Beneficial Response to Megoestrol Acetate in AIDS-related Cachexia and a Possible Megoestrol Withdrawal-associated Syndrome?

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A man with AIDS is described in whom a profound weight loss was converted into a weight gain by treatment with megoestrol acetate, a synthetic progesterone. His appetite improved and was accompanied by a feeling of improved well-being. Following abrupt discontinuation of the drug, there was a significant but transient depression of mood and appetite associated with loss of energy; it is suggested that this complex of symptoms might represent a megoestrol acetate withdrawal-associated syndrome.

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Cachexia is common in patients with progressive HIV infection and often portends a poor prognosis (1). The pathogenesis is complex and often multifactorial; while intercurrent illnesses (such as neoplasia, tuberculosis and gastrointestinal infections) and/or a pure HIV-related enteropathic process (2) may contribute to the weight loss, a poorly understood primary cachexia-inducing pathological process possibly involving an elevation in the basal metabolic rate (3) may also play a part. Some evidence exists that cachectin (tumour necrosis factor, TNF), a substance produced by activated macrophages and known to promote the development of neoplasia-related cachexia (4), is released by alveolar macrophages from HIV-infected patients and may play a part in AIDS-related weight loss (5).

The maintenance of a satisfactory nutritional status in HIV-infected patients is of the utmost importance, since the deleterious effects of malnutrition on the ability to mount an immune response are well known (6); in addition, relentless weight loss adversely affects patient morale. However, simple dietary strategies and/or parenteral nutrition may not prove adequate to halt or reverse the cachexia process, and alternative strategies have been sought. Recently, reports have emerged from the USA of the apparent benefits of megoestrol acetate (MA), a synthetic progesterone, in the treatment of HIV-associated anorexia and weight loss (7–9). We wish to document the first reported successful usage of this agent in Britain, in a homosexual male with AIDS, and report a previously unrecognized possible side effect associated with withdrawal of the drug.

CASE REPORT

A 32-year-old HIV-seropositive homosexual man, who 19 months previously had developed acute *Pneumocystis carinii* pneumonia (PCP), presented with a 3-month history of severe anorexia and unexplained loss of weight (total loss 7 kg, equivalent to 0.58 kg per week). Prior to this he had been in reasonable health, with a stable weight, his medication including regular nebulized pentamidine isethionate (as prophylaxis against recurrent PCP) and intermittent zidovudine. During the latest 3-month period there were no apparent psychological factors, intercurrent infections, neoplasms or drug-related effects (zidovudine had been discontinued 4 months previously owing to unacceptable gastrointestinal upset) that would have accounted for his symptoms. Furthermore he had failed to respond to supplemetary nutrition with high protein/calorie feeds.

In view of this, MA was commenced at a dose of 80 mg q.d.s.; he gained 6 kg in the first month and then, despite a reduction of the dose to 80 mg b.d., a further 2 kg over the next month. During this period the patient noted a dramatic increase in his appetite, and no clinical, biochemical or immunological side effects attributable to the treatment came to light. At this juncture, the patient requested that the drug be withdrawn as he became concerned about the predominance of adipose tissue in his weight gain. Following abrupt discontinuation of the drug, the patient noted a significant depression of mood which was associated with a rapid decline in his appetite and a loss of energy; these symtoms were transient, lasting for 10 to 14 days.

DISCUSSION

In a series of 21 patients who have died of AIDS in this unit over the period 1985–89, 11/21 (53%) have shown weight loss of more than 10% of their premorbid body mass. While it clearly remains essential that all other factors (such as depression, dementia, infection and neoplasia) which might in themselves

be responsible for weight loss be excluded (or, if present, treated) prior to commencement of MA therapy, the response of the present patient to MA is encouraging and suggests that an apparently preterminal loss of weight can be halted and even reversed in some HIV-infected individuals. MA may accordingly have a place in the treatment of patients with pure HIV disease-related weight loss. However, up to the present time those trials that have studied MA have concentrated purely upon patients with full-blown AIDS and have only investigated its effects over relatively short periods of time. Accordingly, the long-term efficacy, safety, and possible value of MA in patients with earlier stages of HIV-related disease, either alone or in conjunction with supplementary nutrition, are still uncertain, and it is essential that the outcome of studies to assess the true efficacy and optimal dosage of the drug are awaited before proposing the more widespread use of this agent. In the present case, the drug was prescribed on compassionate grounds.

An additional point concerns the symptoms of depression and profound fatigue experienced by the present case following abrupt withdrawal of MA. These could perhaps be explained by a "withdrawal syndrome" similar to that described following discontinuation of glucocorticoid therapy (10). However, further work would obviously be needed in order to establish whether the present patient's experience was an isolated incident or part of a more generalized picture.

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