Letters to the Editors

Lead poisoning by self-administration in an exposed worker

Lead poisoning is still a problem in the 21st century. Most cases involve children, but some result from environmental or occupational exposure. Chronic lead poisoning in the workplace is mainly due to inhalation of lead fumes or ingestion of lead compounds (during painting, lead smelting, pottery glazing, storage battery manufacture, etc.) [1, 2]. The case described here appears to be the first report of lead poisoning by a malingerer.

A 51-year-old man admitted to hospital for lead poisoning had been exposed while working in a tin firm for 28 years. He complained of asthenia, weight loss (4 kg), headaches and constipation, but not abdominal colic. Physical examination was normal, particularly for deep tendon and plantar reflexes, and there was no sensory deficit. Biological studies found no anaemia or renal insufficiency. Blood lead concentration was initially $2.6 \mu\text{mol l}^{-1}$ (normal $0.25\text{--}1.25 \mu\text{mol l}^{-1}$), and urine lead concentration after an edetate calcium disodium (CaNa_2EDTA) challenge test was $70 \mu\text{mol } 24 \text{ h}^{-1}$. Erythrocyte protoporphyrin concentration was $2 \mu\text{g g}^{-1} \text{ Hb}$, and delta aminolevulinate concentration was elevated at $80 \mu\text{mol l}^{-1}$. Radiographs of the spine, humerus and femur were normal.

The lead poisoning was initially considered to be of occupational origin. All family members had a normal blood lead concentration, and no other non-occupational sources of lead exposure were found. No abnormal lead concentration was detected in the water. The patient was treated three times with oral 2,3-dimercaptosuccinic acid (DMSA) and intravenous CaNa_2EDTA , and twice with oral DMSA alone. However, the blood lead concentrations were maintained ($4.5, 3.7, 4.5, 5.2, 2.8, 4.2$ and $4.9 \mu\text{mol l}^{-1}$), indicating that poisoning was unlikely to be of occupational origin in a patient who had stopped working 6 months before. Abdominal radiography showed multiple radiopaque foreign bodies in the large intestine, ranging from 0.5 to 15 mm in size (Figure 1). X-ray analysis of some collected stools allowed the extraction of two radiopaque foreign bodies (Figure 1). Analysis of these extracted foreign bodies by electrothermal atomic absorption spectrometry found that they contained 301 mg of lead per gram. This indicated that the patient had induced poisoning by deliberate ingestion of lead compounds. Following psychiatric care and social management, his self-poisoning activity ceased. Abdominal radiography became normal, and blood lead concen-

Figure 1 Multiple radioopaque foreign bodies in the large intestine in abdominal radiography (Inset: X-ray of two radioopaque foreign bodies).

trations returned to the reference range after further chelation treatments.

Factitious disorders, characterized by the deliberate inducement of symptoms for no apparent purpose, are extremely rare causes of lead poisoning [3]. There are only five cases reported in the literature [4–8]. Our case differs from a factitious disorder, as the patient wished to be regarded as having an occupational illness. This case appears to be the first report of malingering [9] related to lead poisoning.

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Different effects of simvastatin and pravastatin on adrenal sensitivity to angiotensin II

The adrenal gland requires a continuous supply of cholesterol for the biosynthesis of steroids including aldosterone. Cholesterol can be derived from *de novo* synthesis by the adrenal gland and uptake of plasma lipoproteins. Simvastatin and pravastatin are 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors widely used for the treatment of hypercholesterolaemia by inhibition of cholesterol synthesis in the liver. Simvastatin, but not pravastatin, also affects cholesterol synthesis in the adrenal gland [1]. Therefore, the effect of simvastatin on steroid biosynthesis may be different from that of pravastatin. The renin-angiotensin-aldosterone (R-A-A) axis is the primary hormonal modulator of blood pressure and fluid homeostasis in humans. However, there is little information about the effect of HMG-CoA reductase inhibitors on the R-A-A axis [2]. This study investigated the long-term (more than 12 months) effect of simvastatin or pravastatin on patients with hypercholesterolaemia by a cross-over design, and estimated the adrenal sensitivity to angiotensin II (AII) by determining the plasma aldosterone :AII ratio [3] at the end of the treatment period.

Two male and six female patients with hypercholesterolaemia (age 53 ± 12 years, weight 60 ± 4 kg) gave informed written consent. The study was approved by the Review Board of Jichi Medical School. The patients received simvastatin 5 mg or pravastatin 10 mg once daily for 12 or more months in the first treatment period. The HMG-CoA reductase inhibitor regimen was then changed to the alternative for the next 12 or more months in the second treatment period. At the end of each treatment period, furosemide (20 mg) was injected intravenously after overnight fasting to elevate the endogenous AII concentration. Blood samples were obtained

just before and 120 min after furosemide injection, and the plasma concentrations of AII, aldosterone, ACTH and potassium were measured. The patients were recumbent for at least 30 min before blood sampling. AII, aldosterone and ACTH were determined by radioimmunoassay methods [4–6]. Urine was collected during the 24 h before furosemide injection, and the urinary excretions of sodium and potassium were also determined. The patients were asked to adhere to their usual dietary habits throughout the study period. No other drugs which influence the R-A-A axis were given during the entire treatment period. Nonsteroidal anti-inflammatory drugs or diuretics were also prohibited for 2 weeks before furosemide injection. Statistical analysis was performed by paired *t*-test and analysis of variance (ANOVA). The Bonferroni/Dunn test was used as a *post hoc* test.

Plasma total cholesterol concentration was reduced by a similar extent by the HMG-CoA reductase inhibitors [mean (95% CI) mg dl⁻¹: basal 254 (234, 275), simvastatin 194 (179, 210), pravastatin 208 (192, 224)]. Plasma aldosterone concentration during simvastatin treatment was lower than that during pravastatin treatment, but it did not reach statistical significance. Plasma AII increased (ANOVA: time, $P = 0.0008$) and serum potassium decreased (ANOVA: time, $P = 0.0003$) while plasma aldosterone and ACTH did not change after furosemide injection. The plasma aldosterone :AII ratio after simvastatin treatment was smaller than that after pravastatin treatment (ANOVA: group, $P = 0.0413$) (Figure 1). The plasma aldosterone :AII ratio decreased after furosemide injection. The reduction in the ratio was significant for simvastatin [difference; mean (95% CI) -3.60 ($-6.27, 0.93$)], but was not significant for pravastatin [difference (95% CI) -7.57 ($-17.16, 2.02$)]. However, because the reduction for pravastatin was larger than that of simvastatin, the aldosterone :AII ratio of the two trials did not differ significantly at 120 min after furosemide injection. There

Figure 1 Plasma aldosterone :AII ratio before and 120 min after furosemide injection. Mean $\pm$ SD, $n = 8$. S: simvastatin, P: pravastatin.

were no significant differences between the treatments in 24 h urine volume [mean (95% CI) ml day⁻¹: simvastatin 2080 (1,614, 2545), pravastatin 1820 (1,427, 2214)] or urinary excretion of sodium [mean (95% CI) mmol day⁻¹: simvastatin 12.0 (7.5, 16.5), pravastatin 11.0 (7.1, 14.8)] and potassium [mean (95% CI) mmol day⁻¹: simvastatin 4.2 (2.6, 5.8), pravastatin 3.3 (2.4, 4.1)] before furosemide injection.

Adrenal sensitivity to AII, as measured by the plasma aldosterone :AII ratio [3], was significantly lower during simvastatin treatment than during pravastatin treatment in this study. Simvastatin, a lipophilic agent, is easily taken up into various tissues including the adrenal gland. In contrast, pravastatin, a hydrophilic agent, does not easily penetrate the organs except for the liver. These physico-chemical profiles partly explain the differences in the inhibition of cholesterol synthesis in the adrenal gland [1] and the adrenal sensitivity to AII shown in this study. Plasma potassium concentration was significantly decreased after furosemide injection, which may be caused by the drug-related massive potassium excretion in the urine. Although plasma AII concentration was elevated following furosemide, plasma aldosterone concentration did not significantly change, resulting in decreased adrenal sensitivity to AII. As aldosterone biosynthesis is regulated not only by AII and ACTH, but also by potassium [7], we think that the decrease in plasma potassium opposed steroid synthesis by the ele-

vated AII concentration. A previous study showed that plasma aldosterone decreases after long-term (9 months) treatment with simvastatin [2]. It is also reported that three patients experienced symptomatic hypotension during simvastatin therapy [8]. The mechanism was unknown, but the episode might be related to the suppression of aldosterone production by simvastatin. Taken together, we think that aldosterone synthesis by AII is potentially impaired by simvastatin, but the simvastatin-related suppression of aldosterone production may only be evident under critical situations, which require sufficient supply of aldosterone to maintain body functions.

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