Plasma Immunoreactive β -Melanocyte-stimulating Hormone and Skin Pigmentation in Chronic Renal Failure

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Summary

Plasma immunoreactive β -melanocyte stimulating hormone (β -MSH) concentrations were greatly increased in patients with chronic renal failure. There was no correlation between the severity of the renal failure or the degree of pigmentation and the plasma β -MSH levels.

Introduction

Patients with chronic renal failure are pigmented, and part of the pigmentation may be due to melanin.¹ We therefore studied plasma β -melanocyte-stimulating hormone (β -MSH) in patients with chronic renal failure.

Patients and Methods

Sixteen men and 12 women with chronic renal failure were studied. Seven were treated by weekly peritoneal dialysis (48 h/week) and 13 by regular haemodialysis (3 $\times$ 6-8 h/week); eight were not treated by dialysis.

Blood was taken from each patient (immediately before dialysis in those so treated), and immunoreactive β -MSH was measured by the method of Thody and Plummer.² Serum creatinine was also measured in some patients. The levels of β -MSH were compared with the normal range for the method, which was obtained from 25 normal individuals. The normal range was lower than that previously reported² because of a more specific extraction procedure.

Skin pigmentation on both the back of the hand and the back was measured in 21 patients using a reflectance photometer with a selenium cell as sensor and a white enamel plate as standard. This measurement correlates well with the clinical grading of pigmentation.¹

Results

The results (fig. 1) showed a great increase in immunoreactive β -MSH in the patients with chronic renal failure. The mean value ($\pm$ S.E.) for patients with chronic renal failure not on dialysis was 109 ± 33 ng/l, for patients with chronic renal failure on peritoneal dialysis 121 ± 37 ng/l, and for patients with chronic renal failure on haemodialysis 225 ± 33 ng/l. The normal value for our method is 13 ± 1.8 ng/l.

No correlations were found between plasma β -MSH and serum creatinine concentrations (fig. 2) between the levels of β -MSH and the degree of skin pigmentation as measured by reflectance (fig. 3) or between to levels of serum creatinine and skin reflectance (fig. 4).

FIG. 1—Plasma immunoreactive β -MSH in normal control subjects and patients with chronic renal failure.

FIG. 2—Lack of correlation between plasma immunoreactive β -MSH and renal function as measured by serum creatinine concentration.

Conversion: SI to Traditional Units—Serum creatinine: 100 μ mol/l $\approx$ 1.13.

FIG. 3—Lack of correlation between plasma immunoreactive β -MSH and pigmentation of skin of dorsum of hand and back as measured by reflectance photometry in 21 patients.

Discussion

The increase in immunoreactive β -MSH which we found in patients with chronic renal failure was presumably due to impaired excretion or metabolism of the hormone by the kidney. If we exclude the unlikely possibility that chronic renal failure stimulates secretion of the hormone measured as immunoreactive β -MSH then our observation suggests that this hormone does not have a significant feedback control mechanism. The lack of correlation between the concentrations of immunoreactive β -MSH, severity of renal failure as indicated by the

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FIG. 4—Lack of correlation between skin pigmentation as measured by reflectance photometry and renal function as measured by serum creatinine in 20 patients.

serum creatinine, and degree of pigmentation may have been partly due to the effect of dialysis, but more probably it was due to the severity of the renal failure, and we are now looking for a relationship in patients with less impairment of renal function.

Our findings may explain the pigmentation of chronic renal failure. Certainly the levels of immunoreactive β -MSH we found are similar to those which occur in Addison's disease and Nelson's syndrome.²⁻⁴ It has been suggested, however, that β -MSH in man exists only as part of the larger lipotrophin (LPH) molecule.⁵ If this is true then the β -MSH we have measured may have been the immunoreactive moiety contained within the parent LPH molecule, and the concentration of LPH may therefore be increased in chronic renal failure. But there are problems in attributing the pigmentation of chronic failure to LPH because this hormone is thought to have only 0.6% of the pigmentary potency of β -MSH.⁶

Several possibilities may explain this discrepancy. Firstly, the pigmentary potency of LPH in the human melanocyte may be greater than its potency in the amphibian melanophore, and it may be wrong to equate mammalian and amphibian pigmentary responses. Secondly, LPH may be a prohormone and an increase

in its plasma concentration may produce an increase in the active hormone (β -MSH) at the target organ, the melanocyte. Thus though we may have been measuring increases in LPH in plasma the pigmentation may still be due to β -MSH formed at the target tissue itself. Thirdly, if β -MSH is normally split off from LPH in vivo (not just at the target organ) it would be cleared by the kidney so that little would be detected in the plasma. In chronic renal failure, by contrast, β -MSH would not be cleared and its accumulation would explain the pigmentation. Thus we may have been measuring a mixture of β -MSH and LPH in the plasma. Lastly, MSH peptides other than β -MSH and LPH may occur in man.

As we are uncertain about the relation between the concentration of active hormone at the melanocyte target and plasma concentration of MSH peptides it is perhaps not surprising that we found no correlation between plasma immunoreactive β -MSH and the degree of skin pigmentation. Also, much of the colour may be due to pigments other than melanin.^{7,8} Thus while the increase in immunoreactive β -MSH we found in chronic renal failure could well be a factor in the pigmentation the precise relation of the MSH peptides to the pigmentation must await resolution of all these difficulties.

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New Serological Test for Malaria Antibodies

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Summary

In an enzyme-linked immunosorbent assay test for malaria antibodies, antibodies to *Plasmodium vivax* and *P. falciparum* in man are detected using a crude antigen prepared from the simian malaria parasite *P. knowlesi*. The test may be suitable for epidemiological studies.

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Introduction

The value of serological studies in supplementing parasitological data in the epidemiological assessment of malaria is generally recognized. Various serological techniques, especially immuno-fluorescence and passive haemagglutination and gel diffusion tests, have been used but none are entirely satisfactory. There is still a place for a test which may be used on a large scale and in which the results are read objectively. The enzyme-linked immunosorbent assay (E.L.I.S.A.) technique developed by Engvall and Perlmann^{1,2} and Engvall et al.³ for measuring antigens and antibodies has been used successfully to measure antibodies to *Trichinella spiralis*.⁴⁻⁶ We therefore decided to see whether it could be applied as a test for the presence of malaria antibodies.

PRINCIPLE OF TEST (fig. 1)

A soluble antigen is immobilized by coating a solid base such as a plastic tube or plate. The test serum thought to contain antibody to the antigen is incubated in the coated tube. Any specific antibody present will react with the antigen. The tube is then washed to remove