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CASE REPORT

Partial Adrenal Suppression with Prolonged Use of Depo-Provera

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ABSTRACT

A 49-year old patient presented with symptoms of adrenal suppression following an attempt to withdraw Depo-Provera or Depot Medroxyprogesterone Acetate (DMPA) injection. She had been receiving DMPA injections for the past 16 years for contraception. She was initially prescribed DMPA by her gynaecologist but later on began obtaining the medication directly from a private pharmacy without prior consultation from her gynaecologist. Clinically, she had been experiencing significant weight gain and appeared cushingoid. Blood investigations confirmed partial adrenal suppression with presence of an adrenal incidentaloma. This case reports a known side effect of DMPA but occurring at a much lower dose than previously described. It also highlights the need to increase the awareness of the insidious side effect of DMPA and to avoid unsupervised use of the drug.

KEYWORDS: Addison, Adrenal Suppression, Depro-Provera, Depot Medroxyprogesterone Acetate (DMPA), cortisol

INTRODUCTION

Depo-Provera (DMPA) is one of the progestin-only methods used for contraception. It was originally approved to treat endometriosis and certain cancers but is most commonly also used as a contraceptive [1]. A 90-day dosage of 150 mg of DMPA has been associated with side effects, including irregular menstruation, anxiety, headaches, weakness, abdominal pain, weight gain and amenorrhoea [2]. However, the effect of DMPA in suppressing the adrenal cortex at a dose of 150mg has never been reported before. We report a case of a woman who had been on DMPA for 16 years and who developed symptoms of adrenal suppression.

CASE PRESENTATION

A 49-year old lady was referred by her General Practitioner for severe lethargy and generalized body pain during her attempt to stop her DMPA treatment. She is a working mother of 5, who was started on DMPA treatment following the birth of her last child 16 years ago. She has not been attending any regular follow-ups with her gynaecologist and obtained the 150 mg three-monthly injections of DMPA from a nearby pharmacy. She has noted progressive weight gain of approximately 30kg within the past 10 years, which she attributed to poor dietary habits and sedentary lifestyle. She became amenorrheic after a year of treatment with occasional spotting.

Five years ago, at the age of 44, she stopped taking the DMPA injection, following advice from her GP. However, a few weeks after stopping the DMPA she became severely lethargic, and suffered headaches and erratic mood swings, which subsequently led to her low mood. She attributed her condition to the cessation of the DMPA and recommenced the injections, which immediately alleviated her symptoms and boosted her energy levels.

She has no other medical condition and denies taking any supplement or traditional medications.

During her current presentation, she was still on DMPA injection to help her with her mood swings and energy levels. She was however still complaining of occasional lethargy, headache, generalized body pains and mood swings but had expressed her wish to discontinue with her DMPA. On clinical examination, she appeared plethoric with apparent moonlike-facies. There was acanthosis nigricans but no paper-thin skin, no striae, no bruising and no hirsutism. There was evidence of proximal myopathy, which was confined to the lower limbs. Her weight was 110kg with a BMI of 47 kg/m2. Her blood pressure was 128/78 (sitting) and 120/70 (standing) with a heart rate of 79 beats per minute. Chest and cardiovascular examination were unremarkable. Her abdomen was soft with no organomegaly.

Laboratory investigations showed reduction in early morning cortisol level at 7am; 140 nmol/L (N=170-536 nmol/L). Serum estradiol level was normal; 106.8 pmol/L (normal level: <18.4-183 pmol/L) as well as progesterone, which was 0.9 nmol/L (normal level: 0.3-2.5 nmol/L). However, her follicular stimulating hormone level was low at 8.76 IU/L (normal level: 26-135 IU/L). Similarly, her luteinizing hormone was also low at 2.92 IU/L (normal level: 7.7-59 IU/L). Renal profile and thyroid function test otherwise were normal.

CT scan of the adrenal showed evidence of left adrenal incidentaloma - 0.9 x 0.9cm. HU (plain): 5-40 (average 23), HU (portovenous): 100-150 (average 125), HU (delayed): 35-55 (average 45) with absolute washout of 78% and relative washout 64%.

DMPA was stopped for the second time and a short synacthen test was performed 3 months later and the results showed partial response of cortisol to synacthen = 0 hour: 156 nmol/L (normal value in morning 170-536 nmol/L), at 30 mins 384.9 nmol/L and at 60 min 429.7 nmol/L (N=increment >200nmol/L above baseline and peak >550 nmol/L. At this juncture, she was still complaining of lethargy and low mood.

She was treated with low dose hydrocortisone 5 mg bd for 1 year before it was stopped. At subsequent clinic follow up sessions, she appeared well, and denied any symptoms of hypo-cortisolism. Six months later, her short synacthen test was normal. She however does have occasional emotional lability and remains amenorheic.

DISCUSSION

The contraceptive effect of three monthly DMPA injections are due to its anti-oestrogenic, anti-androgenic and anti-gonadotrophic actions, which prevent follicular maturation and ovulation and causes thickening of cervical mucus that inhibits sperm entry into the uterus [3].

DMPA has been identified to have a notable cortisol-like glucocorticoid activity on the hypothalmic-pituitary-adrenal (HPA) axis since the 1970s when patients on DMPA presented with cushingoid symptoms, such as weight gain, facial swelling and generalised edema [4].This cortisol-like effect is believed to exert a negative feedback action on the hypothalamus or the pituitary leading to low plasma ACTH, suppression of adrenal function and decreased cortisol secretion. Mild suppression of the hypothalmic-pituitary-adrenal axis has been reported in 10 children who received 100-150mg per week of DMPA for the treatment of precocious puberty [4]. A study done by Hellman *et al* [5] showed a 76% reduction in plasma cortisol concentration in 12 breast cancer patients who were given weekly doses of 400, 700 or 1200 mg of DMPA for 6-24 months. Another study also showed partial adrenal suppression in postmenopausal women with disseminated breast cancer who received high doses of DMPA of up to 250 mg four times daily[6]. Patients who developed adrenal suppression following DMPA treatment were reported to be older and perhaps could be more sensitive to the anabolic effects of DMPA than other patients [7]. Malik et al [8] reported a case-study of eleven patients who had received DMPA following treatment for breast carcinoma and hypernephroma. The duration of DMPA therapy ranged from 6 to 90 months. Four of the eleven patients had low basal cortisol levels and subnormal responses to synacthen and two patients had a borderline response. Eight patients had ACTH levels at or below the detection limit of the assay.

To our knowledge, there have been no reports to date, on partial or complete adrenal suppression due to prolonged use of DMPA, particularly at a dose of 150 mg when used as a contraceptive. Our patient presented with typical symptoms of hypo-cortisolism during the period of cessation of DMPA therapy. This was confirmed by the presence of partial adrenal suppression following the synacthen test. Her CT scan, which showed adrenal incidentaloma, highlights the likelihood that her condition was due to the DMPA therapy. This case highlights 2 major points, which differ from previous reports. The first being the prolonged and unsupervised use of the injectable drug and the second being that even at relatively low doses long-term usage of DMPA can lead to hypo-cortisolism.

CONCLUSION

Depo-Provera or DMPA has been associated with adrenal suppression due to cortisol-like glucocorticoid activity, which provides negative feedback effects on the hypothalamus or pituitary. This results in low plasma ACTH levels and consequently also decreased plasma cortisol. Our patient developed partial adrenal suppression due to prolonged, unsupervised prescription and use of a low dose DMPA. Thus, clinicians should be wary of this insidious side effect of a very common drug even when used at low doses.

Conflict of Interest

Authors declare none.

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