Response of ectopic prostatic ACTH production to metyrapone

B. N. STATHAM
M.B., M.R.C.P. (U.K.)

T. H. PARDOE
M.B., B.Ch.

M. A. MIR
M.B., M.R.C.P.

Department of Medicine, C2 Unit, Welsh National School of Medicine

Summary

A case of ectopic prostatic ACTH production exhibiting a good response to metyrapone is reported.

Introduction

Ectopic hormone production is a rarely recognized complication of prostatic carcinoma. Only 3 well documented cases of adrenocorticotrophin production have been reported (Ewark, Oluyh and Bennett, 1973; Lovern, Farriss and Wettlanfer, 1975; Wenk, Bhaguan and Levy, 1977).

Case report

A 63-year-old man who 3 years previously had undergone a transurethral prostatic resection for adenocarcinoma presented with a 2-month history of 'euphoric' behaviour followed by an excessive thirst and ankle swelling. He was a non-smoker and had been taking ethinyl oestradiol (stilboestrol) 3 mg daily since the prostatic resection. Initial examination revealed an extravagant and extrovert personality in a man previously described as shy. There was no abnormal pigmentation, he was normotensive and had gross bilateral below knee oedema. Investigations revealed impaired renal function and a hypokalaemic alkalosis (serum sodium 157 mmol/l; potassium 1.7 mmol/l; bicarbonate 32.0 mmol/l; urea 14.5 mmol/l); an elevated random plasma glucose at 8.4 mmol/l and a normochromic normocytic anaemia (Hb 12.0 g/dl). X-rays of the chest and skull showed no abnormality. Prostatic acid phosphatase was 5 i.u./l (0-4 i.u./l). Renal tubular function was normal as demonstrated by a normal urinary acidification test and a normal urinary amino acid composition. Plasma cortisol was markedly elevated at >1377 nmol/l (n.r. <800 nmol/l) as was adrenocorticotrophic hormone (ACTH) at 1589 ng/l (n.r. <80 ng/l).

A dexamethasone suppression test was not performed in view of steady deterioration in mental

function and ankle oedema increasingly resistant to diuretic therapy. Metyrapone was then commenced in a dose of 750 mg every 6 hr, together with prednisolone (15 mg/day) to prevent a possible Addisonian crisis. Within 3 days the requirements of potassium supplements declined from 26 g of potassium chloride daily to 5 g/day and his mental state gradually improved. Serum cortisol levels returned to the normal range (359 nmol/l). At this stage there was no evidence of metastatic disease and prolonged survival seemed a possibility.

In view of this, an orchidectomy was uneventfully performed in an attempt to suppress tumour growth. The patient was then discharged home in good health taking metyrapone 750 mg 6 hourly and amiloride 10 mg daily. Two months later he was readmitted with rapidly worsening renal failure and died within 48 hr of admission. A post-mortem examination revealed a poorly differentiated prostatic adenocarcinoma with multiple liver, lung and skeletal secondary deposits, the adrenal glands were hypertrophied (total weight 31 g).

Discussion

This case illustrates several features typical of the previously reported cases of prostatic ectopic ACTH production; the 3-year time lag from the initial diagnosis of a prostatic tumour to the presentation of ectopic ACTH production; the oedema, the hypokalaemic alkalosis and raised plasma glucose have all been reported in previous cases as has the histological picture of an undifferentiated or adenocarcinoma. The response to metyrapone in such a rewarding manner has not previously been noted and bilateral adrenalectomy with its many inherent dangers is the only treatment to have produced an overall survival of 3 months as in this case.

Metyrapone acts as an inhibitor of the 11 β -hydroxylation step necessary for synthesis of glucocorticoids within the adrenal glands, hence its more

common usage as a test of the pituitary-adrenal axis. Common side effects include nausea and vomiting, this has tended to restrict its usefulness both as a diagnostic and a therapeutic manoeuvre. In this case, however, metyrapone was well tolerated and produced a gratifying response for both the patient and his family in a condition for which the long term outlook remains very poor.

References

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