

Premature ovarian failure could be an alarming sign of polyglandular autoimmune dysfunction

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A 31-year-old lady, diagnosed to have premature ovarian failure in the gynecology clinic, was referred for endocrine assessment because of an abnormal thyroid function test. Clinical examination revealed hypotension, and fungal skin infection under her atrophic breasts. Thyroid stimulating hormone (TSH) level was very high. Assessment of the suprarenal function revealed evidence of Addison's disease. Polyglandular autoimmune dysfunction was diagnosed. She was treated with prednisone, fludrocortisone, and levothyroxine with significant improvement of her general condition and blood pressure.

Key words: ovarian failure, polyglandular autoimmune syndrome, hypothyroidism, adrenal failure

Polyglandular autoimmune syndromes (PAS) are series of disorders characterized by autoimmunity against two or more endocrine organs and clinical diversity (Saif 2016). Schmidt first described the association between lymphocytic thyroiditis and adrenocortical dysfunction in 1926 (Betterle et al. 2004). Later the syndromes were classified into a rare juvenile type (PAS I) and a relatively common adult type with (PAS II) or without (PAS III) adrenal dysfunction (Kahaly 2009). Premature ovarian failure (POF) may also have an autoimmune origin and when accompanied by other autoimmune endocrinopathies, may be part of the PASS. A case of PAS presenting by POF is discussed herein.

Subject and Results

A 31-year-old woman, diagnosed to have POF in the gynecology clinic, was referred for endocrine assessment because of an abnormal thyroid function

test. She is married and has one child, born six years ago. She lactated normally for 18 months, but started to complain of amenorrhea shortly after delivery. Thyroid functions were not checked before or during pregnancy. Five years after delivery, she was assessed in the gynecology clinic and diagnosed to have premature ovarian failure. She was already on levothyroxine (0.1 mg daily for two weeks) before being seen in the endocrinology clinic. Clinical assessment revealed weight of 54 kg, blood pressure 85/50 mmHg (reported to be 110/70 mmHg in the gynecology clinic) and regular pulse 70/min. Oral candidiasis and fungal skin infection under her atrophic breasts were evident. Gonadotropin levels were significantly high and estradiol level was very low. TSH level was very high (100 mIU/ml) and free thyroxine (FT4) was low. Thyroid peroxidase (TPO) antibodies were positive. Assessment of suprarenal function revealed evidence of Addison's disease. Morning cortisol level was 60.7 nmol/l (normal range: 138–690 nmol/l) with ad-

Table 1
Assessed parameters before and after treatment.

Parameter	Normal range	Before treatment	After treatment
Body weight (kg)	–	54	69
Blood pressure (mmHg)	–	85/50	110/70
TSH (mIU/ml)	0.3–4.5	100	3.39
FT4 (ng/dl)	0.8–1.8	0.6	1.1
Cortisol (nmol/l) a.m.	138–690	60.7	*
ACTH (pg/ml) a.m.	10–50	69	29
Prolactin (ng/ml)	2–29	49	2.8
Serum potassium (mmol/l)	3.5–5.3	5.7	5.0

TSH – thyroid-stimulating hormone; FT4 – free thyroxine;

ACTH – adrenocorticotrophic hormone

* – not measured

renocorticotrophic hormone (ACTH) 69 pg/ml (normal range: 10–50 pg/ml). Peak cortisol level 30 min after ACTH stimulation was 176.6 nmol/l (normal >496.5 nmol/l). Serum prolactin level was 49 ng/ml (normal range: 2–29 ng/ml). Her fasting blood glucose was 83 mg/dl, serum calcium was 8.8 mg/dl and serum potassium was 5.7 mmol/l. Her liver and kidney functions were normal. Polyglandular autoimmune dysfunction was diagnosed. She was treated with prednisone and fludrocortisone with significant improvement of her general condition and blood pressure. Levothyroxine was stopped temporarily and restarted after two weeks. The dose titration was done over 8 months according to clinical and laboratory follow up. Finally, she was kept on prednisone (2.5 mg twice daily), fludrocortisone (0.1 mg once daily), and levothyroxine (0.125 mg once daily). Her blood pressure was up to 110/70 mmHg and body weight increased gradually to 69 kg. TSH gradually dropped down to 3.39 mIU/ml, serum prolactin to 2.8 ng/ml, and serum potassium to 5.0 mmol/l. Oral candidiasis was treated with miconazole oral gel. The fungal skin infection resolved completely on clotrimazole skin cream.

Discussion

The polyglandular autoimmune syndromes are characterized by the coexistence of at least two autoimmune mediated endocrinopathies. PAS I often appears early in the life with persistent candida infection of the skin and mucous membranes. It usually manifests later with hypoparathyroidism or Addison's disease (Eisenbarth and Gottlieb 2004). PAS II usually peaks between ages 20–60 years and multiple generations are affected by one or more component of the syndrome (Neufeld et al. 1980). Type 1 diabetes is often its first symptom and is usually associated with either autoimmune thyroid disease and/or adrenal failure. A third subtype, which does not involve the adrenal cortex, has also been described in adults (Kahaly 2009).

Our patient was diagnosed in the gynecology clinic as a case of a premature ovarian failure. The discovery of an abnormal thyroid function test was the first clue to the presence of multiple endocrinopathies. The very high TSH and the presence of positive TPO antibodies established the diagnosis of Hashimoto's thyroiditis causing primary hypothyroidism. The fact that her blood pressure dropped after taking levothyroxine for two weeks pointed to the possibility of adrenal failure. This was later confirmed by ACTH stimulation test.

The presence of candida infection of the skin and mucous membranes in addition to the primary ovarian failure suggested the diagnosis of PAS I. But the late onset and the absence of hypoparathyroidism did not confirm that possibility. On the other hand, the age of onset of hypothyroidism and adrenal dysfunction, in association with the ovarian failure, pointed towards PAS II. But the muco-cutaneous candidiasis speaks against this possibility. Balamurugesan and Viswanathan (2016) reported the case of a 27-year-old lady who presented with primary infertility and later diagnosed to have PAS II. Despite the importance of reaching a final diagnosis, the recognition of the multiple endocrine deficiencies was the cornerstone of the life-saving management.

In summary, premature ovarian failure could be an alarming sign of multiple endocrine dysfunction. The management of those patients should be handled by a multi-disciplinary team including gynecology and endocrinology specialists. Full assessment of possible other endocrine disease associations would be recommended.

References

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