

PELLAGRA-LIKE REACTION DUE TO PAS AND ISONIAZID TREATMENT

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Since the introduction of new drugs in the treatment of tuberculosis, a number of side-effects of the various preparations have been reported. The overall incidence of the drug intolerance in 1,744 T.B. patients was 12.2% as reported in a study by Berté et al. in 1964.

The most common reaction to streptomycin is eighth cranial nerve toxicity. Nausea, headache, urticarial rash, anaphylactic shock, liver and kidney damage are other manifestations of adverse effects due to streptomycin.

The toxic effects of Para-aminosalicylic acid (PAS) are:—gastro-intestinal disorders, skin rash, pruritis, hepatitis, myalgia, arthralgia, eosinophilia, leukopenia, haemolytic anaemia (Bower, 1964), methaemoglobinaemia (Simmel, 1962), allergic pneumonia and psychotic reaction (Chandra, 1963).

The most frequently encountered adverse effects of isoniazid are dryness of the mouth, headache, gastro-intestinal upset, difficult micturition, twitching and dizziness. Occasionally, peripheral neuropathy, euphoria, psychosis, hepatitis, skin rash and rarely pellagra-like rash (Aspinall, 1964), purpura (Duncan, 1963), agranulocytosis and convulsions are observed.

Two or three of the above drugs are commonly used in combination in the treatment of tuberculosis. There are, however, the alternative drugs available when patients become resistive or show hypersensitivity to the above drugs. These are:—ethionamide, parazinamide, cycloserine, viomycin, kanamycin and capreomycin, which are also liable to produce similar or other toxic side effects. A patch test may be helpful in predicting safety or likelihood of recurrence of allergy when re-administering one of these drugs. (Brown et al. 1966).

We are reporting the pellagra-like toxic effects of PAS and isoniazid used in the treatment of pulmonary tuberculosis in a mentally retarded, spastic patient.

Case History

A 34 year old male, mentally retarded patient (I.Q. 50) who also suffers from spastic paraplegia, was found to have pulmonary tuberculosis in December, 1961. He was admitted to our hospital T.B. ward for treatment. His initial treatment began with a daily dosage of streptomycin—1G, PAS—15G and isoniazid—150 mg. After 12 weeks of treatment, streptomycin was discontinued. The patient remained on PAS and isoniazid until May, 1964, when both drugs were discontinued because of toxic effects which clinically resembled pellagra.

(a) *Cutaneous lesions*—there was increased pigmentation of the exposed parts of the body, with a sharp line of demarcation from healthy skin and also increased pigmentation of pigmented areas. The skin was dry and rough (Fig. 1).

(b) *Gastro-intestinal disorder*—the tongue was smooth and red, with angular stomatitis, poor appetite and constipation.

(c) *Peripheral neuropathy*—the patient constantly complained about difficulty in micturition and various aches and pains in different parts of the body. He also suffered from hyperaesthesia. His reflexes were very brisk and he had impaired coordination.

(d) *Psychotic episodes*—he became extremely anxious, apprehensive and agitated and developed ideas of reference and persecution. At times he was confused, disorientated, depressed, deluded and refused treatment.

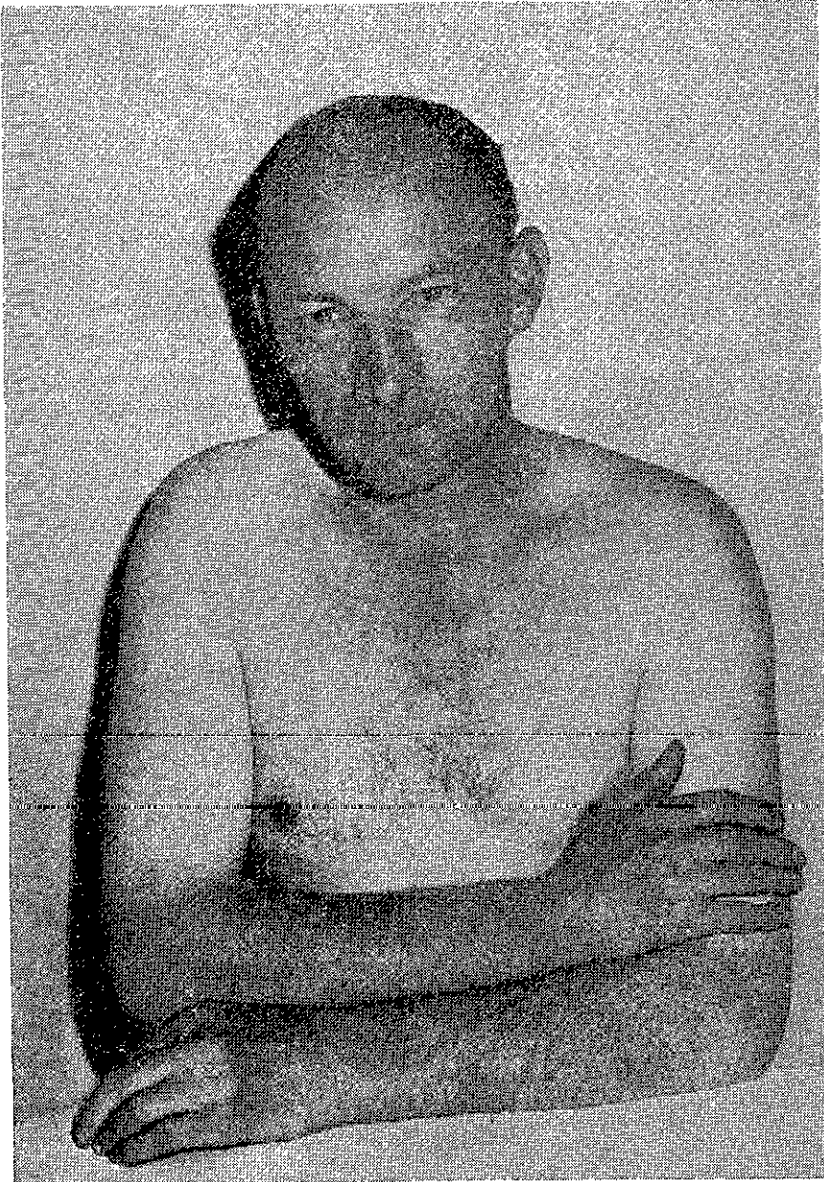


Fig. 1. Frontal view of patient showing increased pigmentation of the skin on exposed parts of the body.

Investigations

- Blood:** Full blood count—normal.
Blood urea—31 mg. per 100 ml.
Serum cholesterol—195 mg. per 100 ml.
- Urine:** Specimen—normal concentration.
Total N—0.8%.
Cystine—normal.
Benedicts—no reduction.
Protein—no precipitate.
Sulkowitch—calcium normal.
Ferric chloride—purple-black colour due to PAS.
Keto acids—no reaction.
Porphobilinogen—none detected.
Amino acid chromatogram—strong “Glycine” pattern.

Throughout the pellagra-like phase, patient's temperature and blood pressure remained normal but he lost nearly 5.50 kg. in weight.

Treatment

When PAS and isoniazid were withdrawn, vitamin B complex forte and yeast tablets, three times daily, with nicotinamide 300 mg. daily, with full and varied diet were administered. Patient showed rapid physical and mental improvement and gained weight steadily. After a few weeks he returned to his normal state of health. Fortunately, his pulmonary T.B. lesion was healing well and remained static and required no further anti tuberculous treatment. Vitamin therapy was gradually reduced and in November, 1966, discontinued altogether. In November, 1967, patient was discharged from the T.B. ward to a general ward of the hospital for mentally retarded patients, where he has since remained well.

Summary

Adverse effects of the drugs used in the treatment of tuberculosis are noted and pellagra-like reaction, due to PAS and isoniazid therapy in a 37 year old mentally retarded, spastic, tuberculosis male and its treatment is reported.

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