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Suramin and Prostate Cancer: The Role of Hydrocortisone

S.J. Harland and G.M. Duchesne

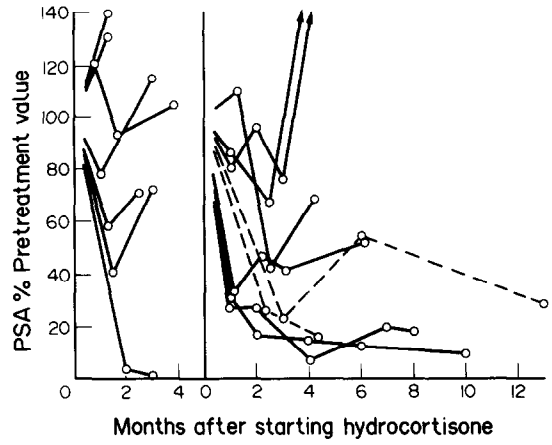

Fig. 1. Changes in PSA (continuous line) and prostatic acid phosphatase (broken line) levels in 15 patients with metastatic prostate cancer treated with hydrocortisone 20 mg twice daily. For clarity, patients treated for less than 4 months are shown in the left-hand graph.

RECENT PRESENTATIONS [1–3] have described a high response rate when suramin is used in metastatic prostate cancer that has escaped endocrine control. The fact that in this disease, whose prognosis has remained essentially unaltered for the last 50 years, remissions are being induced with high frequency by an agent with novel mechanisms of action (including binding of tumour growth factors) has led to much interest and some enthusiasm. Indeed, its significance has been compared to the development of nitrogen mustard and aminopterin [4]. The enthusiasm may be inappropriate: the responses seen in prostate cancer may be related to the co-administration of hydrocortisone, given because of the high frequency of drug-induced adrenocortical insufficiency. This suggestion has on occasion met with the view that objective responses to low-dose hydrocortisone do not occur (40 mg daily was used in at least two of the above studies).

Some 10–15% of circulating androgens are derived from non-testicular sources, the most important being the adrenal gland. Suppression of adrenal androgens should be considered a possibility with any agent that causes adrenal insufficiency. If replacement therapy with steroids is also used it becomes inevitable [5, 6]. We have carried out serial prostate-specific antigen (PSA) levels in 15 prostate cancer patients treated with hydrocortisone 40 mg daily.

The median age of the group was 69 (range 54–88) years. Bone disease was present in 14 patients. 3 patients had measurable nodal disease. All had failed first-line endocrine treatments, the median duration of response to which was 24 (9–72) months, perhaps making this group rather more favourable than most populations for whom the median response duration is 18 months. Previous treatments included orchidectomy (12), casodex (4), cyproterone acetate (3), goserelin (2), flutamide (1) and stilboestrol (1).

Only 1/3 patients with measurable disease responded. However, 8 out of 15 patients entered tumour marker remission, defined as a fall of at least 50% (Fig. 1). All patients whose marker fell below 80% (12 of them) experienced subjective benefit with pain reduction (though some patients received radiotherapy simultaneously) and in most cases weight gain. This symptomatic improvement was not seen in the three patients whose prostate-specific antigen levels did not fall. Of those patients fulfilling the criterion for marker remission, the median duration of remission is 6 (2–16) months.

Treatment of metastatic prostate cancer with steroids is not new [7, 8] but detailed quantitation of response in terms of tumour markers may not have been previously described at this dose level. Clearly it is relevant when considering the activity of the suramin/hydrocortisone combination in which the contribution of the hydrocortisone—in the case of prostate cancer—is not negligible. It is probably significant that where hydrocortisone has been omitted [9] the results have been poor.

Correspondence to S.J. Harland.
S.J. Harland and G.M. Duchesne are at the Institute of Urology and Department of Oncology, University College and Middlesex School of Medicine, London W1N 8AA, U.K.
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