A CASE OF CHILDHOOD PELLAGRA WITH PSYCHOSIS

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PELLAGRA is a rare disease in Great Britain. The majority of cases occur among patients in mental hospitals and institutions (Stannus and Gibbons, 1934), and more recently it has been described as an accompaniment or complication of a chronic psychosis (Hardwick, 1946). Sporadic cases do arise in the general population (Davis and Hinden, 1941), but it is likely that in many instances the disease goes unrecognized (Deeny, 1942). Pellagra is particularly uncommon in British children (Greenfield and Holmes, 1939), although observers in areas where the disease is rife are of the opinion that it is found more frequently in children than in adults (Weston and Weston, 1948).

Mental symptoms are frequent in pellagra and may, in fact, precede the other manifestations (Sydenstricker, 1943). Severe psychoses occur in untreated cases and depressive, manic and paranoid reactions have been described (Hardwick, 1946). In children, however, symptoms are usually mild and mania or delirium is not often present (Holt and McIntosh, 1953); therefore this case of pellagra with a psychotic reaction in a 10-year-old English schoolboy may be of interest.

CASE REPORT

M.H., male, aged 10 years 8 months, was admitted to the Children's Department of the Maudsley Hospital in May, 1953. The history was of dermatitis of 5 months' duration and the sudden onset of severe mental disturbance 6 days prior to admission.

Family and Social History

The father, an unstable personality with a criminal record, deserted his wife soon after the patient's birth and the mother, a woman of low average intelligence, had experienced considerable difficulty keeping the family together. They had changed residence frequently and were at the present time in poor financial circumstances living in cramped quarters in a relative's house in South London. Three elder siblings were healthy with no history of nutritional disorder.

Personal History

The patient had lived in England all his life. Birth and early development were normal apart from "teething convulsions". At the age of 7 years he had spent 6 months in an institution because of housing difficulties, and had changed schools several times. A report from his present school described him as a slow but average scholar.

Previous Personality

Up till the age of 8 years he was described as active, friendly, obedient and rather submissive in his relationships with other children. On his return from the institution he was shy and fearful in company, lacked energy and initiative, slept poorly at night, awakening with frightening dreams, and became excessively dependent on his mother. Although more settled after a time, he remained anxious and inhibited.

Dietary History

The patient had been a finicky eater for many years, his mother being hard put to satisfy his tastes within the limits of her income. He would not eat fresh meat, fish or green vegetables, preferring tinned meats, spaghetti, tinned beans, potatoes and bread, and took only small amounts of milk. These likes and dislikes were confirmed in hospital, where he always left meat and green vegetables untouched unless supervised.

History of Illness

In February, 1952, he first developed a sunburn-like reddening of the skin over his face, back of neck, knees, backs of hands and wrists, the skin later becoming scaly and dark. This condition gradually cleared during the next 3–4 months, but he occasionally complained of stiffness in his legs and appeared unsteady on his feet at times. There was an episode of diarrhoea lasting 3 days in September, 1952. In January, 1953, his mother noticed that he was unusually irritable and morose, had a poor appetite, slept badly, and was less active at play, tending to keep to himself. In April, 1953, the dermatitis recurred. The boy was sensitive and anxious about his appearance, kept his hands in his pockets and asked, "Am I going mouldy?" He complained frequently of fatigue and aching and stiffness in his legs. Four days prior to the onset of mental symptoms he was brought home from school with the story that, while competing in a race, he seemed to lose control of his limbs and staggered about in an uncoordinated fashion. Six days prior to admission he became acutely ill with insomnia, frequent crying spells, restlessness, agitation, and demands not to be left alone. He expressed strange ideas: that there was an object inside his body, he was unable to taste his food, his neck was loose, his limbs had become skinny, his head felt empty and he could not think properly any more. His mother also stated that he seemed afraid to swallow his saliva for fear he would be poisoned, and accused his family of disliking him, blaming first his mother and later his brother for his condition.

Examination on Admission

The patient was of average height with sallow complexion and dark hair. Muscular development was normal and there was no evidence of marked weight loss, or clinical anaemia. Temperature was normal. The skin showed erythema with pigmentation and desquamation affecting the exposed areas, i.e. the cheeks, the back and sides of his neck, the backs of wrists and hands and encircling both knees. The areas were sharply defined from healthy skin, particularly on the neck and hands. (The patient was examined by Professor A. W. Woodruffe and Dr. L. Forman, who described the skin lesions as typical of pellagra.)

Tongue was moist and clean, and slightly reddened at the tip. No cheilosis, angular stomatitis, or other mucous membrane lesion was present.

Cardiovascular, respiratory and gastro-intestinal systems showed no clinical abnormality. Blood pressure 100 mm. systolic, 80 mm. diastolic. Pulse 90.

Nervous System

Bilateral nystagmoid jerkings were present on lateral gaze, but there was no other abnormality in the cranial nerves or special senses. Resistance to passive movement was increased in both lower limbs. Power and co-ordination were normal. All tendon reflexes were brisk but equal on both sides. Plantar responses were flexor. There was slight unsteadiness of gait. Accurate sensory testing was not possible but there appeared to be subjective impairment of sensation to cotton-wool and pin-prick over the hands and feet.

Mental State

He lay quietly in bed and took little interest in his surroundings. His expression was apprehensive, he responded slowly to instructions and appeared bewildered. He knew his name but was disorientated for time and place and was unable to recall events in the past few days. Simple tasks and calculations were poorly performed and attention and concentration soon waned. He did not talk spontaneously but answered questions shortly and in a whisper before resuming his fixed, anxious expression. When questioned about any changes in his body, he became very disturbed and began to weep, saying "I can't feel myself. My legs have gone skinny. My head is empty and I can't think about things like I used to." When asked what was wrong with him, he touched his thigh and abdomen and became very agitated, attempting to get out of bed in a confused fashion. After reassurance, he described how "a finger with yellow stuff on the tip touched my leg in the night. Now it's in my stomach and it's burning me inside." He stated that his family did not like him and were responsible for his illness because of something he had done. During the day he remained in a confused dream-like state interspersed with short periods of intense anxiety when he wept loudly and clutched his chest, crying "I can't breathe. My heart has stopped and I will die. My brain has gone soft." His agitation and confusion were most marked in the evenings. He urinated in his bed and on the floor and repeatedly tried to run out of the ward. He was observed one evening sitting bolt upright with a terrified expression as if afraid to move. He then began to weep and scream "Look out! It's there in the bed. It's the finger," and tried to run away.

Progress and Treatment

The patient took a full hospital diet and copious fluids, but tended to be constipated. He remained confused and agitated and the bizarre delusions and vivid hallucinations were constantly present. He was markedly disturbed at night requiring fairly heavy sedation.

Treatment was begun with an initial dose of nicotinic acid 200 mgm. by mouth followed by nicotinamide 100 mgm. T.I.D. He was given a high protein and carbohydrate diet supplemented with marmite and milk.

There was a conspicuous improvement within 48 hours. He was less agitated, more in

touch with his surroundings, and slept well without sedation. He no longer reacted so violently to his hallucinations and delusions and these cleared by the fourth day. Disorientation remained and he now appeared vague and apathetic. The neurological findings were unchanged.

The dermatitis improved rapidly, clearing completely within 14 days. By this time all signs of acute mental and neurological disturbance were absent and the picture emerged of a dull, polite boy with little interest or initiative, content to wander about alone or gaze vacantly into space. He was reluctant to discuss his symptoms, but realized he had been ill. He had no clear recollection of the delusions and hallucinations, describing them as "bad dreams". He later became more alert, sociable and active, and on discharge from hospital 3 months later was described as "back to normal". Advice was given to his mother on the preparation of a balanced diet and maintenance dose of nicotinamide and yeast tablets was prescribed.

Pathological Investigations

Haemoglobin 84 per cent. (13·1 gm.). Red blood corpuscles 5·1 million per c.mm. Packed cell volume 43 per cent. Mean corpuscular volume 84 cu. microns. Leucocytes 12,300 per c.mm. Polymorphs 77 per cent., lymphocytes 20 per cent., monocytes 3 per cent. Cells appeared normal on the stained film. Erythrocyte sedimentation rate 5 mm. fall in the first hour. Wassermann reaction—negative. Cerebrospinal fluid. Pressure 120 mm. water. No block. Cells: 1 lymphocyte per cu. mm. Protein 40 mgm. per 100 ml. Chlorides 760 mgm. per 100 ml. Sugar: normal. Pandy test—negative. Wassermann reaction—negative. Lange test—no change. Urine examination: no abnormality. Liver function tests: no abnormality. Serum proteins: total protein 6·8 gm. per 100 ml. Albumin 4·3 gm. per 100 ml. Globulin 2·5 gm. per 100 ml. Stool examination: no abnormality.

Biochemical Investigations

No porphyrins or urorosein were found in the urine. The urinary output of nicotinic acid, nicotinamide and N_1-methylnicotinamide was estimated (over a three-day period) in the patient and a normal control while on an identical standard diet. Nicotinamide 100 mgm. was then administered on each of three days and the estimation repeated. The values obtained did not establish any abnormality in the major known excretion products of nicotinic acid, thus indicating that a disturbance in absorption and metabolism of nicotinamide was not an aetiological factor in this case.

The patient's urine showed a high output of indican in 24-hour volume specimens, a finding which has been frequently observed in pellagra (Spies and Butt, 1947), but which appears to be of particular significance in this case (Rodnight and McIlwain).

Electroencephalographic Examination

The record showed a mild abnormality only during overbreathing as is sometimes seen in toxic conditions. There were no paroxysmal nor localizing features in the record.

Psychological Investigation

A full psychological investigation was carried out after recovery to determine evidence of residual intellectual impairment. The earlier test results when compared with the previous educational level were suggestive of deterioration. Scores on the Binet Form L. were: Mental Age: 7 years 2 months; I.Q. 67, and performance on memory items was particularly poor. The patient appeared vague and bewildered and the scores were not considered a reliable indication of "true" intellectual level. Successive test performances showed a gradual improvement and scores on a wide range of tests three months after recovery gave no evidence of impairment. Scores on the Binet Form M. were: Mental Age: 9 years 6 months; I.Q. 88, which was commensurate with school progress prior to illness.

Follow-up After Discharge

The family moved away from London in October, 1953, but the patient was kept under supervision by the local school medical officer. A year later he was reported to be quite well mentally and physically, the only symptoms since discharge from hospital being a short spell of diarrhoea at the end of the summer while he was without his maintenance dose of vitamin tablets. His school work was described as satisfactory.

COMMENTARY

The aetiology of pellagra has been a source of speculation and discussion since the first occurrence of the disease in the eighteenth century (Chick, 1951). Pellagra is now considered to be a multiple deficiency disease with disturbed metabolic relationships involving nicotinic acid, pyridoxine, tryptophane and possibly protein and other members of the vitamin B complex (Bicknell and Prescott, 1953). The clinical signs of pellagra have been experimentally produced in man using diets low in nicotinamide and tryptophane supplemented with

other B vitamins (Goldsmith *et al.*, 1952). Tryptophane is a precursor of nicotinic acid and its administration leads to an increased excretion of nicotinic acid metabolites in normal subjects and pellagrins (Sarett and Goldsmith, 1949) and brings about healing of the lesions in pellagra (Vilter, Mueller and Bean, 1949). The importance of the protein content of the diet has long been appreciated, and the above relationship may explain the pellagra-preventive effects of foods low in nicotinic acid but rich in good protein (Goldsmith *et al.*, 1952).

The exact amounts of the different constituents of the patient's diet were difficult to determine. It may however be accepted from his clinical condition that M.H. (of 34 kg.) was obtaining adequate calories and protein from the foodstuffs listed in the dietary history. Thus he did not gain in weight whilst on a controlled and adequate diet in hospital. Tabulated data on such foodstuffs shows that a diet composed of them and yielding 2,500 cal./day and 70 gm. of protein is very unlikely to contain less nicotinamide than the accepted average requirement of 12 mgm./day. As vitamin requirements vary greatly in different individuals and, indeed, in the same individual from time to time as the result of growth, inherent metabolic pattern and physical activity, it is not easy to estimate needs or intake with any degree of accuracy. The requirements for some nutrients are dependent on other components in the diet and an insufficiency of one may affect the requirement and utilization of others (Yudkin, 1951). Thus the present symptoms of deficiency in nicotinic acid are most likely to have arisen through M.H.'s requirement for the substance being above the average.

It has been suggested that chronic partial deficiency of nicotinic acid lasting many months or years produces functional or biochemical disturbances which are relatively mild whereas complete or almost complete depletion rapidly produced, causes severe or even fatal functional disturbances (Sydenstricker, 1943). The course of the illness in this patient would seem to support this hypothesis. It is likely that a state of sub-clinical nicotinamide deficiency had existed for some time prior to the appearance of the dermatitis. The symptoms reported by his mother of irritability, insomnia, apprehension and fatigue, have been described as initial features of the disease in adults (Frostig and Spies, 1940) and in children (Spies and Butt, 1947). The acute mental disturbance occurred during the second appearance of the dermatitis and followed soon after an episode of strenuous physical activity. This additional stress appears to have further disturbed the already precarious balance between metabolic demands and dietary intake.

The clinical picture of pellagra in childhood varies in some respects from that in adults. Spies and Butt (1947) explain this difference by the fact that in the adult nutritional deficiencies affect mature tissues, whereas in children they are engrafted on tissues in the process of growth and development. The striking dissimilarity in environment also influences the symptomatology: the infant or child leading a sheltered existence compared with the active and exposed life of the adult. In children glossitis and mucous membrane lesions are usually mild (Weston and Weston, 1948). Violent gastro-intestinal symptoms are less frequent and constipation rather than diarrhoea may predominate (Holt and McIntosh, 1953). It is of interest that diarrhoea was a minor feature of this patient's illness and that mucous membrane lesions were confined to a mild glossitis.

The nervous system is less severely affected in children but cerebral symptoms are an integral part of the disease and are present to some extent in every fully developed case. In the milder cases the children are dull, irritable, emotionally labile, easily fatigued and may show lack of progress at school (Ford, 1953). In more severe cases there may be an apparent deterioration in intellectual

capacity, the formerly bright and intelligent child appearing backward or even mentally defective (Greenfield and Holmes, 1939).

Evidence of spinal cord involvement is found when the disease has been present for a year (Dodd, 1941). Tremor, ataxia, spasticity and increased reflexes with extensor plantar responses have been described. Histological examination showed degeneration in the spino-cerebellar tracts and severe involvement of motor cortex and basal ganglia (Greenfield and Holmes, 1939).

Psychotic reactions are unusual and few are reported in the literature. Hutchison and Paterson (1923) recorded a psychotic reaction in a ten-year-old girl with a history of pellagra of some years' duration. She was described as "childish" and nervous in the years prior to the appearance of the dermatitis. On admission to hospital she appeared mentally defective, was extremely emotional and unreasonable with hallucinations of sight and hearing. She believed an attempt was being made to poison her and that someone was trying to cut her throat at night. This case is of particular interest because of the similarity in certain respects to the one presented in this paper. In both instances the patients were the same age and the illness of more than a year's duration. Both presented paranoid delusions and terrifying visual hallucinations, noticeably worse at night—features noted by Kanner (1952) as characteristic in children with delirious reactions of infectious or toxic origin.

The mental symptoms in pellagra, unless of long standing, are usually reversible and are particularly responsive to treatment with nicotinamide. Nicotinic acid is a constituent of enzyme systems which are essential for carbohydrate metabolism. The energy of nervous tissue is largely derived from the metabolism of glucose and a break in this process results in a disturbance of cerebral function. Thus a metabolic disturbance has been suggested as the underlying cause of the disorder of consciousness, memory and perception which occurs in pellagra (Himwich, 1951).

Summary

A case of pellagra in childhood is described with particular reference to the occurrence of a confusional psychosis. A metabolic peculiarity resulting in an increased requirement for nicotinamide is postulated as a possible factor in the cause of the illness.

A satisfactory response to treatment with nicotinamide was obtained and psychological testing showed no evidence of mental deterioration.

Acknowledgments

I am indebted to Dr. Kenneth Cameron, Physician to the Children's Department, The Maudsley Hospital, for permission to publish this case report and for his advice and encouragement. Professor H. McIlwain and Mr. R. Rodnight of the Biochemistry Department initiated and carried out the biochemical investigations. Miss M. Newell was responsible for the psychological investigation.

References

Bicknell, F., and Prescott, F., *The Vitamins in Medicine*, 1953. 3rd ed., p. 352. London: William Heinemann.

Chick, H., *Nutr. Abst. and Revs.*, 1951, **20**, 523.

Davis, E., and Hinden, E., *Lancet*, 1941, *i*, 10.

Deeny, J., *Brit. Med. J.*, 1942, *i*, 157.

Dodd, K., in Seale Harris's *Clinical Pellagra*, 1941, p. 341. St. Louis: C. V. Mosby & Co.

Ford, F. R., *Diseases of the Nervous System in Infancy and Childhood*, 1952. 3rd ed., p. 768. Oxford: Blackwell Scientific Publications.

Frostig, J. P., and Spies, T. D., *Amer. J. Med. Sci.*, 1940, **199**, 268.

Goldsmith, G. A., Sarett, H. D., Register, U. D., and Gibbens, J., *J. Clin. Invest.*, 1952, **31**, 533.

Greenfield, J. G., and Holmes, J. MacD., *Brit. Med. J.*, 1939, *i*, 815.

Hardwick, S. W., *J. Ment. Sci.*, 1946, **92**, 310.

Himwich, H., *J. Nerv. Ment. Dis.*, 1951, **114**, 450.

HOLT, L. E., JR., and MCINTOSH, R., *Holt's Pediatrics*, 1953. 12th ed., p. 294. New York: Appleton Century Crofts Inc.
HUTCHISON, R., and PATERSON, D., *Brit. Med. J.*, 1923, *ii*, 646.
KANNER, L., *Child Psychiatry*, 1948. 2nd ed., p. 449. Oxford: Blackwell Scientific Publications.
RODNIGHT, R., and MCILWAIN, H., *J. Ment. Sci.*, 1955, **101**, 884.
SARETT, H. P., and GOLDSMITH, G. A., *J. Biol. Chem.*, 1949, **177**, 461.
SPIES, T. D., and BUTT, H., in G. G. Duncan's *Diseases of Metabolism*, 1947. 2nd ed., p. 440. London: W. B. Saunders Company.
STANNUS, H. S., and GIBSON, C. R., *Quart. J. Med.*, 1934, n.s. **3**, 211.
SYDENSTRICKER, V. P., *Proc. Roy. Soc. Med.*, 1942, **36**, 169.
VILTER, R. W., MUELLER, J. F., and BEAN, W. B., *J. Lab. Clin. Med.*, 1949, **34**, 409.
WESTON, W., and WESTON, W. JR., in Brenneman's *Practice of Paediatrics*, 1948. Vol. 1, Ch. 34, p. 1. Hagerstown: W. F. Prior & Co.
YUDKIN, J., *Lectures on the Scientific Basis of Medicine*, 1951–2. Vol. 1, p. 364. University of London: The Athlone Press.