Sudden Onset of Psychosis in Association with Vitamin-B₁₂ Deficiency

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Psychiatric disturbance due to avitaminosis B₁₂ is well documented (Holmes, 1956; Wiener and Hope, 1959; Fraser, 1960; Smith, 1960), but the precipitation of such a situation by folic acid cannot fortunately be common, since the dangers of neurological damage by folic acid in the presence of vitamin-B₁₂ deficiency are now well known (Spies and Stone, 1947; Israëls and Wilkinson, 1949; Conley and Krevans, 1955). The results were so dramatic in a case which recently came to our attention that we feel the details are deserving of record.

CASE HISTORY

A 53-year-old housewife presented in February 1966 with a four-year history of intermittent numbness and tinglings in the arms and legs which had been diagnosed elsewhere at the onset as being due to cervical spondylosis and treated by neck traction with partial relief. After a minor traumatic episode six months before presentation the symptoms had become more pronounced and unremitting and she had also developed weakness of fine movements of the hands. During the last six months she had felt depressed.

On inquiring into her past history it was found that she had been treated by "acid" for anaemia 15 years previously—this was probably hydrochloric acid—and that it had been discontinued after some 12 months. In March 1965 she was admitted to another hospital for hysterectomy for menorrhagia. At this time a blood count showed: Hb 50% (7.4 g./100 ml.); P.C.V. 25%; M.C.H.C. 30%; W.B.C. 4,000/cu. mm., normal differential; reticulocytes 6%; M.C.D. 7.8 μ by halometry; appearances of film compatible with rapid red cell regeneration with some hypochromia, but macrocytosis not striking. A histidine loading test for formimino-glutamic acid was weakly positive. Blood transfusion, iron, and folic acid were given with good response, but tests to exclude vitamin-B₁₂ deficiency were not carried out and she continued taking folic acid, 10 mg. t.d.s., until admission.

On examination she was a fit-looking, well-nourished woman who appeared depressed. There was no clinical anaemia, but glossitis was severe. In the central nervous system she was orientated in time and space. Cranial nerves were normal. Power was generally diminished in all four limbs, especially in the distal muscle groups. She had impaired sense to pinprick of the hands and feet and impaired proprioceptive and vibration senses of the feet and lower legs. Tendon reflexes were symmetrically depressed, the supinator and knee reflexes being absent. Gait and Romberg's tests were normal.

Investigations showed: Hb 12.4 g./100 ml., with normal indices and normal film; W.B.C. 4,500/cu. mm., with normal differential; E.S.R. 3 mm. in first hour; total serum protein 5.7 g. (albumin 3.2 g.). Electrophoresis showed slight increase in β -globulin. Liver-function tests were normal. Pyruvate-tolerance test: fasting, 2.55 mg./100 ml.; 30 minutes after 50 g. of glucose, 4.0 mg./100 ml.; 60 minutes, 3.7 mg./100 ml.; 120 minutes, 2.8 mg./100 ml. The normal blood pyruvate level is 0.5 to 1 mg./100 ml. and after glucose should not exceed 1.4 mg./100 ml.

Four days after admission she suddenly became frankly psychotic with delusions, requiring large doses of chlorpromazine. The mental picture was characterized by confusion with paranoid

delusions and auditory hallucinations. She was convinced that others in the ward were saying horrible things regarding her and that she was about to undergo a serious brain operation.

Vitamin-B₁₂ deficiency was suspected, and after the injection of cyanocobalamin 1,000 μ g. for the Schilling test her mental aberration started to improve within 24 hours, and after 48 hours there was marked improvement. The Schilling test showed only 5.3% excretion of the oral dose in 24 hours, rising to 13.3% after 100 mg. of hog intrinsic factor.

Further investigation by Kay's augmented histamine test meal showed achlorhydria, and a barium meal with follow-through was normal apart from a bald gastric fundus. Bio-assay showed serum vitamin B₁₂ 62 μ g./ml. and folate 100 m μ g./ml. Xylose excretion was 2.1 g. after a 5-g. dose. Faecal fats were 12.8 g. in the first 24 hours, 7.8 g. in the second 24 hours, and 6.4 g. in the subsequent 24-hour periods.

Within a few days the mental symptoms had completely resolved, and over the ensuing weeks there was considerable symptomatic improvement in the peripheral neuropathy and she had only occasional mild paraesthesiae in the hands and feet. The power has improved, but at the time of writing impaired vibration sense and diminished tendon reflexes were still present.

COMMENT

The evidence of vitamin-B₁₂ deficiency secondary to pernicious anaemia seems conclusive from the bio-assay and Schilling test results in this case, though there would also seem to be an element of malabsorption in the small intestine not involving vitamin B₁₂, as shown by the high faecal fat excretion values. The rapid improvement in the mental symptoms after parenteral vitamin B₁₂ strongly favours deficiency of this vitamin as the cause of the psychosis, which began with dramatic suddenness at a time when the blood picture was normal and the clinical findings indicated peripheral neuropathy rather than the spinal involvement typical of subacute combined degeneration of the cord. A similar sequence of events was described in three cases by Strachan and Henderson (1965). It was fortunate that the psychosis developed while the patient was under observation in hospital so that treatment could be instituted promptly. We feel that this case illustrates once again the danger of prolonged folic acid therapy without prior exclusion of vitamin-B₁₂ deficiency.

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REFERENCES

- Conley, C. L., and Krevans, J. R. (1955). *Ann. intern. Med.*, 43, 758.
Fraser, T. N. (1960). *Lancet*, 2, 458.
Holmes, J. M. (1956). *Brit. med. J.*, 2, 1394.
Israëls, M. C. G., and Wilkinson, J. F. (1949). *Ibid.*, 2, 1072.
Smith, A. D. M. (1960). *Ibid.*, 2, 1840.
Spies, T. D., and Stone, R. E. (1947). *Lancet*, 1, 174.
Strachan, R. W., and Henderson, J. G. (1965). *Quart. J. Med.*, 34, 303.
Wiener, J. S., and Hope, J. M. (1959). *J. Amer. med. Ass.*, 170, 1038.