

Schmidt's syndrome associated with sarcoidosis

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Summary

We present a case of Schmidt's syndrome (autoimmune Addison's disease and hypothyroidism) associated with sarcoidosis. There have been only four previous reports of Schmidt's syndrome with sarcoidosis, and a possible fifth with negative autoantibodies. We have been able to find only four other reports of adrenal failure (without hypothyroidism) in sarcoidosis. It is important to be aware of the potential for masking the diagnosis of Addison's disease by steroid treatment.

Keywords: Schmidt's syndrome, Addison's disease, hypothyroidism, sarcoidosis

A 34-year-old woman presented in August 1988 with an eight-week history of dry cough, pleuritic chest pain, dyspnoea on exertion, and generalised weakness. Examination was normal apart from bilateral basal crepitations in the lungs. Chest X-ray showed diffuse miliary nodular shadowing. She had a restrictive lung function: FEV1 2.02 l (predicted 2.91), FVC 2.02 l (predicted 3.43), KCO 1.29 (predicted 2.11). Mantoux test was negative. The diagnosis of sarcoidosis was confirmed by a transbronchial lung biopsy showing granulomatous inflammation with numerous giant cells. At that time, serum urea, electrolytes, glucose, and calcium were normal. She was also found to be hypothyroid (free thyroxine 3.6 pmol l⁻¹, thyroid-stimulating hormone 63.6 mU l⁻¹). Antithyroid antibodies were positive: antithyroglobulin titre 1:40, antithyroid microsomal antibody titre 1:6400.

Treatment was started with prednisolone 15 mg daily and thyroxine 0.1 mg daily, with a dramatic symptomatic improvement. The chest X-ray and lung function returned to normal. Subsequently her steroid dose was reduced slowly. After six months on a prednisolone dose of 1 mg, she complained of feeling tired, although there were no features on chest X-ray or lung function testing to suggest active sarcoidosis and her thyroid replacement was adequate. An attempt to discontinue prednisolone in September 1989 resulted in a deterioration of her lung function but she was stabilised on a dose of 2.5 mg prednisolone on alternate days.

In December 1990, she was admitted to hospital as an emergency with diarrhoea and vomiting. On admission her blood pressure was 100/60 mmHg, and her electrolytes were abnormal: sodium 124 mmol l⁻¹, potassium 4.9 mmol l⁻¹. Stool culture was negative. At the

time she was thought by the admitting team to have gastroenteritis, and her steroid dose was increased to 30 mg for a few days to cover the intercurrent illness. She improved, the prednisolone dose was reduced, and she was discharged on her previous dose of 2.5 mg on alternate days.

In August 1991 she presented again with malaise, nausea, and postural hypotension, with serum sodium 128 mmol l⁻¹, potassium 5.3 mmol l⁻¹, and urea 8 mmol l⁻¹. The diagnosis of adrenal insufficiency was confirmed by a low cortisol (30 nmol l⁻¹), with no increase following synacthen injections, either acutely or over five days. Adrenocorticotropin was elevated at 243 ng l⁻¹. Adrenal antibodies were present in the blood. Ambulant aldosterone level was low (90 pmol l⁻¹; recumbent reference range 100 - 450).

She was treated with cortisol 30 mg and fludrocortisone 50 g daily, and has remained well since. She had had five years of secondary infertility with biochemical evidence of anovulatory cycles (day 21 oestradiol 610 pmol l⁻¹, progesterone 19 nmol l⁻¹, follicle-stimulating hormone 4 IU l⁻¹, luteinising hormone 5 IU l⁻¹, prolactin 320 mU l⁻¹), but she became pregnant and a healthy female child was delivered by caesarian section in February 1994.

Discussion

Schmidt's syndrome was initially described in 1926 as the association of idiopathic Addison's disease and lymphocytic thyroiditis. Subsequently the association with autoimmune failure of other endocrine glands has been recognised (see box 1). Four previous reported cases of sarcoidosis associated with Schmidt's syndrome in which adrenal and thyroid autoantibodies were present were reviewed by Walz and From.¹ In another case, both Addison's disease and hypothyroidism were present but adrenal and thyroid autoantibodies were not detected.² The authors speculated that granulomatous involvement of the endocrine glands might be responsible, but the patient also had vitiligo which is commonly associated with autoimmune endocrine disorders.

We know of no previous reported cases of Schmidt's syndrome with sarcoidosis who subsequently had a successful pregnancy. We know of four other published cases of Addison's disease, without hypothyroidism, associated with sarcoidosis.³⁻⁶ In one case, autopsy showed the adrenal cortex replaced by fibrous tissue which the authors thought may have been a result of healed granulomatous infiltra-

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tion.³ Sarcoid granulomatous involvement of the adrenal glands was suggested but not proven in the other cases. Adrenal antibodies were negative in one of these cases,⁵ but in others an autoimmune aetiology has not been excluded. Hypothyroidism due to sarcoid involvement of the thyroid is recognised, but in our case the presence of antibodies indicates an autoimmune aetiology. Granulomatous infiltration should not be assumed to be the cause of any endocrine disorder in a patient with sarcoidosis without good evidence.

In retrospect, the episode of 'gastroenteritis' in our patient was probably an Addisonian crisis. Because she had been on long-term steroids, the dose was increased for a supposed intercurrent infection, fortuitously treating the condition but delaying the correct diagnosis.

This illustrates the potential for camouflage of adrenal insufficiency in patients taking systemic steroids for sarcoidosis or other conditions, which was highlighted by Jacobs *et al.*⁶

A number of other autoimmune conditions have been reported in association with sarcoidosis, including Hashimoto's thyroiditis (without adrenal failure), autoimmune thrombocytopenia, and connective tissue diseases. There is no evidence of a common aetiology between Schmidt's syndrome and sarcoidosis, and it is possible that the association occurred by chance. However, the possibility that there may be an association between sarcoidosis and autoimmune disease deserves consideration.

Autoimmune conditions associated with Schmidt's syndrome

- hypothyroidism
- Addison's disease
- vitiligo
- pernicious anaemia
- primary ovarian failure
- insulin-dependent diabetes mellitus
- Graves' disease
- hypoparathyroidism
- primary testicular failure

Box 1

Learning points

- there may be an association between sarcoidosis and Schmidt's syndrome or other autoimmune disorders
- granulomatous infiltration should not necessarily be assumed to be the cause of any endocrine disorder in a patient with sarcoidosis
- the symptoms and signs of Addison's disease may be masked in patients who are taking systemic steroids for sarcoidosis or for other diseases
- autoimmune ovarian failure is associated with Schmidt's syndrome. However, fertility can be impaired by untreated hypothyroidism or Addison's disease, or sarcoidosis, without any intrinsic ovarian disease

Box 2

1 Walz B, From GLA. Addison's disease and sarcoidosis: unusual frequency of co-existing hypothyroidism (Schmidt's syndrome). *Am J Med* 1990; **89**: 692-3.

2 Seinfeld ED, Sharma OP. TASS syndrome: unusual association of thyroiditis, Addison's disease, Sjogren's syndrome, and sarcoidosis. *J R Soc Med* 1983; **76**: 833-5.

3 Maycock RL, Bertrand P, Morrison CE. Manifestations of sarcoidosis. Analysis of 45 patients with a review of nine series selected from the literature. *Am J Med* 1963; **35**: 67-89.

4 Irvine WJM, Toft AD, Feek CM. Addison's disease. In: James VHT ed. *The adrenal gland*. New York: Raven Press, 1979; pp 131-64.

5 Umeki S, Moriya O, Kihari T. Second case of sarcoid Addison's disease (Letter). *Am J Med* 1987; **82**: 186-7.

6 Jacobs TP, Whitlock RT, Edsall J, Holub DA. Addisonian crisis while taking high-dose glucocorticoids. An unusual presentation of primary adrenal failure in two patients with underlying inflammatory diseases. *JAMA* 1988; **260**: 2082-4.