SHORT REPORTS

Hypercalcaemia associated with tuberculosis

Hypercalcaemia has been known to be associated with tuberculosis since 1931 and has recently been reported to occur commonly.[1] The hypercalcaemia is generally asymptomatic and mild. We describe a case with symptoms and also report a study of the prevalence of hypercalcaemia in 89 tuberculous patients.

Case report

A 25-year-old man presented with a history of rigors, night sweats, and productive cough for two weeks. He smoked 10 cigarettes a day, drank alcohol socially, and took no medication. On examination he was feverish (38·6°C), chest radiography confirmed the signs of right upper lobe consolidation and collapse, and his sputum grew *Mycobacterium tuberculosis*. Biochemical analyses (Technicon SMAC) showed hypercalcaemia (plasma calcium concentration 2·72 mmol/l (10·9 mg/100 ml)) and hypoalbuminaemia (serum albumin 27 g/l). He was given rifampicin 600 mg, isoniazid 300 mg, pyridoxine 6 mg, ethambutol 1500 mg, and streptomycin 1 g daily. After 19 days he became drowsy, polyuric, dehydrated, and his plasma calcium concentration was 3·33 mmol/l (13·3 mg/100 ml). The results of serum and urine electrophoresis and thyroid function tests were unremarkable and serum parathyroid hormone was undetectable. He was given phosphate by mouth and forced fluids, and he rapidly became more conscious. The plasma calcium concentration became normal by 12 weeks and remained normal two years later.

We reviewed the 89 consecutive untreated patients (64 male, 25 female) with culture-positive pulmonary tuberculosis admitted to the Royal Adelaide Hospital from January 1976 to June 1978. Hypoalbuminaemia was present in 32 (36%), and to allow for protein binding of calcium we corrected the admission and discharge plasma calcium concentrations for hypoalbuminaemia using an average correction factor.[2] We also selected age- and sex-matched controls from the general hospital medical inpatient population who had similar plasma albumin concentrations but normal plasma alkaline phosphatase activities (<95 U/l) and creatinine concentrations (<0·12 mmol/l). All routine chemical estimations were performed on Technicon SMAC and our mean (±2SD) normal range for plasma-corrected calcium concentration was determined in December 1977 in 100 healthy laboratory workers as 2·19-2·41 mmol/l 8·8-9·6 mg/100 ml). Chest radiographs on admission were graded for extent of disease according to the criteria of the National Tuberculosis Association, New York (1969). The difference between the controls and tuberculous patients was assessed by Student's t test and the χ^2 test using Yate's correction.

The admission plasma-corrected calcium concentration (±SEM) in tuberculous patients was 2·44±0·01 mmol/l (9·8±0·04 mg/100 ml)—significantly higher than in controls (2·34±0·01 mmol/l (9·4±0·04 mg/100 ml)) ($t=5$, $p<0·001$). Forty-five (51%) tuberculous patients and 23 (26%) controls had plasma-corrected calcium concentrations above the normal range (mean ±2SD) on admission ($\chi^2=10·5$, $p<0·001$). At three standard deviations above the mean 38 (43%) patients and 11 (12%) controls were abnormal ($\chi^2=19$, $p<0·001$), and at four standard deviations above the mean 20 (22%) patients and 8 (9%) controls were abnormal ($\chi^2=5·1$, $p<0·05$). At the time of discharge only 30 (34%), 16 (18%), and 10 (11%) tuberculous patients had corrected calcium concentrations greater than 2, 3, or 4 standard deviations above the mean. This was not significantly different from the controls. The admission plasma calcium concentrations in patients with severe radiographic changes were significantly higher than in patients with minimal or moderate disease (2·51±0·02 mmol/l (10·0±0·08 mg/100 ml) n=31, $t=3·5$, $p<0·001$) compared with 2·39±0·01 mmol/l (9·6±0·04 mg/100 ml) (n=58).

Comment

The difference between the prevalence of hypercalcaemia on admission in tuberculous and control patients, the effect of treatment on this difference, and the correlation between the extent of tuberculosis and hypercalcaemia suggest that tuberculosis often causes hypercalcaemia. Hypoalbuminaemia may mask hypercalcaemia. This presumably explains why Abbasi *et al*,[1] who did not correct for hypoalbuminaemia, could show hypercalcaemia only several weeks after admission (when the plasma albumin concentration had increased). The apparently high prevalence of hypercalcaemia in the control patients is attributable to our use of average rather than individual correction factors.[2] The difference in prevalence of hypercalcaemia on admission (>mean+2SD) between tuberculous and control patients is 26%, which agrees with Abbasi *et al*[1] and is higher than the reported prevalence in sarcoidosis (17%).[3] Hypercalcaemia is associated with several granulomatous diseases (tuberculosis, sarcoidosis, histoplasmosis, coccidioidomycosis, and berylliosis) but the mechanism is obscure.

Although some patients may have had mild hyperparathyroidism unmasked by dehydration this can be only a minor component, since the prevalence of hypercalcaemia in our patients (26%) is much higher than the reported prevalence of hyperparathyroidism (1-6·2 per thousand)[4] and we are not aware that hyperparathyroidism predisposes to tuberculosis. The hypercalcaemia of tuberculosis is usually asymptomatic but as reported above and by others[5] it may be severe. Knowledge of the association and care with vitamin supplements should avoid most problems.

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Anti-static mattress as reservoir of pseudomonas infection

Postoperative urinary infections in this hospital have been systematically recorded since 1972. Pseudomonas infections are unusual. Twenty-three occurred between November 1975 and February 1979, but 17 of these, all postprostatectomy, occurred in two short periods: eleven from mid-July to late September 1976 and six between late August and early October 1977. The first outbreak was recognised and the source eliminated, but the smaller outbreak was recognised only in retrospect.

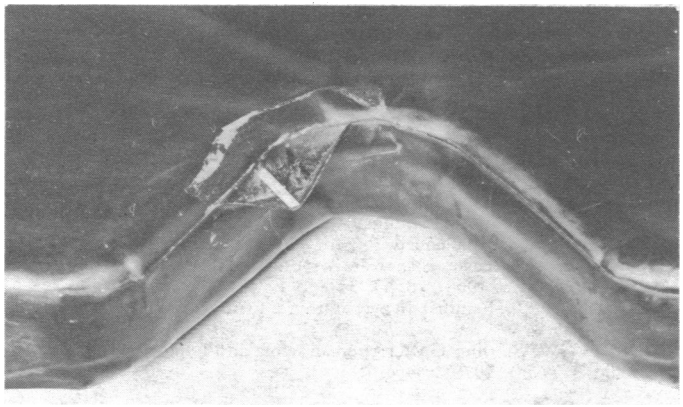
Study and results

When the first outbreak was recognised extensive bacteriological investigation into all possible sources of pseudomonas infection was initiated, including environmental surveys of the male and female wards and the theatre, bladder-washing fluids, cystoscopes, Bigolow's apparatus, all antiseptics, sinks, drains, dusters, and mops. Pseudomonas were isolated from a waste pipe, a table top, a curtain rail, a viewing box, and a locker top in the male ward but from nowhere in the theatre or female ward. It was considered that this contamination was the result of the infections rather than their cause, because pyocine typing incriminated several strains of pseudomonads which seemed to rule out cross-infection, and the cases continued to appear despite tightening up nursing and cleaning procedures.

At this point one of us (IMP) remembered that some years previously *Pseudomonas pyocyanea* had been isolated from a pocket formed by the sealing of the anti-static table mattress in the theatre coming apart and forming a trap for water. No infections had been noted but the mattress was replaced. Inspection of the existing mattress revealed numerous large pockets which, when pressed, extruded fluid containing several types of pseudomonads. This explained the multiplicity of strains causing the infections. Autoclaving this mattress twice weekly before replacement stopped the outbreak. The mechanism of infection was now clear Bladder-wash fluids

spilled over the operation site filled the pockets, the body of the mattress soaked up fluid, and the whole became an ideal nidus for pseudomonads. Washing over with antiseptics was ineffectual because the organisms were inaccessible and pseudomonads are relatively resistant. The weight of a patient in the lithotomy position extruded an aerosol, if not actual liquid, containing pseudomonads right on to the operation site.

Nothing further was noted until November 1979, when a routine bacteriological survey of the theatre after redecoration revealed a pocket in the mattress (figure) from which a heavy growth of pseudomonads was obtained. No infections had been noted at this time but a retrospective survey disclosed the six cases in August to November 1977. The mattress had been frequently renewed and it is not unlikely that this outbreak too had been due to this source and had stopped when the mattress was replaced.



End of anti-static mattress showing rupture of sealing and resulting pocket.

Comment

This hazard may cause outbreaks of infection even when the theatre and laboratory staff are fully aware of the possibility. It should be more widely known. The manufacturers have improved the design of the mattress. The latest model in this hospital is more satisfactory but potential pockets still exist, especially where strips of material are used to reinforce corners. Theatre staff should check their mattresses for even the smallest pockets.

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Are pigmented gall stones caused by a "metabolic" liver defect?

Increased concentrations of unconjugated bilirubin, which can precipitate as insoluble calcium salt, are found in the gall-bladder bile of patients with pigmented stones.[1] The source of biliary unconjugated bilirubin is still under discussion since it might be secreted by the liver or produced by hydrolysis of conjugated bilirubin in the gall bladder.[2] We present here data which show a persistently abnormal concentration of unconjugated bilirubin in the bile of patients with pigmented stones and support the hypothesis of a primary liver defect.

Patients, methods, and results

Twelve patients who underwent cholecystectomy were selected according to the type of gall stone as assessed by visual inspection and then confirmed by chemical analysis.[3] Pigmented stones were found in five patients (mean age 53 years) and cholesterol stones in the other seven (mean age 46 years). Gall-bladder bile collected at cholecystectomy was cultured for bacteria and assayed for total bilirubin and conjugated and unconjugated bilirubin as described by Boonyapisit *et al.*[4] Six months after the operation hepatic bile was obtained by duodenal aspiration the morning after an overnight fast and cultured and assayed as before. Routine liver function tests (serum bilirubin, transaminases, alkaline phosphatase, serum protein electrophoresis) and blood tests (blood count and haemoglobin, reticulocyte count) performed before cholecystectomy and six months after surgery gave normal values. The results were analysed by Student's *t* test.

No difference in biliary total bilirubin concentrations was found between patients with pigmented stones and those with cholesterol stones (see table). Unconjugated bilirubin values expressed as percentage of total bilirubin were significantly higher in those with pigmented stones than in those with cholesterol stones not only in gall-bladder bile but also in hepatic bile collected six months after surgery. Aerobic and anaerobic cultures performed on gall-bladder bile from both groups of patients gave negative results.

Comment

Our data indicate that patients with pigmented gall stones who have no overt haemolysis or cirrhosis do not show abnormal biliary concentrations of total bilirubin, but have higher concentrations of unconjugated bilirubin than those with cholesterol stones. These higher values do not seem to be related to bacterial hydrolysis of conjugated bilirubin. Even though these findings do not exclude other factors such as hydrolysis of conjugated bilirubin by biliary endogenous β-glucuronidase,[5] they support the existence of a "metabolic" liver defect responsible for the persistent increase in the secretion of unconjugated bilirubin into the bile in patients with pigmented stones.

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Total bilirubin and unconjugated bilirubin values in bile of patients with different types of gall stones

	Gall-stone composition (% dry weight)				Gall-bladder bile		Hepatic bile	
	Bilirubin	Bile salts	Cholesterol	Residue	Total bilirubin (μmol/l)	Unconjugated bilirubin (%)	Total bilirubin (μmol/l)	Unconjugated bilirubin (%)
Patients with:								
Pigmented stones ..	51·5±0·5*	2·1±0·1	18·7±0·6	27·7±0·2*	3215±359	4·8±0·8*	131±18·8	3·7±0·9*
Cholesterol stones ..	0·7±0·1	1·4±0·3	79·3±2·4	18·6±0·4	2685±256	0·9±0·5	87±13·7	0·5±0·3

*$p < 0.01$ compared with value in patients with cholesterol stones.
Conversion: SI to traditional units—Total bilirubin: 1 μmol/l ≈ 0·06 mg/100 ml.