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. Adrenocorticotropic 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.³⁻⁵ In one case, autopsy showed the adrenal cortex replaced by fibrous tissue which the authors thought may have been a result of healed granulomatous infiltr-
tion. Sarcoi
d granulomatous involvement of
the adrenal glands was suggested but not
proven in the other cases. Adrenal antibodies
were negative in one of these cases, but in
others an autoimmune aetiology has not been
excluded. Hypothyroidism due to sarcoi
d 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 sarcoi
dosis, including Hashimoto’s thyroiditis (with-
out adrenal failure), autoimmune
thrombocytopenia, and connective tissue dis-
eases. There is no evidence of a common
aetiology between Schmidt’s syndrome and
sarcoidosis, and it is possible that the associa-
tion occurred by chance. However, the possi-

tility 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
- 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

Schmidt's syndrome associated with sarcoidosis.

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