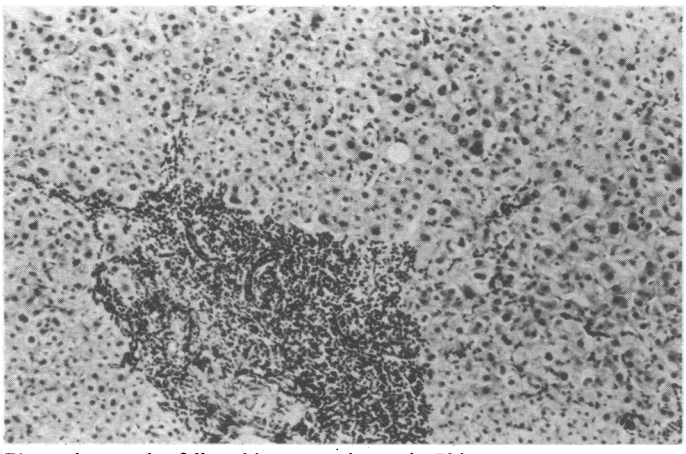

Photomicrograph of liver biopsy specimen. (×70.)

blood flow study[1] was carried out using a constant infusion method with ^{131}I-labelled rose bengal. The estimated hepatic blood flow was 1230 ml/min (normal). The hepatic vein was patent; the wedged (left) hepatic vein pressure was 15/10 mm Hg, with a mean of 8 mm Hg, and inferior vena cava pressure was 5/2 mm Hg.

Comment

Investigation showed this patient had portal hypertension of the intrahepatic, presinusoidal type.[2] This has been described in various myeloproliferative disorders and lymphoma,[3 4] but not in reports on Waldenström's macroglobulinaemia, which included a series of 40 cases,[5] although several of these patients had heavily infiltrated portal tracts. Our patient's estimated hepatic blood flow was normal, indicating that increased resistance to blood flow through the infiltrated portal tracts was causing portal hypertension rather than increased splanchnic blood flow in association with the splenomegaly. Treatment has been started with cyclophosphamide, which, if it reduces the portal tract infiltration, may also reduce the degree of portal hypertension.

I wish to thank Dr C D Holdsworth, Dr F E Preston, and Mr W Morris-Jones for permission to report this case, and Mrs N Hobson for technical help in performing the hepatic blood flow study.

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Factitious hypercalcaemia

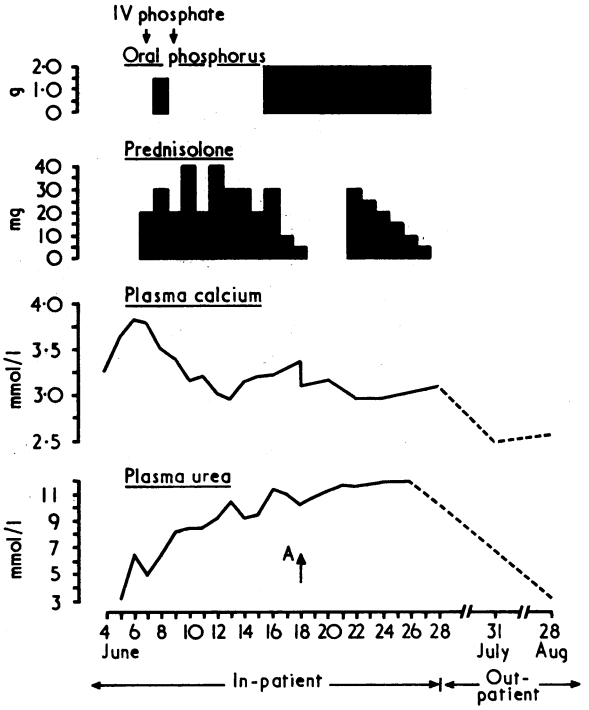
Deliberate self-intoxication with vitamin D does not appear to have been reported. In the case described here it occurred in a patient with the Munchausen syndrome.[1] The case also illustrates the value of parathyroid hormone assay in refuting a tentative diagnosis of hyperparathyroidism. The diagnosis of vitamin D intoxication was established by finding an extremely high level of serum 25-hydroxycholecalciferol.

Case report

A 34-year-old woman with a long history of deep venous thrombosis and recurrent pulmonary embolism had the first of several episodes of right loin pain in July 1972. It was discovered that her plasma calcium concentration was 2·9 mmol/l (11·4 mg/100 ml) and she was admitted for further investigation. The results of physical examination were unremarkable. Hypercalcaemia was confirmed, and the phosphorus excretion index (+ 0·09) was at the upper limit of normal, but otherwise full biochemical and radiological investigations gave normal results. Within two days she began vomiting. Concomitantly her plasma calcium rose rapidly to more than 3·5 mmol/l (14 mg/100 ml), requiring urgent rehydration and treatment with prednisolone (see figure) and two infusions of a 2·9 % sodium phosphate and 0·26 % potassium acid phosphate mixture.

Preparations were made for emergency exploration of her neck as hypercalcaemia was uncontrolled, and her blood urea was rising. At this point it was reported that parathyroid hormone was undetectable in her serum by immunoradiometric assay.[2] Aspects of her behaviour had already aroused suspicion and she was found to be in possession of about 500 strong calciferol tablets (stated strength 1·25 mg) and ampoules of calcium gluconate for injection. When confronted with this discovery she initially denied all knowledge, but then claimed that she added the vitamin D to a tumbler of water in which she kept her false teeth. During psychiatric interview there was definite communication block and a diagnosis was made of behaviour consistent with a hysterical personality disorder. It was subsequently discovered that since the age of 14 she had attended no fewer than thirteen hospitals, five being London teaching hospitals, with a wide variety of complaints including pyrexia of undetermined origin, cystitis, venous thrombosis, and abdominal pain (negative laparotomy).

The original sample of serum was found to contain 1298 nmol/l (520 ng/ml) 25-hydroxycholecalciferol (normal range 10·0-80·0 nmol/l (4-32 ng/ml)),[3] confirming vitamin D intoxication. After discharge from hospital her plasma calcium and urea concentrations fell to normal (see figure), but she has subsequently defaulted from follow-up.



Biochemical and therapeutic data. The arrow marked A indicates the point at which the patient was found to be in possession of calciferol tablets and ampoules of calcium gluconate for injection.

Conversion: SI to traditional units—Calcium: 1 mmol/l ≈ 4 mg/100 ml. Urea: 1 mmol/l ≈ 6 mg/100 ml.

Comment

Clearly this patient's illness was a manifestation of the Munchausen syndrome. Hyperparathyroidism was tentatively diagnosed before the report of serum parathyroid hormone assay became available. Although some patients with hyperparathyroidism have serum parathyroid hormone concentrations within the normal range, they usually also have a minimal rise in plasma calcium concentration.[4] Additional features which cast some doubt on such a diagnosis were the persistently normal plasma bicarbonate and chloride concentrations; unusually low plasma alkaline phosphatase, levels ranging from 3·8 to 6·3 King Armstrong units; and the unstable concentrations of the plasma calcium. There was no obvious reason for the initial rapid rise in plasma calcium, and, in our experience, such instability without clear cause is unusual in hyperparathyroidism. Preece *et al*[5]

have reported values of 25-hydroxycholecalciferol of over 749 nmol/l (300 ng/ml) in vitamin D intoxication, and the value in the present case was even greater. It is not clear how much calciferol was being ingested, but the lack of response of the hypercalcaemia to treatment with prednisolone could have been due to consumption of a very high dose.

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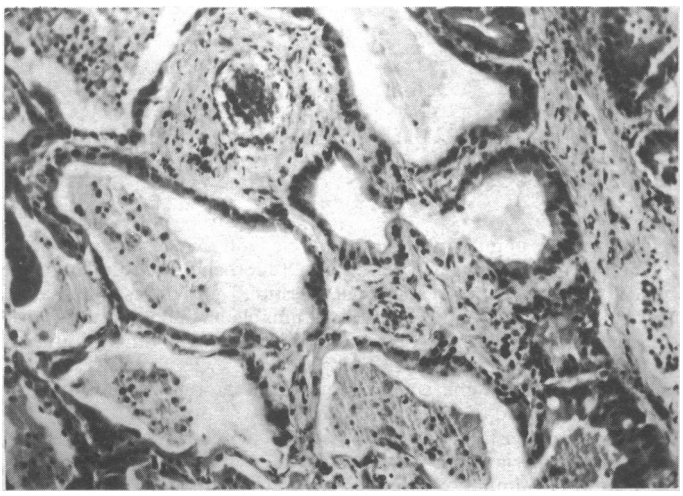
Aflatoxin inhalation and alveolar cell carcinoma

Aflatoxin, a toxic metabolite of the mould *Aspergillus flavus*, is one of the most potent carcinogens known.[1] Epidemiological studies in tropical areas have shown that the high incidence of primary liver cancer in their populations may be related to the ingestion of contaminated food.[2 3] This paper reports a case of pulmonary adenomatosis due possibly to inhalation of aflatoxin.

Case report

A chemical engineer aged 68 worked for three months on a method of sterilising Brazilian peanutmeal which was contaminated by the mould *Aspergillus flavus*. Three months after finishing this work he became ill with high fever and began to expectorate thick, white sputum. *X*-ray examination showed cavitation in the left lower lobe of the lung. At first the process was considered to be due to tuberculosis, and later to mycotic disease. After two months further lesions developed in both lungs. The condition of the patient became worse and he died 11 months after the onset of his illness. Necropsy showed enlarged, heavy lungs diffusely infiltrated with firm yellow-white or reddish lesions.



Section of lung. Interalveolar septa well preserved. Alveoli lined with high cylindrical or cubical epithelium. (Haematoxylin and eosin. × 95.)

Histological examination (see fig) showed bands of fibrous tissue in the parenchyma. The alveoli were lined with high cylindrical or cubital epithelium with giant multinucleated cells, some containing mucous vacuoles in their plasma. The interalveolar septa were well preserved. Mitotic figures were rare. The picture was that of pulmonary adenomatosis. No metastases or tumours in other organs were found. Bacteriological examination was negative. A sample of lung tissue was taken for chemical investigation. Thin-layer chromatography of the extract showed a blue fluorescent spot in 365 nm UV light similar to that of a commercial sample of aflatoxin B_1 (Calbiochem, California), the same colour change as standard B_1 when treated with 50% H_2SO_4, and an RF value identical to that of the commercial aflatoxin sample B_1. A colleague of this patient who had been doing the same work had died three years before of pulmonary adenomatosis, but no chemical investigations were done in his case.

Discussion

The pathogenesis and aetiology of primary pulmonary adenomatosis is not clear. It often develops at the site of fibrous scars of inflammatory origin or in a lung chronically damaged from other causes. Eversole and Rienhoff[4] suggested that it is due to congenital malformations, while Spencer[5] thought it was caused by the inhalation of irritant substances together with other factors that lead to chronic damage to the lung. It seems that men who inhale toxic mould during their work might well be at risk.

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Pulmonary asbestosis and autoimmunity

Experimental animals exposed to silica particles form rheumatoid factor.[1] Rheumatoid factor and antinuclear antibodies have also been found in persons exposed to asbestos and in patients with pulmonary asbestosis.[2] Autoimmunity might therefore be implicated in causing the pulmonary lesions of asbestosis. The inhaled asbestos fibres would cause cellular damage, tissue antigens would be released, and autoimmune antibodies formed. Furthermore, HLA-27 antigen, known to be associated with diseases of possible autoimmune aetiology,[3] is often present in patients with asbestosis.

Antophyllite, a relatively rare kind of asbestos, is mined in Finland. The incidence of pulmonary tuberculosis and of pulmonary carcinoma is high,[4] and they occur not only in the factory workers but also in people living close to the mines.[5] If autoimmune mechanisms played a part in the pathogenesis of their disease we would expect to find rheumatoid factor or antinuclear antibodies in their sera. We therefore examined the sera of all the quarry and fibre mill workers for the presence of rheumatoid factor and antinuclear antibodies.

Methods and results

In all, 66 sera were studied from men who had been working with asbestos for 2 to 38 years, the average being 15·2 years. None had severe asbestosis. We used the Waaler-Rose test for the rheumatoid factor and the fluorescent antibody test for antinuclear antibodies, as used routinely in our laboratory. Both positive and negative control sera were included in all test series.

A Waaler-Rose titre >1/32 was found in seven (10·7%) and a titre of >1/64 in three (4·5%) of the 66 sera. Antinuclear antibodies were seen in only one serum. The titre with FITC conjugated antihuman immunoglobulin was 1/80 and with antihuman IgG 1/10. These findings are the same as those in the normal healthy population.