Medical Memoranda

Case of Extreme Hypersensitivity to Almost All Antituberculous Drugs

British Medical Journal, 1969, 4, 540

One of the main difficulties in the modern treatment of tuberculosis is side-effects—hypersensitivity and toxic reaction—of antituberculous drugs.

The following is a report of a patient who showed extreme hypersensitivity to almost all antituberculous drugs except ethambutol.

CASE REPORT

A 57-year-old man with a history of chronic bronchitis since childhood and a family history of tuberculosis (his mother and wife both having died of pulmonary tuberculosis) was first radiographed in 1949. He was found to have multiple calcified opacities in both lung fields but no active tuberculous focus. From that time he was followed up at the chest clinic with routine x-ray examination of the chest. In April 1961 the chest x-ray picture showed reactivation in the form of apical cavitation with tuberculous infiltration in the left apex. The sputum was also smear- and culture-positive for tubercle bacilli. He was put on to antituberculous chemotherapy with 1 g. of streptomycin and two cachets daily of Pycamisan (isoniazid and para-aminosalicylic acid). After four weeks he showed a severe drug reaction in the form of extensive generalized exfoliative dermatitis. The streptomycin and Pycamisan were stopped and cortisone was given in increasing doses until the severe skin reaction was controlled.

When the rash had subsided an attempt was made to desensitize the patient to streptomycin and P.A.S. A single test dose of 1 mg. of streptomycin was given under cover of a daily dose of 300 mg. of cortisone, but there was an immediate reaction with exacerbation of the skin condition. The streptomycin was discontinued immediately and cortisone doses were increased to 400 mg. daily.

When the rash had subsided again, in about two weeks, a test dose of 10 mg. of P.A.S. was given with still higher doses of cortisone, but the rash recurred and tests showed grossly abnormal liver function, with high serum transaminases (S.G.O.T. 260 units/ml. and S.G.P.T. 830 units/ml.), considerably raised serum bilirubin (4 mg./100 ml.), raised alkaline phosphatase (26 K.A. units), and reversed albumin-globulin ratio. Nevertheless, the skin condition and liver function returned to normal within two months. Isoniazid was then tried in a test dose of 50 mg. daily, but on the third day the rash reappeared. The isoniazid was stopped and cortisone doses were again temporarily increased to control the rash and then changed to prednisone 75 mg. daily; this was also gradually reduced by 1 mg. a day to a maintenance dose of 25–30 mg. daily, which was essential to control his rash. During this time he was tried on tetracycline 2 g. daily because of recurrent episodes of purulent bronchitis and because of its slight antituberculous action. No adverse reaction to this antibiotic occurred.

Six months after the start of steroids he complained of girdle-pain with lower chest pain. X-ray examination of the spine showed osteoporosis and compression of the second and third thoracic vertebrae, almost certainly due to prolonged high dosage of steroids, and so a further gradual reduction in steroid dosage was made. Anabolic steroids and calcium were also started.

During his period of hospital stay he was also tried on test doses of 250 mg. of ethionamide, 250 mg. of cycloserine, and 500 mg. of pyrazinamide, but to all of them he reacted with further recurrence of rash and pyrexia. In spite of the absence of any prolonged effective antituberculous therapy and very high doses of steroids, his tuberculous disease settled well, and sputum became smear- and culture-negative within about eight months. He was discharged in March 1962 taking prednisone 7 mg. and tetracycline 2 g. daily. After discharge he was followed up at the chest clinic with frequent sputum tests and chest x-ray examinations.

He remained well until March 1966, when he was readmitted with a mild cerebrovascular episode and a sputum culture was found to be positive for tubercle bacilli. He was again tried on isoniazid in a small test dose of 10 mg., but again he showed pronounced hypersensitivity in the form of anaphylactic shock and dermatitis, which required high doses of prednisone. After about four weeks a single test dose of 50 mg. of ethionamide was given under cover of 50 mg. of prednisone daily, which also resulted in further exacerbation of the rash. Ethionamide was stopped and prednisone was first increased to 75 mg. daily and then gradually tapered to nil in about two months. During this period he was also given tetracycline 2–3 g. daily with prednisone and other palliative therapy, and as his cerebrovascular episodes improved gradually and a sputum culture was negative he was discharged in July 1966 taking prednisone in tapering doses, with tetracycline 2 g. daily and Betnovate cream (betamethasone valerate) for local application to the skin rashes.

He was readmitted in May 1967 with a history of productive cough and a feeling of generalized malaise and tiredness. Sputum was again found to be smear- and culture-positive. This time the new antituberculous drug, ethambutol, in a test dose of 25 mg. daily, with continued tetracycline and prednisone, was given, but there were no signs of hypersensitivity, so the ethambutol doses were gradually increased to the recommended dosage of 700 mg. b.d. over several weeks. During this period he started to have attacks of faintness and pronounced hypotension lasting for a few minutes when the prednisone was reduced to 5 mg. daily. The prednisone was increased and later changed to cortisone, since it was clear that suprarenal suppression had resulted from large and prolonged steroid dosage. Estimation of steroids excreted in the urine while the patient was on 15 mg. of cortisone daily showed a reduced figure of 1.9 mg./24 hours as 17-ketosteroids, and 7.0 mg./24 hours as 17-hydroxycorticosteroids, suggesting some degree of suprarenal suppression.

To start with, this man's sputum was smear- and culture-positive for tubercle bacilli and remained so from April to December 1961. From December 1961 onwards his sputum remained smear- and culture-negative. In March 1966 sputum again became smear- and culture-positive and remained so until November 1967, with one or two negative tests in between. In May 1967 he was started on ethambutol, and after about four months of full doses his sputum became smear- and culture-negative and has remained so to the time of writing (August 1969). He remained on ethambutol 1 g., tetracycline 1 g., and cortisone 75 mg. daily. His tuberculosis on this treatment appeared to be well controlled, with reasonably good general health.

COMMENT

It is interesting that in spite of the inability of this man to tolerate any antituberculous drug except tetracycline (later ethambutol) and the necessity for very high steroid doses, his tuberculosis became quiescent for a time. The high doses of steroids resulted in osteoporosis and compression of the thoracic vertebrae, with suprarenal suppression. The fainting attacks and hypotension were abolished by maintenance dosage of cortisone 75 mg. and fludrocortisone 0.1 mg. daily.

Ethambutol proved completely free of side-effects and there is every indication that it has, with a small dose of tetracycline, successfully controlled the tuberculous process.

I am grateful to Dr. W. H. Helm, consultant physician, City Hospital, York, for permission to publish this case and for his valuable advice; and to Dr. W. Davidson, chest physician, Fairfield Hospital, York, for his guidance and help.

R. AGRAWAL, M.B., B.S., B.SC.
Senior House-officer in Medicine, Fairfield and City
Hospitals, York.