Pregnancy in a woman with premature ovarian failure

Nicholas Finer¹, Ignac Fogelman² and Gianfranco Bottazzo³

Departments of ¹Medicine and ²Nuclear Medicine, Guy's Hospital and Medical School, St. Thomas Street, London Bridge SE1 9RT and ³Department of Immunology, Middlesex Hospital Medical School, 40–50 Tottenham Street, London W1P 9PG, UK.

Summary: We report the case of a 32 year old woman with premature ovarian failure associated with ovarian autoantibodies, autoimmune Addison's disease and primary hypothyroidism who became pregnant following the treatment of her thyroid and adrenal deficiencies.

Introduction

When ovarian failure occurs with a premature menopause it is usually associated with elevated gonadotrophin levels and the absence of follicles in the ovary. However, a syndrome of ovarian failure with persisting ovarian follicles is recognized and has been variously termed the 'savage', 'resistant' or 'insensitive ovary syndrome' (Tulandi & Kinch, 1981). The mechanism for this condition is not known but on rare occasions ovarian function may recover and pregnancies have been reported (Tulandi & Kinch, 1981). Premature gonadal failure is, however, relatively common in Addison's disease – in one series it was present in over 25% of women (Irvine & Barnes, 1972). It is usually ovarian in origin with hypergonadotrophism and low oestrogen levels. Laparoscopy may show lymphocytic infiltration of the ovaries, or the presence of streak ovaries in cases of primary amenorrhoea (Irvine & Barnes, 1972). Gonadal failure is particularly common in those subjects with 'idiopathic' disease and may precede the onset of adrenal insufficiency by many years (Turkington & Lebovitz, 1967). Ovarian (steroid cell) autoantibodies are IgG antibodies that react with steroid producing cells in the gonads. They may be present in up to 50% of patients with Addison's disease without gonadal failure, and may also occur when adrenal autoantibodies are not present (Sotsiou et al., 1980). Amenorrhoea or an early menopause was always present in subjects with autoantibodies to both adrenal cortex and ovarian theca interna cells (Irvine & Barnes, 1972; Sotsiou et al., 1980). This case report describes a patient with Addison's disease and premature ovarian failure associated with these autoantibodies who became pregnant.

Case report

A 32 year old woman presented with a classical history of Addison's disease. She had felt increasingly tired and weak over a period of six months, with dizziness on standing and then nausea and vomiting. She gave a history of 7 years' primary infertility, which had been investigated elsewhere and attributed to an early menopause. For 18 months she had had complete amenorrhoea.

On examination she was pigmented, thin and had postural hypotension. Investigations confirmed Addison's disease with 09.00 h plasma cortisol of 86 nmol/l and no cortisol response to Synacthen. Adrenocorticotropic hormone (ACTH) levels were elevated at >500 pg/ml (normal <71 pg/ml). Her thyroid was not palpable. Serum thyroxine (T₄) was 14 nmol/l (normal range 65–155 nmol/l) and serum thyrotropin (TSH) elevated at >25 mU/l, thus confirming the diagnosis of primary myxoedema. Gonadotrophins were compatible with ovarian failure; follicle stimulating hormone (FSH) >20 U/l (normal <5 U/l and luteinizing hormone (LH) <50 U/l (normal 16 U/l; plasma oestradiol was undetectable (<40 nmol/l). Serum prolactin was normal (327 mU/l) and there was no evidence of hypoparathyroidism. Antibody studies showed adrenal (titre 1/320) and ovarian-steroid cell (1/320) autoantibodies, detected by immunofluorescence. Mitochondrial (1/10), stomach gastric parietal cell (1/640), smooth muscle antibodies (1/20) and thyroid microsomal haemagglutinating antibodies (1/160) were also detected. Thyroglobulin, pituitary and pancreatic islet cell antibodies were negative.

The patient was commenced on hydrocortisone 30 mg/d, fludrocortisone 50 µg/d and L-thyroxine 100 µg/d. Six weeks after starting this treatment she menstruated and gonadotrophins were found to have

Correspondence: I. Fogelman, M.D., M.R.C.P.
Accepted: 25 June 1985

© The Fellowship of Postgraduate Medicine, 1985
Clonidine was 237 fallen: hormone replacement, and the subsequent pregnancy all indicate that she had reversible ‘ovarian failure’.

All the previously reported cases of ovarian failure in association with ovarian autoantibodies were irreversible. Ovarian autoantibodies have been shown to be cytotoxic to ovarian cells in vitro (McNatty et al., 1975) but whether they cause ovarian failure in vivo may depend upon other factors such as the individual’s cell-mediated immune response. While it is recognized that autoimmune disorders may follow a fluctuating course (Doniach et al., 1979) ovarian antibody titres were constant in this case. In the ‘resistant ovary syndrome’ pregnancy is rare and reported cases have usually occurred after oestrogen or gonadotrophin therapy. Thus the explanation for the recovery of ovarian function in our patient following replacement hormone treatment is not clear. It is unlikely that physiological doses of steroids would have any immunosuppressant effect.

This case is exceptional but it provides a further reminder that ovulation may still occur after a premature menopause and indeed pregnancy may ensue.

Addendum

We are pleased to report that this patient subsequently delivered a healthy boy.

References


Pregnancy in a woman with premature ovarian failure.

N. Finer, I. Fogelman and G. Bottazzo

*Postgrad Med J* 1985 61: 1079-1080
doi: 10.1136/pgmj.61.722.1079

Updated information and services can be found at:
http://pmj.bmj.com/content/61/722/1079

**Email alerting service**
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Notes**

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/