

Treatment of a case of allergic asthma with a synthetic human ACTH preparation

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Summary

The following case history documents the first patient treated with synthetic human ACTH. It was prescribed for an asthmatic child because of suspected allergy to both porcine ACTH and tetracosactrin. It proved both effective clinically and free of any adverse effects.

Case report

A. W. was first referred to the chest clinic at this hospital in January 1972 at the age of 9 years and 4 months. In the spring of 1970 she had developed hay fever, and the following winter began having attacks of clinical asthma. The symptoms were worse at night and also precipitated by exercise and excitement. Her general practitioner had prescribed sodium cromoglycate (Intal compound, Fisons Ltd) but during the year prior to referral she had missed a considerable amount of schooling. Skin testing revealed marked sensitivity to house dust mite, with a lesser reaction to house dust and grass pollen. She was advised to continue with her Intal. When she was reviewed in March, 1972 her condition had deteriorated and she received her first injection of porcine ACTH (40 units of Acthar Gel—Armour Pharmaceutical Company Limited). Three days later she was admitted to the Paediatric Unit in status asthmaticus, but responded to a further injection of porcine ACTH given in conjunction with oral salbutamol. An immunoglobulin assay (IgG, IgA and IgM) and sweat test gave normal results, but her FEV₁ after maximal bronchodilation was reduced at 1.21 l/min (expected mean for height + 2 s.d. 1.61 l/min). When discharged she was receiving Intal, salbutamol and Acthar Gel 40 units twice weekly. On this regime her FEV₁ returned to the normal range, but after 7 weeks a skin rash was noted and allergy to porcine ACTH suspected. Tetracosactrin (Synacthen Depot, Ciba Laboratories) 0.5 ml twice weekly was therefore substituted. Despite some initial improvement the rash persisted, and after 9 weeks the tetracosactrin dosage was reduced to 0.5 ml weekly. Once again some initial improvement in the rash occurred but was not maintained, and the tetracosactrin was discontinued because of this after a further 8 weeks in August.

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In November 1972 her clinical state was such that steroid therapy was again required and she was re-admitted for a trial of a synthetic human ACTH preparation (Seractide Gel—Armour Pharmaceutical Company Limited), her skin rash having resolved completely meanwhile. Her basal cortisol level was $6.5 \mu\text{g}/100 \text{ ml}$ (normal range $6\text{--}20 \mu\text{g}/100 \text{ ml}$), and this rose to $18.8 \mu\text{g}/100 \text{ ml}$ 30 min after an injection of 40 units of Seractide Gel. No adverse reaction occurred and she was allowed home on weekly injections of 40 units of this hormone. Weekly treatment was continued for a total of 14 weeks and then fortnightly injections were given for a further 3 months. During the whole of this time she remained clinically well, and no rash or other adverse side effects were noted. In June, 1973 the ACTH was discontinued and she remained in good health until this year, when she has required admission on two occasions over the last 2 months. On the first occasion Seractide Gel was used, but during the second admission she received 80 units of porcine ACTH which produced clinical improvement without any adverse reaction.

During the time when this patient's rash was present, porcine ACTH, tetracosactrin and salbutamol were being administered. The Committee on Safety of Medicines, Register of Adverse Reactions, Volume 1, records that four out of forty-four side effects reported for salbutamol during 1969–71 were skin reactions. It is unlikely that salbutamol was responsible in this instance, however, as the child has continued to take this drug over the last 2 years without sequelae.

Allergic reactions to animal preparations of ACTH have been reported previously (Landon, Friedman & Greenwood, 1967), these having been attributed to that section of the amino acid polypeptide which is species variable, i.e. the amino acid sections between positions 25 and 31 inclusive.

Similarly, although it was originally thought that synthetic corticotrophin peptides were not antigenic, allergic reactions to tetracosactrin have now been recorded (Jensen & Sneddon, 1969; Patriarcha, 1971).

A cross sensitivity between porcine corticotrophin, human corticotrophin and tetracosactrin is unusual, but has been suggested by Forssman & Mulder (1971). A cross sensitivity with Seractide might, therefore, have been expected in this patient, but did not occur. This is particularly interesting as the first twenty-four amino acids in the molecule are identical to those in both porcine corticotrophin and tetracosactrin. It is possible, therefore, that the skin reaction in this child was unrelated to ACTH therapy, despite its close temporal association.

Seractide has been synthesized according to the formula proposed for Human ACTH by Lee, Lerner & Buettner-Janusch (1961), and while Rinniker *et al.* (1972) have recently disputed the positioning of the amino side chain in the 25–31 amino acid sequence, the preparation was clinically effective, and no adverse reactions were observed during continual use over a 6-month period.

References

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