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بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

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Management of Hormone-Refractory Prostate Cancer

Essay submitted in partial fulfillment of the degree of M.Sc. in Urology
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Cairo 2001

بسم الله الرحمن الرحيم

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أجتماع لجنة الحكم على الرسالة المقدمة من
الطبيب / محمد عبد الرسول
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بناء على موافقة الجامعة بتاريخ ١٥ / ٤ / ٢٠٠٧ تم تشكيل لجنة الفحص والمناقشة للرسالة المذكورة أعلاه على النحو التالى :-

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بعد فحص الرسالة بواسطة كل عضو منفردا وكتابة تقارير منفردة لكل منهم إنعقدت اللجنة مجتمعة فى يوم الخميس بتاريخ ١٩ / ٤ / ٢٠٠٧ بقسم المسالك البولية مدرج الكلية بكلية الطب - جامعة القاهرة وذلك لمناقشة الطالب فى جلسة علنية فى موضوع الرسالة والنتائج التى توصل إليها وكذلك الأسس العلمية التى قام عليها البحث .

قرار اللجنة : بعد مناقشة الرسالة قبول الرسالة في جلسة علنية يوم الخميس ١٩ / ٤ / ٢٠٠٧

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Abstract

Most of the patients of advanced prostate cancer respond to hormonal therapy, however this response is usually temporary and last for only limited period of time then the tumor becomes resistant to hormonal treatment. In the last decade, there has been a great development in the treatment of hormone-refractory prostate cancer. This development has been achieved in the second line hormonal therapy and in the new chemotherapeutic regimens which demonstrate more than 50% response rate in clinical trials. Also, gene therapy has been introduced in the management of hormone-refractory prostate cancer with promising results in the preliminary experiments. Finally, there has been a great achievement in the improvement of quality of life in advanced cancer patients using the modern regimens of radiotherapy and radioisotopic treatment. This essay presents a review of the new different modalities of management of hormone-refractory prostate cancer.

Keywords

Hormone-refractory, cancer, prostate, HRPC, chemotherapy, hormonal therapy

INTRODUCTION

Prostate cancer represents a prime model of endocrine dependent tumors in men. Although patients respond dramatically (subjectively and objectively) to a variety of androgen deprivation procedures, this effect is usually palliative and temporary. The development of a hormone-refractory state is categorical and irreversible phenomenon observed in the majority of patients and occurs within an almost predictable time frame after the initiation of androgen deprivation. Extensive data derived from large-scale, prospective studies involving patients with stage D2 disease treated with virtually all combinations and permutations of androgen deprivation maneuvers indicate that the medians in time to progression and survival have ranged from 12 to 18 months and 2 to 3 years *(Crawford et al, 1989)*.

The treatment of hormone-refractory prostate cancer has been undergoing a revolution over the last decade. Traditionally, metastatic disease that failed hormonal therapy was found to be unresponsive to chemotherapeutic regimens, and many urologists and oncologists stopped treating this disease aggressively. In the 1990s, several chemotherapeutic regimens were developed, and many of these regimens demonstrated a greater than 50% response rate in clinical trials and under assessment in the phase III setting.

This essay shows the recent trend in the management of hormone- refractory prostate cancer, including up-to-date discussion of pain management and supportive care.

THE BIOLOGY OF HORMONE-REFRACTORY PROSTATE CANCER

It is known that prostate cancer cells, like certain normal prostate epithelial cells, can depend on a critical level of androgenic stimulation for their net continuous growth and survival ***(Resnick and Grayhack, 1975)***. On this basis androgen ablation has been used as standard systemic therapy for metastatic prostate cancer. There are a multitude of excellent means of ablating serum androgens, including chronic treatment with luteinizing hormone releasing hormone analogues alone and in combination with antiandrogens, surgical orchiectomy, or both. A recent, large, randomized prospective clinical trial compared the effectiveness of gold standard androgen ablation (i.e., surgical orchiectomy) as monotherapy with a combination approach of orchiectomy plus concomitant antiandrogen treatment in patients with metastatic prostate cancer ***(Eisenberger et al, 1998).*** The data suggest that there is no additional advantage of combination approaches when compared with orchiectomy alone in terms of the time to progression or overall survival ***(Eisenberger et al, 1998).*** None of the patients with definitive metastatic disease were cured by such androgen ablation therapy regardless of how aggressively it was given ***(Eisenberger et al ,1998).*** Thus, androgen ablation therapy is not curative for metastatic prostate cancer because it does not eliminate the portion of prostate cancer cells within a patient with metastatic disease that no longer depend on the effects of androgen for stimulation of their continuous growth and survival. These cancer cells are androgen-independent and thus hormone refractory.

The entire issue of the development of resistance to androgen ablation therapy is based on the fact that at least a portion of the cells present within a patient with prostate cancer before therapy is begun depend on androgenic stimulation for their proliferative growth and survival. If a tumor does not have at least some cells that initially require androgen stimulation for their survival, no response to subsequent androgen ablation therapy would