Diffuse histoplasmosis in a patient with sarcoidosis

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Summary
A case is presented of a woman with a long history of sarcoidosis who developed diffuse histoplasmosis. Although association between these two entities has been described before, there are only a few case reports of histoplasmosis among sarcoid patients. Diagnosis was finally established by bone marrow biopsy which saved the patient's life.

Keywords: histoplasmosis, sarcoidosis

*Histoplasma capsulatum*, a dimorphic fungus and a soil saprophyte, is distributed throughout the world. Although histoplasmosis occurs worldwide, endemic regions in the US are in the Ohio-Mississippi River Valley, with microfoci in other areas. It is usually asymptomatic or self-limiting, except in patients who have a predisposing immunodeficiency.

Disseminated histoplasmosis predominantly affects the lungs and reticuloendothelial system, but it may affect any part of the body. The diagnosis becomes particularly difficult when systemic diseases such as tuberculosis or sarcoidosis predispose to dissemination of histoplasmosis. We report a case of diffuse histoplasmosis that developed in a patient with sarcoidosis.

Case report

A 29-year-old black woman had presented to the hospital with fever and cough of several weeks duration. Pulmonary sarcoidosis was diagnosed by mediastinal lymph node biopsy in 1987, followed by progressive renal failure. A percutaneous renal biopsy revealed focal glomerulosclerosis. The patient's pulmonary symptoms were successfully treated with corticosteroids, but renal function soon deteriorated to end-stage renal-disease requiring haemodialysis. She received a one-haplotype-identical living renal transplant from her mother in 1989. Her graft was functioning well two years post-transplant, when she moved from Boston to Dayton, Ohio. During the second year after her transplant, she inadvertently stopped taking azathioprine for several weeks. Her renal function deteriorated and a renal biopsy revealed severe acute and chronic rejection with prominent eosinophils in the interstitium. No granuloma was visible. Despite pulse solumedrol therapy her graft kidney could not be salvaged and she was started on ambulatory peritoneal dialysis.

Two months later she developed persistent fever with night sweats, chills, diarrhoea and weight loss. There was no evidence of infection or recurrence of sarcoidosis despite an extensive work up that included blood cultures, chest X-rays and gallium scan. The transplanted kidney was thought to be the source of infection and she underwent transplant nephrectomy with complete resolution of her symptoms. She was switched to haemodialysis after the surgery. The patient remained off corticosteroids and immunosuppressive agents for more than a year.

While on haemodialysis, she had a recurrence of high-grade fever with night sweats, weight loss and non specific diarrhoea. Physical examination was unremarkable. All infectious work up, including chest X-rays, blood cul-

![Figure 1](https://pmj.bmj.com/content/73/856/101/F1)

**Figure 1** Histological appearance of bone marrow with noncaseating granuloma (short arrow) of *Histoplasma capsulatum* infection, bone marrow biopsy material from posterior iliac crest, before steroid therapy. Long arrow indicates granuloma (Hematoxylin, Eosin X 11)

![Figure 2](https://pmj.bmj.com/content/73/856/101/F2)

**Figure 2** Intracytoplasmic appearance of *Histoplasma capsulatum* in a mononuclear cell within bone marrow aspirate smear preparation, after initiation of steroid therapy (Wright & Giemsa, X 700)
Pulmonary histoplasmosis: clinical spectrum

**Acute**
- asymptomatic
- self-limiting influenza-like syndrome
- severe dyspnea
- pneumonia

**Chronic**
- granulomas
- mediastinal and pleural fibrosis
- chronic lung cavities
- histoplasmosmas
- 'Buckshot' calcifications

**Chest X-ray**
- normal
- one or two patchy infiltrates
- mediastinal or hilar adenopathy
- diffuse miliary opacities
- pleural effusion and cavitiation are uncommon

**Box 1**
Selenium-induced thyroid dysfunction

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Summary
Administration of the anti-oxidative trace element selenium is currently being evaluated for its benefits in patients with inflammatory diseases. However, little is known about the risks of selenium. We report on a patient in whom, along with standard therapy, administration of large intravenous doses of selenite for sepsis secondary to pneumonia resulted in development of marked hypothyroidism. In addition, severe iodine deficiency was noted, and supplementation with iodine led to normalisation of thyroid function.

Keywords: selenium, iodine deficiency, hypothyroidism, euthyroid sick syndrome

Case report
A 66-year-old man with chronic glomerulonephritis and no history of thyroid disorder was admitted for treatment of severe pneumonia following removal of a tongue cancer. Laboratory results showed an elevated white blood cell count of $15 \times 10^9/\text{l}$ with a left shift, and elevated creatinine (309.4 $\mu\text{mol/l}$) and blood urea nitrogen (29.6 mmol/l) levels. Thyroid function tests revealed serum levels of thyroid-stimulating hormone (thyrotropin) of 2.0 mIU/l (normal 0.4 to 4.0), free $T_3$ of 1.7 ng/l (2.3 to 4.2), and free $T_4$ of 0.5 mg/l (normal 0.8 to 1.8), consistent with euthyroid sick syndrome. Thyroid auto-antibodies were negative. Shortly

The clinical benefit of selenium, an essential trace element with anti-oxidative effects, is currently under investigation.$^{12}$ Target compounds containing selenium include the anti-oxidative enzyme glutathione peroxidase and type I deiodinase which catalyzes hepatic thyroxine ($T_4$) to triiodothyronine ($T_3$) conversion.$^3$ We report on a patient who developed marked hypothyroidism following administration of large doses of selenium. Supplementation with iodide effectively restored normal thyroid function.

Side-effects of selenium

- odour of garlic on the breath
- fatigue, nausea
- diarrhoea, abdominal pain
- red discoloration at the base of the nails
- alopecia
- pulmonary oedema
- polyneuropathy
- increased $T_3/T_4$ ratio, hypothyroidism (in the presence of iodine deficiency)
- infertility

Learning points

- hypothyroidism may be misdiagnosed in patients with histoplasmosis
- histoplasmosis may be a concomitant infection in patients with sarcoidosis
- hypothyroidism may induce a chronic inflammatory illness such as sarcoidosis

Box 2


Box 1

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