SHORT REPORTS

Tromsø Heart Study: vitamin D metabolism and myocardial infarction

The high mortality rates from myocardial infarction in northern Norway lead to the establishment of the Tromsø Heart Study (THS) in 1974.¹ An investigation by Lindén,² suggested that a high intake of vitamin D might be a precipitating cause of myocardial infarction in this area of Norway. We therefore studied data from the THS to determine whether vitamin D was a risk factor for myocardial infarction.

Patients, methods, and results

In 1974-8, 30 participants in the THS¹ developed myocardial infarction; 23 had been free from any known disease at the start of the study. For each of these 30 patients we selected two controls of the same age (within a year) who had had serum samples taken in the same month as the patient.

In 1978 deep-frozen serum samples from the THS were thawed and the concentration of 25-hydroxy vitamin D (25-OHD) measured, principally as described by Bouillon.³ Calcium and magnesium were analysed by atomic absorption spectrophotometry and albumin and phosphate by standard colorimetric procedures. Group specific component (Gc protein), which is the vitamin-D binding protein, was assayed by immunoprecipitation in a Gemaec fast analyser.⁴

The table shows mean values of some of the risk factors and of 25-OHD and Gc protein in the 23 patients free of disease at the start of the study and their controls. The observed differences were largely unchanged when all 30 patients and their 60 controls were compared.

Mean concentrations of 25-OHD and Gc protein measured in 1978 and risk factors recorded at the start of the Tromsø Heart Study in 23 men in whom myocardial infarction was diagnosed during the following four years and in 46 male controls matched according to age and month of blood sampling

	Patients		Controls		Significance† (P)
	Mean	SD	Mean	SD	
25-OHD (nmol/l)	59.0	24.1	63.4	27.2	
Gc protein (mg/l)	315	69.3	283*	82.9	
Cholesterol (mmol/l)	8.12	1.95	7.41	1.38	<0.05
Triglycerides (mmol/l)	2.13	1.06	1.38	0.78	<0.0025
Blood pressure (mm Hg):					
Systolic	133.8	19.7	128.8*	15.4	
Diastolic	82.7	11.2	80.6*	10.5	
Smokers (%)	91		83		

*n = 45.

†Unpaired Student's *t* test.

Conversion: SI to traditional units—Cholesterol: 1 mmol/l ≈ 38.6 mg/100 ml. Triglycerides: 1 mmol/l ≈ 88.5 mg/100 ml.

There were no significant differences between the patients and controls in weight, height, or haemoglobin concentration. 25-OHD concentrations¹ were slightly lower in the patients than in controls, though the difference was not significant. The most striking difference was the non-fasting triglyceride concentration, which was much higher in the patients.

Comment

Consumption of fish and fish oil, and hence of vitamin D, has been assumed to be substantially higher in northern Norway than in other regions. Our results do not support this view, as vitamin D concentrations in both patients and controls were comparable to those in other populations.⁵ We measured 25-OHD, the main circulating metabolite of vitamin D, and methods that measure the 25-hydroxylated metabolites of cholecalciferol and ergocalciferol are generally accepted to reflect the overall vitamin D status of the organism.⁵

Gc protein was higher among the patients than among the controls, though not significantly so. These higher Gc protein values tended to decrease even further the concentrations of free 25-OHD among the patients. Indeed, correcting 25-OHD concentration for Gc protein

concentration produced a statistically significant difference between the groups ($P=0.024$), with the patients having a lower concentration of free 25-OHD.

It has been postulated that vitamin D could influence the incidence of coronary heart disease by raising the serum cholesterol concentration. But at the concentrations found in our study there was no significant correlation between vitamin D status and the serum cholesterol concentration (linear regression, least squares method).

The hypertriglyceridaemia among the patients was our most striking finding, and our preliminary suggestion is that the difference between patients and controls was caused by dietary differences. We propose to study triglyceride values further.

The strength of the present study is its prospective nature. We believe that our data are, to a large extent, free from bias caused by seasonal or age-dependent variations or changes caused by a coronary attack. Our results give no reason to suggest that the vitamin D intake or the vitamin D status of the population of northern Norway account for their higher risk of myocardial infarction.

We thank Edith Holstad for technical help.

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² Lindén, V, *British Medical Journal*, 1974, **3**, 647.

³ Bouillon, R, van Kerkhove, P, and Demoor, P, *Clinical Chemistry*, 1976, **22**, 364.

⁴ Blom, M, and Hjørne, N, *Clinical Chemistry*, 1975, **21**, 195.

⁵ Favus, M J, *Medical Clinics of North America*, 1978, **62**, 1291.

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Remission of a syndrome indistinguishable from motor neurone disease after resection of bronchial carcinoma

Motor neurone disease may occur in association with carcinoma.¹ The association may be coincidental, as malignant disease is common and motor neurone disease occurs in 2.45/100 000 population.² We report a case of bronchial carcinoma presenting as a syndrome resembling motor neurone disease. After pneumonectomy the syndrome remitted.

Case report

A 54-year-old man presented with a six-month history of progressive weakness of the legs and painful knees, tender swelling of the right breast, and haemoptysis. He smoked 40 cigarettes a day. Examination showed clubbing of the fingers and toes and right-sided gynecomastia. There was slight wasting of the muscles of the shoulder girdle, extensor digitorum brevis, and gastrocnemius and severe wasting of the quadriceps. Tone was increased in the legs, and the quadriceps were fasciculating. Intrinsic hand muscles and finger extensors were weak. There was pronounced weakness of hip flexion, adduction, and abduction, but extension was normal. Dorsiflexion and plantar flexion of the ankles were weak. Brisk reflexes were elicited in the left arm and both knees and ankles. Abdominal reflexes were present and plantar responses were unequivocally extensor.

Chest radiography showed a mass at the left hilum extending into the upper lobe. Bone-scan and other radiological findings were normal apart from minimal degenerative changes in the cervical and lumbar spine. Fibreoptic bronchoscopy showed irregularity and widening of the subcarina between the lingula and left upper lobe. Biopsy yielded neoplastic cells. Cerebrospinal fluid was normal. The right lateral popliteal nerve had a motor conduction of velocity 48 m/s (normal). Electromyography with a central needle electrode in the right vastus medialis and rectus femoris showed no

definite spontaneous activity but poor relaxation and severe contraction fasciculation. Twitching was associated with a polyphasic unit of long duration firing about five times a second. Units were prolonged and polyphasic up to 3 mV. The interference pattern was reduced. We concluded that the quadriiceps weakness was neurogenic and that the pattern of electrophysiological abnormality was consistent with motor neurone disease.

Left radical pneumonectomy was performed with good clearance of lymph nodes from the mediastinum. The neoplasm was a large-cell carcinoma with a suspicion of adenocarcinomatous tubules in places. All fasciculation immediately resolved and pain in the knees disappeared.

Six months later there was much less wasting of quadriceps and no fasciculation. Right quadriceps and hamstrings were slightly weak but the left leg was normal. Reflexes in the legs were normal and plantar responses flexor. Clubbing was reduced, and the gynecomastia had gone. Electromyography of the right vastus medialis and rectus femoris showed no fibrillation or fasciculation and, though the interference pattern was mildly reduced, the motor units looked normal. Some polyphasic units were seen in the right tibialis anterior but they were not prolonged or increased in amplitude. There was no evidence of a lower motor neurone lesion.

Comment

Carcinomatous neuromyopathies occur in 16% of men with bronchial carcinoma.³ Brain *et al* reported on 11 patients with a syndrome indistinguishable from motor neurone disease—though running a more benign course—associated with malignancy.¹ Five had bronchial carcinoma, one of whom partially improved after resection. They concluded that motor neurone disease may be a manifestation of carcinomatous neuromyopathy. Our patient achieved complete remission, which we believe suggests a causal relation between the carcinoma and the neurological syndrome.

We thank Dr C J Earl and Dr F H Scadding for their help and advice in preparing this case report.

¹ Brain, Lord, Croft, P B, and Wilkinson, M, *Brain*, 1965, **88**, 479.

² Jokelainen, M, *Journal of the Neurological Sciences*, 1976, **29**, 55.

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Acute tubular necrosis after exposure to diesel oil

Exposure to diesel oil has been implicated in two previous reports of acute oliguric renal failure.^{1,2} Our case represents the first such report from Britain and provides further evidence that diesel oil should be considered a nephrotoxin.

Case report

A 47-year-old man presented with a month's history of epigastric and loin pains, thirst, nocturia, nausea, anorexia, and severe exhaustion, and a week's history of scrotal swelling. This unusual presentation prompted an inquiry into possible toxic exposure, and he admitted to cleaning his hands and arms with diesel oil over several weeks while building a home extension. On examination he looked pale and ill and had bilateral loin tenderness and scrotal oedema. Initial investigations showed: haemoglobin 11.9 g/dl, white cell count $6.7 \times 10^9/l$, erythrocyte sedimentation rate (ESR) 76 mm in the first hour, blood urea 6.5 mmol/l (39 mg/100 ml); plasma sodium 141 mmol(mEq)/l, plasma potassium 4.1 mmol(mEq)/l, plasma bicarbonate 26 mmol(mEq)/l, total protein 77 g/l, and serum albumin 43 g/l; urine analysis showed no protein, cells, casts, or growth.

Two weeks later he developed pitting ankle oedema and further investigation showed: haemoglobin 9.4 g/dl, reticulocytes 0.2%; blood urea 17.0 mmol/l (102 mg/100 ml), plasma sodium 139 mmol/l, plasma potassium 5.0 mmol/l, total protein 66 g/l, serum albumin 35 g/l, serum creatinine 910 μ mol/l (10.3 mg/100 ml); urine analysis normal, 24-hour urine protein 0.19 g, and creatinine clearance 14.2 ml/min. Intravenous urography

showed a faint nephrogram, normal-size kidneys, and no evidence of obstruction.

His urine output fell to 100 ml in 24 hours but he responded to frusemide with diuresis of 1500–2500 ml per 24 hours with disappearance of his oedema. His blood urea peaked at 28 mmol/l (169 mg/100 ml) during the diuretic phase. Renal biopsy showed the classic findings of nephrotoxic acute tubular necrosis—namely, patchy degeneration and necrosis of proximal and distal tubular epithelium with preservation of basement membranes.³ There were 14 normal glomeruli and some interstitial oedema. He subsequently made a good recovery with a haemoglobin concentration of 12.6 g/dl, ESR 27 mm in the first hour, blood urea 6.5 mmol/l (39 mg/100 ml), and serum creatinine only slightly raised at 140 μ mol/l (1.6 mg/100 ml) three months later.

Comment

The intermittent but frequent use of diesel oil before the onset of this patient's illness may explain the subacute development of renal failure. Nevertheless, the patient had histologically proved acute tubular necrosis. Detailed questioning revealed no history of exposure to any other nephrotoxin. Reidenberg *et al*¹ described a patient with acute oliguric renal failure following 10 days' exposure to diesel oil vapour in the cab of a lorry. Abdominal cramps and epigastric and loin tenderness, and oedema were prominent features, as in our patient. Strong evidence for absorption of diesel oil through the skin was offered by the patient described by Barrientos *et al*.² He developed acute oliguric failure on the same day as washing his hair with diesel oil, but renal biopsy—performed much earlier than in our patient, on the second oliguric day—showed only tubular dilatation with casts and a "light proliferation" of mesangial cells in the glomeruli. Considering the widespread use of diesel oil, toxic effects are extremely rare, although contact dermatitis is well recognised.⁴ Nevertheless, diesel oil by topical exposure or vapour inhalation should be accepted as a rare cause of acute renal failure.

Requests for reprints should be sent to Dr B I Hoff brand.

¹ Reidenberg, M M, *et al*, *American Journal of the Medical Sciences*, 1964, **247**, 25.

² Barrientos, A, *et al*, *Archives of Internal Medicine*, 1977, **137**, 1217.

³ Jones, D B, in *Pathology*, ed W A D Anderson and J M Kissane, p 959. Philadelphia, Mosby, 1977.

⁴ Borrie, P, *Roxburgh's Common Skin Diseases*, p 169. London, Lewis, 1975.

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Insulin oedema

Oedema occurring soon after starting insulin treatment is occasionally mentioned in textbooks on diabetes mellitus,¹ but we have found few descriptions of cases. We here report one such case.

Case report

A 31-year-old man was admitted as an emergency with a 5-day history of vomiting, diarrhoea, and increasing confusion. He had been fit, and there was no family history of diabetes. He was disorientated, dehydrated, and smelled of acetone. Urine tests showed large quantities of sugar and ketones, and his blood glucose concentration was 52.8 mmol/l (951 mg/100 ml). He was given intramuscular injections of 5 units of soluble insulin every hour and appropriate intravenous fluids. He responded well, and after eight hours his blood glucose concentration had fallen to 13 mmol/l (234 mg/100 ml). He was eventually stabilised on 50 units of Monotard insulin daily.

After seven days he developed ankle oedema, which became generalised over the next 24 hours and was particularly noticeable on the face; he resembled a patient with the nephrotic syndrome. His weight increased from 63 kg on the second day, when he had already been rehydrated, to 67 kg on the eighth day. His blood pressure and electrocardiograph were normal, and he felt well. Twenty-four-hour urinary protein output was 2.43 g/l and no erythrocytes or casts were seen. Serum total protein concentration was 60