Lysozyme and hypokalaemia

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Summary

Serum potassium, lysozyme and urinary lysozyme measurements were made in 98 patients with tuberculosis, 18 with sarcoidosis and 30 with acute myeloid leukaemia. Serum K concentration fell below 3.5 mmol/l in 17 of the 30 leukaemic patients and only 7 of these had raised serum lysozyme concentrations. None of the patients in the tuberculosis-sarcoidosis group with lysozymaemia or lysozymuria developed hypokalaemia. This study suggests that raised lysozyme concentrations are not causally related to hypokalaemia.

Introduction

Hypokalaemia is a frequent complication associated with acute myeloid leukaemia (Muggia *et al.*, 1969; Pruzanski and Platts, 1970; Mir *et al.*, 1975). Some workers (Muggia *et al.*, 1969; Pickering and Catovsky, 1973) have attributed the hypokalaemia to raised serum concentrations of a small molecular weight protein, lysozyme (muramidase), which is elaborated by primitive white blood cells in acute myeloid leukaemia (AML). This view was questioned by Mir *et al.* (1975), who carried out potassium balance studies in 32 patients with AML, and found that concentrations of serum and urinary lysozyme did not correlate with those of serum potassium. However, the role of lysozyme as a cause of hypokalaemia cannot be investigated satisfactorily in AML since leukaemic patients develop proximal renal tubular dysfunction (Mir and Delamore, 1974) which may cause hypokalaemia, and many patients receive a wide variety of antibiotics such as gentamicin, polymyxin, etc., which have been known to cause hypokalaemia (Klastersky *et al.*, 1973; Rodriguez, Green and Bodey, 1970).

In order to settle the question whether raised lysozyme concentrations have any causal relationship with hypokalaemia, one would need to study the frequency of hypokalaemia in a disease in which raised concentrations of lysozyme occur but in which the abnormalities that are associated with

AML and may cause hypokalaemia, are not found. Tuberculosis and sarcoidosis are 2 such conditions; raised serum lysozyme levels have been reported in both (Perillie, Khan and Finch, 1973; Pascual, Gee and Finch, 1973) but other potential causes of hypokalaemia usually associated with AML have not been reported in these 2 diseases. This study was undertaken to explore the relationship between lysozyme and serum potassium concentration in tuberculosis and sarcoidosis.

Patients and methods

Ninety-eight patients with tuberculosis, 18 with sarcoidosis and 30 with AML were studied. All patients were unselected. In the tuberculous group, 28 patients (all of Asian origin) had glandular tuberculosis and the diagnosis was established by biopsy in all. *Mycobacterium tuberculosis* was grown from the sputa of the remaining 70 patients. Diagnosis of sarcoidosis was made on the grounds of a consistent clinical picture and a positive reaction to Kveim antigen. Standard haematological techniques were used in establishing the diagnosis of AML and its variants. Serum electrolytes were measured at admission and twice/week in admitted patients. Further measurements were made in the clinic at each attendance. Serum and urinary lysozyme concentrations were measured by the turbidimetric method of Parry, Chandan and Shahani (1965). Standards for this reaction were prepared from crystalline egg-white muramidase (Sigma) and a suspension of lyophilized *Micrococcus lysodeikticus* (Sigma) in phosphate buffer was used as substrate.

Results

Raised serum lysozyme levels

Of the 98 patients in the tuberculous group, 37 (38%) had raised serum lysozyme concentrations (control 3-13 µg/ml). Nineteen of these 37 patients had glandular tuberculosis, and in 18 others the disease was well advanced with involvement of more than one zone of one lung (11 patients) or both lungs

(7 patients). Thirteen of the 18 patients (72%) with sarcoidosis had raised serum lysozyme concentrations. In the leukaemic group of 30 patients, 15 (50%) had raised serum lysozyme concentrations. Thus, 50 patients in the tuberculosis-sarcoidosis group had elevated lysozyme concentrations with a mean of $19.1 \pm 2.4 \mu\text{g/ml}$ (s.e. mean). The mean concentrations in the 15 leukaemic patients with elevated lysozyme was $31.7 \pm 3.6 \mu\text{g/ml}$. This was significantly ($P < 0.01$) higher as compared with the tuberculosis-sarcoidosis group.

Hypokalaemia

Seventeen of the 30 patients with AML developed hypokalaemia (serum $\text{K}^+ < 3.5 \text{ mmol/l}$) at some stage during the course of their illness. Only 7 of these patients had raised serum lysozyme concentrations; one patient had lysozymuria but his

3 had normal serum lysozyme concentrations and 4 hypokalaemia.

Discussion

Serum lysozyme was elevated in a high proportion of patients with granulomatous infiltration of the glands. Patients with lymphoma were also studied, and a raised serum lysozyme concentration appeared to be a useful test in differentiating tuberculous or sarcoid involvement of hilar and mediastinal glands from lymphoproliferative disorders. This subject has been discussed elsewhere (Lodha and Mir, 1980). The purpose of the present study was to investigate whether raised concentrations of serum lysozyme were associated with low serum K^+ concentrations in sarcoidosis and tuberculosis. Hypokalaemia developed in 57% of the patients with AML and seemed to bear no definite relation to serum or urinary lysozyme concentration. In particular some patients in the tuberculous group had high concentrations of serum lysozyme but none of these developed hypokalaemia.

Osserman and Lawlor (1966) put forward the suggestion that lysozyme may be responsible for hypokalaemia in AML, since raised concentrations of lysozyme were found in some leukaemic patients with hyperkaluria. However, lysozymuria has been found in various renal tubular disorders as a manifestation of the disease (Butler and Flynn, 1961; Prockop and Davidson, 1964). Furthermore, leukaemic patients with normal serum lysozyme concentrations develop proximal renal tubular dysfunction (Mir and Delamore, 1974). Hypokalaemia in AML occurs in well over 50% of patients and is probably multifactorial (Mir *et al.*, 1975; Mir and Delamore, 1978).

Rosenthal, Maglio and Moloney (1972) showed that prolonged elevation of serum lysozyme in chloroleukaemic rats causes lysozymuria and hyperkaluria. Both tuberculosis and sarcoidosis are chronic diseases and serum lysozyme concentrations probably remain elevated longer in these diseases than they do in AML which is an acute disease with a rapid onset and, in most cases, runs an acute course. Some of the patients with glandular tuberculosis and sarcoidosis in this study were seen for longer than 18 months; elevated concentrations of lysozyme were observed but none of the patients developed hypokalaemia. This study provides further support for the thesis put forward by Mir *et al.* (1975) that lysozymaemia and lysozymuria do not cause hypokalaemia.

Acknowledgments

We thank Dr I. W. Delamore, Consultant Physician, Dr J. C. Chang, Consultant Haematologist, Manchester Royal Infirmary, and Dr B. Gill, Medical Assistant, Oldham

FIG. 1. Relationship between serum lysozyme and potassium concentrations in 50 patients with tuberculosis and sarcoidosis (●) and 30 patients with acute myeloid leukaemia (O) (control serum lysozyme 3–13 $\mu\text{g/ml}$; normal serum K^+ 3.5–5.5 mmol/l).

serum lysozyme concentration was normal. Figure 1 shows correlation between concentrations of serum lysozyme and those of serum K^+ in all the groups. As can be seen, none of the 50 patients with raised serum lysozyme concentrations in the tuberculosis-sarcoidosis group had hypokalaemia. Of the 5 leukaemic patients with serum K^+ concentration of $< 3 \text{ mmol/l}$, 3 had normal lysozyme concentrations.

Lysozymuria

Eleven patients in the tuberculosis group had lysozymuria (control $< 1 \mu\text{g/ml}$); 6 of these had normal serum lysozyme concentrations. None of the 18 patients with sarcoidosis had lysozymuria. Of the 30 patients with AML, 8 had lysozymuria; of these 8,

Chest Clinic, for allowing us to study the patients under their care.

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