versus Subcapsular orchidectomy for treatment of advanced prostatic carcinoma: Comparison of serum testosterone and PSA levels. J Bras Urol. 1999; 25:221-224.
- 8. Maatman TJ, Gupta MK, Montie JE. Effectiveness of castration versus intravenous estrogen therapy in producing rapid endocrine control of metastatic cancer of the prostate. The Journal of urology. 1985 Apr;133(4):620-1.
- 9. Limonta P, Marelli MM, Moretti RM. LHRH analogues as anticancer agents: pituitary and extrapituitary sites of action. Expert opinion on investigational drugs. 2001 Apr 1;10(4):709-20.
- Labrie F. Adrenal androgens and intracrinology. InSeminars in reproductive medicine 2004 Nov (Vol. 22, No. 04, pp. 299-309). Copyright© 2004 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA.
- 11. Collette L, Studer UE, Schröder FH, Denis LJ, Sylvester RJ. Why phase III trials of maximal androgen blockade versus castration in M1 prostate cancer rarely show statistically significant differences. The Prostate. 2001 Jun 15;48(1):29-39.
- 12. Schmitt B, Wilt TJ, Schellhammer PF, DeMasi V, Sartor O, Crawford ED, Bennett CL. Combined

androgen blockade with nonsteroidal antiandrogens for advanced prostate cancer: a systematic review. Urology. 2001 Apr 30;57(4):727-32.

- Geller J, Albert J, Yen SS, Geller S, Loza D. Medical castration of males with megestrol acetate and small doses of diethylstilbestrol. The Journal of Clinical Endocrinology & Metabolism. 1981 Mar;52(3):576-80.
- Crawford ED, Eisenberger MA, McLeod DG, Spaulding JT, Benson R, Dorr FA, Blumenstein BA, Davis MA, Goodman PJ. A controlled trial of leuprolide with and without flutamide in prostatic carcinoma. New England Journal of Medicine. 1989 Aug 17;321(7):419-24.
- 15. Janknegt RA, Abbou CC, Bartoletti R, Bernstein-Hahn L, Bracken B, Brisset JM, Da Silva FC, Chisholm G, Crawford ED, Debruyne FM. Orchiectomy and nilutamide or placebo as treatment of metastatic prostatic cancer in a multinational double-blind randomized trial. The Journal of urology. 1993 Jan;149(1):77-82.
- Prostate cancer Trialist's collaboration group. Maximum androgen blockade in advanced prostate cancer: an overview of 22 randomized trials with 3283 deaths in 5710 patients. Lancet 1995;346:365-369.
- 17. Caubet JF, Tosteson TD, Dong EW, Naylon EM, Whiting GW, Ernstoff MS, Ross SD. Maximum androgen blockade in advanced prostate cancer: a meta-analysis of published randomized controlled trials using nonsteroidal antiandrogens. Urology. 1997 Jan 1;49(1):71-8.
- Eisenberger MA, Simon R, O'Dwyer PJ, Wittes RE, Friedman MA. A reevaluation of nonhormonal cytotoxic chemotherapy in the treatment of prostatic carcinoma. Journal of Clinical Oncology. 1985 Jun;3(6):827-41.
- Lam JS, Leppert JT, Vemulapalli SN, Shvarts O, Belldegrun AS. Secondary hormonal therapy for advanced prostate cancer. The Journal of urology. 2006 Jan 31;175(1):27-34.
- Wang J, Halford S, Rigg A, Roylance R, Lynch M, Waxman J. Adjuvant mitozantrone chemotherapy in advanced prostate cancer. BJU international. 2000 Oct 1;86(6):675-80.