Nephropathy and neuropathy induced by a germanium-containing compound

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Introduction

Germanium (Ge; atomic number 32, atomic weight 72.59) is the middle element of periodic group IV which includes C, Si, Sn, and Pb and has been used mainly in the industrial field as a semiconductor. It is a ubiquitous biomaterial and almost all foods contain it in minute amounts [1]. Germanium-containing compounds have some biological activities such as erythropoietic [2] and antibacterial [3] effects. Carboxyethylgermanium sesquioxide (Ge-132) has been reported to have antitumour effects in experimental murine ascites tumours [4]. On the other hand, germanium-containing compounds have been demonstrated to be toxic to the liver, kidney, muscle and nerves [5–9]. In Japan, some people take GeO₂ as an elixir. We observed one patient in whom both nephropathy and neuropathy were thought to be the result of germanium toxicity.

Case

A 53-year-old man was admitted to our hospital complaining of severe general weakness, anorexia and weight loss (16 kg in 3 months). Over the preceding 17 months, he had taken a total of 400 g of lysine germanium oxide in powder form as a daily health-giving agent. Anorexia appeared 14 months after he had begun to take the compound and weight loss followed. Tests at a private clinic revealed azotaemia (BUN 60 mg/dl, creatinine 2.6 mg/dl). Tingling sensation in palms and soles and asthenia of the extremities, especially the lower extremities, developed after 15 months of taking the medication. Two months later he was admitted to our hospital for further evaluation.

At the time of admission he appeared ill; the height and the weight were 176 cm and 74 kg respectively. On physical examination heart rate was 100/min and blood pressure 110/70 mmHg. Neurological examination revealed grade IV motor strength and negative deep tendon reflex in lower extremities and persistent tingling sensation of the palms and soles. Laboratory tests revealed impaired renal function (BUN 62 mg/dl, creatinine 3.0 mg/dl, creatinine clearance 39 ml/min, serum uric acid 18.8 mg/dl, FEUA 3.1%) and anaemia (haemoglobin 10.5 g/dl). Urinalysis was normal except for isotonic urine. Lactate dehydrogenase was 519 IU/l (normal 100–225), creatinine phosphokinase 2005 IU/l, myoglobin above 500 ng/ml (normal below 50), serum protein 6.6 g/dl, serum albumin 3.8 g/dl, calcium 5.8 mg/dl, ionized calcium 0.79 mmol/l (normal 1.05–1.35), phosphorus 6.1 mg/dl, intact parathyroid hormone 5 pg/ml (normal 10–65), 1,25(OH)₂ vitamin D3 7.9 pg/ml (normal 16–60), sodium 133 mmol/l, potassium 2.9 mmol/l, chloride 91 mmol/l, total CO₂ 21 mmol/l, AST 43 IU/l and ALT 18 IU/l. Urinary concentration of β₂-microglobulin was 0.63 μg/ml (normal 0.1–0.16). Blood Ge concentration was 62.7 μg/l and urine Ge concentration 2190 μg/l (normal below 5 μg/l) [8]. Renal sonogram showed no morphological abnormalities. The nerve conduction study and needle electromyography suggested sensorimotor polyneuropathy, predominantly involving sensory nerves. Nerve or muscle biopsy was not performed because of patient’s refusal. The light microscope examination of a renal core biopsy showed that the glomeruli were slightly increased in size and with normal cellular features and a segmentally increased mesangial matrix (Figure 1). There was severe necrosis with finely granular PAS-positive deposits in tubular epithelial cells and the interstitium showed focal moderate fibrosis (Figure 2). Fluorescence microscopy revealed no evidence of immune complex or autoimmune deposits in the glomeruli. Electron-dense inclusions in the mitochondria of tubule cells, detected in several previous cases, were not found by electron microscopy.
This patient had impaired renal function and sensorimotor polyneuropathy. The histological examination of the kidney revealed generally normal glomeruli with no immune-complex or antibody deposits and focal necrosis with intracellular PAS-positive deposits in both proximal and distal tubular epithelial cells. The proximal tubular epithelial cell necrosis, which was not seen in other previous cases, might be due to the relatively high amount of germanium taken by the patient (about 400 g), and reflected by the high urinary concentration of $\beta_2$-microglobulin in our case. Germanium concentration of the urine was higher than those of previous cases [8].

The neurological examination suggested that the sensorimotor polyneuropathy was the main cause of the extremity weakness. The confirmative study, such as nerve biopsy, was not performed because of patient’s refusal but the temporal relationship between symptoms and the drug usage, the clinical findings and previous reports suggest that the neuropathy is the result of the Ge toxicity.

Laboratory tests of this patient showed hypocalcaemia and low concentration of serum parathyroid hormone. Tubulointerstitial nephritis may cause hypocalcaemia, hyperphosphataemia, and low concentration of 1,25(OH)$_2$ vitamin D3, but low concentration of parathyroid hormone is unusual. It may be possible that germanium accumulation in the parathyroid gland, similar to thyroid gland [9], may cause hypoparathyroidism and severe hypocalcaemia. Further histological confirmation in human or animal studies is needed to prove this assumption.

References


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