METHYL-PREDNISOLONE IN PULMONARY TUBERCULOSIS WITH DIABETES MELLITUS

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Both diabetes mellitus and pulmonary tuberculosis were regarded as contraindications to cortico-steroid therapy when such treatment first became available. Steroids have now become standard adjuvant therapy to the usual antituberculous drugs in most cases of fulminant pulmonary tuberculosis and the Tuberculosis Society of Scotland report (1957, 1958) confirmed the value of such combined treatment. Even small doses of cortico-steroids seem to have a definite value as shown by Weinstein and Kohler (1959).

At the Dreadnought Seamen’s Hospital, cases of advanced, bilateral or fulminant pulmonary tuberculosis are frequently seen, more especially among Indian and Pakistani seamen. The reasons for this are not pertinent to the present paper but experience has suggested that patients from the Indian sub-continent often have a poor response to tuberculous infection whilst amongst the Chinese the reverse seems to obtain. For these reasons we frequently have recourse to cortico-steroids and on more than one occasion we have seen diabetes mellitus diagnosed only after glycosuria has occurred, apparently as a direct result of a gluco-corticoid action.

Diabetes mellitus has generally been regarded as contraindicating the use of cortico-steroids in any but the most compelling emergencies. Quite recently Oakley et al. (1959) have shown that in insulin resistant diabetes, due to insulin antibodies, steroids may counteract what is, perhaps, an auto-immune reaction and in this way overcome an insulin resistance. The present case presents the combination of pulmonary tuberculosis with diabetes mellitus, both proving resistant to standard treatment until steroids in the form of methyl-prednisolone were included in the therapeutic régime.

Case Report

C.F., a Goanese seaman, aged 63, was admitted to the Dreadnought Seamen’s Hospital on May 23, 1959. He gave a history of diabetes of 20 years duration for which he had had only intermittent treatment with insulin. In 1957, a chest X-ray had been suspicious of tuberculosis but no further investigations had been undertaken. For one week before admission he had noticed cough with blood-stained sputum and pain, pleuritic in character, in the right lower chest.

On examination he was cachectic with temperature 101°F. The urine contained 2 per cent. of sugar and ketone bodies were present. The sputum was purulent and blood streaked. Chest examination showed dullness to percussion and diminished breath sounds at the right lung base. There was tenderness of the muscles of the calves, the knee and ankle tendon reflexes were absent and vibration sense was absent at the ankles. Peripheral arterial pulses at the ankles were normal. Sputum examination on admission showed numerous acid-fast bacilli and Loewenstein-Jensen culture subsequently proved positive for M. Tuberculosis which showed full sensitivity to streptomycin, PAS and isoniazid. Chest X-ray showed bilateral disease with infiltration throughout the left lung and in the lower part of the right upper lobe with an area of consolidation in the anterior basal segment of the right lower lobe. There was a dense opacity below the left clavicle, probably due to confluent disease. Fasting blood-sugar was 300 mg. per cent. and the glucose tolerance curve was of diabetic type. E.S.R. was 32 (corrected for P.C.V. 40 per cent.) and blood urea was 26 mg. per cent.

From the time of admission he was treated with streptomycin, 1 g. daily, PAS 6 g. t.d.s. and daily intravenous injections of high potency vitamins.
in the form of Parentrovite. This dosage of streptomycin is heavy for a small man aged 63 but it was considered to be justified by the gravity of the illness. It was continued for more than three months until an episode of vertigo and ataxia on September 26, 1959, compelled us to discontinue it. The initial diabetic treatment was soluble insulin 20 units in the morning and 20 units in the evening and a 200 g. carbohydrate diet. On this régime the urine remained loaded with sugar and ketosis continued in spite of an increase to 40 units of insulin b.d. This was changed to six-hourly insulin regulated according to urinary sugar and although the ketosis lessened, his general condition remained very poor, glycosuria was continuous ½ to 2 per cent. together with ketosis, and his evening temperature continued to rise to 100 to 101°F.

Two weeks after admission isoniazid was added to the treatment but, after a further week, there had been no improvement and his weight, 96 lb. on admission, had fallen to 89 lb. After considerable hesitation it was decided to use corticosteroid therapy in spite of the presence of uncontrolled diabetes and on June 11, 1959, he was started on methylprednisolone (Medrone) 4 mg. b.d. Even this small dose proved sufficient and three days later his temperature was normal for the first time during the illness and the patient's general condition and alertness both showed striking improvement. The diabetic control, which was watched carefully during this period, also showed a remarkable improvement; glycosuria fell to 0 to ½ per cent. by the fourth day and insulin requirement to 20 units b.d. by the seventh day and to 12 units b.d. by the fourteenth. Three weeks after starting to take steroids there was an obvious overall improvement and the loss of weight had been arrested.

From this point onwards diabetic control again became more difficult with increasing glycosuria and the insulin requirement rose progressively so that on July 21, 1959, in spite of insulin dosage of 24 units b.d. the blood sugar two hours after the mid-day meal was still 333 mg. per cent. In spite of increasing dosage of insulin diabetic control remained apparently unsatisfactory but the patient's weight began to increase while the chest X-ray showed clearing of the lesion at the right base and increased translucency of the opacity below the left clavicle. Control of the diabetes was improved by the addition of tolbutamide 1 g. b.d. on July 31, 1959, and the insulin requirement fell to 28 units b.d. after this addition.

After the episode of vertigo and ataxia on September 26, 1959, streptomycin was stopped.
and treatment was continued with P.A.S. and isoniazid. At this time it was thought wise to tail off the methyl-prednisolone. This withdrawal had no obvious effect on the diabetic control which remained reasonably steady on the same dosage of insulin and tolbutamide. Sputum has been negative since September 2, 1959, and serial chest X-rays show progressive clearing. His weight at the time of writing has risen to 108 lb., but evidence of peripheral neuritis persists.

The essential data relating to temperature, weight, glycosuria, etc., and the initial treatment both of the tuberculosis and diabetes mellitus have been compressed on the accompanying chart (Fig. 1).

Discussion

The combination of tuberculosis and diabetes mellitus has always presented a most difficult problem in treatment and has long been known to carry a bad prognosis. The introduction of insulin for diabetes and collapse therapy for tuberculosis produced some improvement in the outlook but the main advance followed the introduction of the various anti-tuberculous drugs from 1945 onwards. Very severe cases of tuberculosis are mercifully becoming less common in this country but they are still seen with sufficient frequency to make the adjuvant action of cortico-steroids of much more than academic interest. Tuberculosis, or any other serious infection, makes diabetic control more difficult and as a general rule cortico-steroids by their gluco-corticoid action may be expected to increase the severity of the diabetes still further. In this case the addition of steroid therapy brought about a dramatic improvement in both conditions simultaneously. It is thought likely that the primary action of methyl-prednisolone was to suppress the inflammatory reaction to tuberculosis and that this resulted in easier control of the diabetes. Methyl-prednisolone is known to have a diabetogenic action similar to that of prednisolone (Kleeman et al., 1958, and West, 1958), but this action did not become apparent for three weeks after treatment was started. The small dosage of steroid used proved sufficient to make control of tuberculosis possible but was not small enough to avoid the diabetogenic action.

The value of treatment with cortico-steroids in this combination of diseases seems to be clearly demonstrated in this case, and the response to cautious dosage was remarkable.
Methyl-Prednisolone in Pulmonary Tuberculosis with Diabetes Mellitus

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doi: 10.1136/pgmj.36.411.33

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