Learning points

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

Box 2

- 1 Sharma OP. Histoplasmosis: a masquerader of sarcoidosis. *Sarcoidosis* 1991; 8: 10–13.
- 2 Goodwin RA, Shapiro JL, Thurman GH, et al. Disseminated histoplasmosis: clinical and pathological correlation. *Medicine* (Baltimore) 1980; 59: 1–33.
- 3 Tebib JG, Piens MA, Guillaux M, Colomb D, Garin JP, Tete R. Sarcoidosis possibly predisposing to disseminated histoplasmosis. *Thorax* 1988; 43: 73–4.
- 4 Winterbauer RH, Kraemer KG. The infectious complication of sarcoidosis. *Arch Intern Med* 1976; 136: 1156–62.
- 5 Wheat JL, French MLV, Wass WL. Sarcoid like manifestation of histoplasmosis. *Arch Intern Med* 1989; 149: 2421–5.

meters were normal, the patient may have had underlying immunodeficiency since she was on haemodialysis.

In summary, the occurrence of histoplasmosis in patients with sarcoidosis requires careful evaluation. Active histoplasmosis must be carefully excluded in patients suspected to have sarcoidosis, as corticosteroid treatment may result in rapid progression of disseminated histoplasmosis in patients misdiagnosed as having sarcoidosis.⁹

- 6 Sathapatayavongs B, Batteiger BE, Wheat LJ, Slama TG, Wass JL. Clinical and laboratory features of disseminated histoplasmosis during two large urban outbreaks. *Medicine* 1983; 62: 263–70.
- 7 Israel HL, DeLamater E, Sones M, Willis WD, Mirmelstein A. Chronic disseminated histoplasmosis. *Am J Med* 1952; 12: 252–60.
- 8 Reimann HA, Price AH. Histoplasmosis resembling sarcoidosis. *Trans Assoc Am Physicians* 1949; 62: 112–5.
- 9 Sills M, Schwartz A, Weg JG. A consequence of progressive dissemination in the index case after steroid therapy. *Ann Intern Med* 1973; 79: 221–4.

Selenium-induced thyroid dysfunction

Lorenz C Hofbauer, Christine Spitzweg, Roland A Magerstädt, Armin E Heufelder

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 $15 \times 10^9/l$ 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 $0.4–4.0$), free T_3 of 1.7 ng/l ($2.3–4.2$), and free T_4 of 0.5 mg/l (normal $0.8–1.8$), consistent with euthyroid sick syndrome. Thyroid auto-antibodies were negative. Shortly

Side-effects of selenium

- odour of garlic on the breath
- fatigue, nausea
- diarrhoea, abdominal pain
- red discolouration at the base of the nails
- alopecia
- pulmonary oedema
- polyneuropathy
- increased fT_3/fT_4 ratio, hypothyroidism (in the presence of iodine deficiency)
- infertility

Box 1

Division of
Endocrinology,
Medizinische Klinik,
Klinikum Innenstadt,
Ludwig-Maximilians-
Universität, Ziemssen-
straße 1, D-80336
Munich, Germany
LC Hofbauer
C Spitzweg
RA Magerstädt
AE Heufelder

Correspondence to Armin E.
Heufelder, MD

Accepted 7 March 1996

The clinical benefit of selenium, an essential trace element with anti-oxidative effects, is currently under investigation.^{1,2} 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.

after admission, haemodynamic and respiratory functions deteriorated and the patient was transferred to the intensive care unit for supportive therapy and intravenous administration of broad-spectrum antibiotics for presumed sepsis. In addition, intravenous supplementation with selenite (2500 µg total over seven days) was given according to an investigational protocol. Six days after selenite had been started, the patient's condition had stabilised with normal vital functions. However, his mental status progressively worsened with marked lethargy and poor attention span. Thyroid function tests now showed a rise in free T₃ (2.9 ng/l), a decline of free T₄ (0.4 mg/l), and an elevated basal thyrotropin (12.1 mIU/l), suggesting hypothyroidism. In addition, marked iodine deficiency, as reflected by low 24-h urinary iodine excretion of 15 µg (normal 45–700 µg), was noted. Selenium-induced hypothyroidism precipitated by marked iodine deficiency was suspected. Following supplementation with iodide (200 µg per day), the patient's mental status and thyroid function normalised within three weeks (thyrotropin 2.25 mIU/l, free T₃ 2.5 ng/l, free T₄ 0.8 mg/l).

Discussion

Selenium deficiency is common in people over 60 years of age, and may impair activity of selenium-containing type I deiodinase and T₄-to-T₃ conversion.⁴ Oral supplementation of normal individuals with selenium has been reported to induce type I deiodinase activity, thereby enhancing the T₄-to-T₃ conversion rate and lowering T₄ serum levels without a concomitant increase in thyrotropin.⁵ Similarly, a recent study suggested that oral administration of selenium in euthyroid, elderly individuals may alter thyroid function.⁴ In this study, T₄ was the most sensitive

Learning points

- physicians should be aware of adverse effects of trace elements
- administration of selenium may alter thyroid function and promote hypothyroidism in iodine-deficient individuals
- iodine deficiency should be corrected prior to selenium administration

Box 2

parameter of selenium deficiency and subsequent repletion. While selenium deficiency may play a role in the low T₃ syndrome, an adverse prognostic marker in critical illness, it appears to protect against some consequences of iodine deficiency and may attenuate the severity of hypothyroidism in iodine-deficient individuals. As suggested by our patient, short-term reversal of selenium deficiency via parenteral administration of large doses of selenium may induce thyroid dysfunction and frank hypothyroidism. This may be particularly relevant in individuals with marked iodine deficiency and impaired selenium clearance due to renal failure. Marked iodine deficiency may have contributed to thyroid dysfunction in our patient, since stimulation of type I deiodinase activity and hepatic T₄-to-T₃ conversion occurred in the presence of poor iodine reserve, thus limiting thyroid hormone synthesis. In summary, physicians should be aware of unexpected metabolic effects following indiscriminate administration of the 'natural' trace element selenium (box 1). Potential beneficial effects of using selenium to counteract oxidative stress^{1,3} must be carefully balanced against the potential risk of aggravating thyroid dysfunction. We recommend that, prior to its use, iodine deficiency should be sought and corrected, as illustrated by a recent study.⁶

1 Michiels C, Raes M, Toussaint O, Remacle J. Importance of Se-glutathioneperoxidase, catalase, and Cu/Zn-SOD for cell survival against oxidative stress. *Free Radic Biol Med* 1994; 17: 235–48.

2 Willett WC, MacMahon B. Diet and cancer - an overview (part II). *N Engl J Med* 1984; 319: 697–703.

3 Berry MJ, Larsen PR. The role of selenium in thyroid hormone action. *Endocr Rev* 1992; 13: 207–19.

4 Olivieri O, Girelli D, Azzini M, *et al.* Low selenium status in the elderly influences thyroid hormones. *Clin Sci* 1995; 89: 637–42.

5 Contempre B, Duale NL, Dumont JE, *et al.* Effect of selenium supplementation on thyroid hormone metabolism in an iodine and selenium deficient population. *Clin Endocrinol* 1992; 36: 579–83.

6 Contempre B, Dumont JE, Ngo B, *et al.* Effect of selenium supplementation in hypothyroid subjects of an iodine and selenium deficient area: the possible danger of indiscriminate supplementation of iodine-deficient subjects with selenium. *J Clin Endocrinol Metab* 1991; 73: 213–5.