

MENTAL SYMPTOMS IN PELLAGRA AND NICOTINIC ACID DEFICIENCY

By L. P. VARMA, M.B., B.S.

Medical College Hospital, Patna

MENTAL symptoms have been regarded as one of the characteristic features of pellagra since 1735 when Gasper Cassal studied the first case and called it 'Mal de la Rose'. The present name was given by an Italian physician, Francesco Frapolli, who published a careful account of the disease in 1771. Since then, cases of pellagra have been reported by workers all over the world.

The psychiatric importance of pellagra

The psychiatric importance of pellagra is considerable. It has been estimated that from 4 to 10 per cent of all pellagrins show mental symptoms (Henderson and Gillespie, 1940). In England, pellagra has been noted in lunatic asylums since 1913. There were 21 deaths from pellagra in 1922, mostly from the Lancashire

(Continued from previous page)

Summary

1. Seventeen of over one hundred cases of kala-azar treated with 4:4' diamidino-stilbene subsequently developed a neurological syndrome.

2. The principal features of this syndrome are paræsthesia and partial anæsthesia in the trigeminal area with loss of sensation of light touch, with preservation of sensation of pain, temperature and pressure.

3. The lesion is in the principal sensory nucleus of the trigeminal nerve in the pons, and is probably of the nature of a toxic degeneration. Diamidino-stilbene is the toxic factor responsible, and the selective toxic action is probably due to the ethylene component of this compound.

4. The condition is not dangerous to life and is not progressive; in most patients there is a tendency to slow recovery.

5. In cases having troublesome paræsthetic symptoms, all therapeutic measures (non-surgical) have been found to be useless except injections of solution of cobra venom (1:100,000) in gradually increasing doses which produces some degree of subjective improvement.

REFERENCES

- | | |
|---|--|
| ADLER, S., and TCHERNO-MORETZ, I. (1939). | <i>Ann. Trop. Med. and Parasit.</i> , 33 , 313. |
| BRAIN, W. R. (1933) .. | <i>Diseases of the Nervous System</i> . Oxford University Press, London. |
| DEVINE, J. (1938) .. | <i>Ann. Trop. Med. and Parasit.</i> , 32 , 163. |
| <i>Idem</i> (1940) .. | <i>Ibid.</i> , 34 , 67. |
| FULTON, J. D., and YORKE, W. (1942) .. | <i>Ibid.</i> , 36 , 134. |
| NAPIER, L. E., and SEN GUPTA, P. C. (1942). | <i>Indian Med. Gaz.</i> , 77 , 71. |
| <i>Idem</i> (1943). | <i>Ibid.</i> , 78 , 177. |
| NAPIER, L. E., SEN GUPTA, P. C., and SEN, G. N. (1942). | <i>Ibid.</i> , 77 , 321. |

Mental Hospital, Rainhill, and during the period 1913 to 1918 there have been 104 deaths from pellagra among the asylum inmates. Goldberger found that in certain asylums in the United States the number of lunatics developing pellagra each year was a constant proportion of the total (Manson-Bahr, 1940). Conditions are however quite different in the mental hospitals of this country. It is interesting to note that during the period 1936 to 1940 not a single case of pellagra has been reported from the Indian Mental Hospital, Kanke, which is the biggest mental hospital in this country and caters for the three provinces of Bihar, Bengal and Orissa (Dhunjibhoy, 1938, 1939, 1940, 1940a; Das, 1942). As early as 1915, Singer (Strecker and Ebaugh, 1935) realized the psychiatric importance of this disease and described it under three broad groups. His first group consisted of patients who developed mental symptoms, mostly depression and delirious states as a result of the disease itself. In the second group he placed those cases of manic depressive psychosis, dementia præcox and psychoneurosis in which pellagra had acted as a precipitating factor. His third group was formed of those patients who were already suffering from certain organic diseases of the brain, such as arteriosclerotic dementia, senile or presenile psychosis and general paralysis, patients in whom pellagra subsequently developed.

Miller and Ismail (1920) made an investigation into the incidence of the pellagra psychosis in Egypt and found that such cases formed 27.6 per cent of all admissions made into the Khanka Mental Hospital. They studied 757 cases. The cases were classified on admission into acute confusional psychosis; mania, acute, recurrent and febrile; melancholia, simple and recurrent; dementia, imbecility, adolescent insanity, epileptiform insanity and general paralysis of the insane.

Mental symptoms in pellagra reported in this country

Pellagrins showing mild depression, melancholia, mania, restlessness, irritability and clouding of the consciousness have been studied in this country by Lowe (1931), Raman (1933), Gupta (1935), Panja (1935), Dhyagude and Khadilkar (1939), Goodall (1940), Ahmed (1942, 1942a), Batra (1942), Patel and Shah (1942), Patel and Motashaw (1942), Heilig (1943), Napier and Chaudhuri (1943) and Dey (1943). Lowe (1931) studied 40 cases of pellagra occurring among the lepers at the Leprosy Hospital, Dichpali, Hyderabad, Deccan, and noticed marked mental symptoms in three of them. One showed marked melancholia with periods of mania and suicidal tendency. Another patient became semicomatose and had periodic attacks of epileptiform fits. A third case showed extreme depression verging on melancholia and finally committed suicide by

drowning. Lowe's patients who showed marked mental symptoms invariably died. Mody (1935) reported a typical case of pellagra with characteristic skin and gastro-intestinal manifestations. He was taciturn and morose and often suffered from hallucinations. His mental attitude was pessimistic as he believed that he would never get well. Treatment was however effective in removing the other manifestations of pellagra though the mental condition remained stationary. Raman (1940) reported two cases of pellagra with mental symptoms. In one of them, mental symptoms were so severe that the patient could be controlled only with hyocine injections. With treatment, the general condition of the patient improved but the mental condition did not show any amelioration. He had later on to be transferred to a mental hospital, where he subsequently died.

Mental symptoms in pellagra and their response to treatment

The prognosis of pellagra has considerably improved with the introduction of nicotinic acid therapy. Fouts *et al.* (1937) treated four cases of 'alcoholic pellagra' with relatively large doses of nicotinic acid and noticed improvement in their mental condition within 24 hours of the treatment. Smith *et al.* (1937) obtained good results with 50 mg. of nicotinic acid given daily over a period of 12 days, the patients showing improvement in their mental condition in about 48 hours. Spies *et al.* (1939) found dramatic improvement in treated patients showing acute mental symptoms. These symptoms, varying from slight confusion to delirium and mania, disappeared rapidly, often overnight. The maniacal patients became calm and the confused patients mentally clear. Apathy and lassitude gave way to interest. After therapy, they readjusted themselves and often had excellent memory of their actions, ideas and surroundings during the psychotic period. Patients suffering from irritability, abdominal pains, weakness and difficulty in walking improved considerably under the combined therapy of nicotinic acid and vitamin B₆ (Spies *et al.*, 1939a). Similar results have been obtained by Matthews (1938), Rachmilewitz and Glueck (1938), Bogart (1938), Goodall (1940), Ahmed (1942), Batra (1942), Patel and Shah (1942), Patel and Motashaw (1942) and Dey (1943). This is only one side of the picture as we often come across cases in which nicotinic acid does not cause any improvement in the mental condition of the patient.

The case described below is one of this nature.

Case 1.—A Hindu male, cultivator, aged 38 years, of Gaya district, came under the author's observation on the 14th May, 1942, with the following complaints: (1) diarrhoea for the last 5 months, and (2) weakness and inability to do any work for the last 2 months.

The patient is the third child of healthy parents. There is no history of mental illness in the family. He was married at the age of 18 years and has three healthy children.

His diet consisted of rice, pulse, vegetables and milk. He is not addicted to any intoxicant and is an orthodox Brahmin.

He has not had good health from 1935 or 1936. His main troubles have been occasional attacks of diarrhoea, dysentery, constipation and flatulence. Since then he has been constantly losing weight. He was robust and healthy before, but is now emaciated.

He was a happy, care-free man. He loved his children and took an interest in his work. He had many friends in his village. His uncle noticed a change in his character in 1939. He became irritable and quarrelsome. He began to avoid the company of his friends. His children were afraid of him as he beat them on the slightest pretext. He did not take care of his property and always accused him (his uncle) of misappropriation. His attitude to his wife also changed.

The patient was pale, thin and emaciated. His weight was 98 lb. and height 5 feet 6 inches. There were symmetrical patches of scaly dermatitis with marked pigmentation, sharply demarcated from the surrounding skin on the dorsum of the feet and front of the legs.

His tongue was flabby with indentations on the margin. The abdomen was tumid and tympanitic, with gurgling in the iliac fossæ. He was passing five to six loose motions daily. Repeated examination of the stool revealed no abnormality. Neurological examinations revealed nothing.

Mental examination: He was found sitting in a sad and apathetic mood. He took no interest in his surroundings. He dressed carelessly and was often found lying naked in his bed. He passed fæces and urine in the bed, and did not have the bed cleaned. His facial expression was vacant; saliva was dribbling from his mouth. When he ate, he did not wash his mouth but left it till some one cleaned it for him. He did not relish food but took it when it was given. He was always absent-minded and depressed. Questions had to be repeated several times before a response could be elicited from him. Speech was slow and coherent but rarely spontaneous. Memory for both recent and remote events was impaired. Orientation in time was impaired. Orientation in place and person was good. His judgment was poor. He had insight into his illness.

He was put on the following treatment: (1) nicotinic acid 50 mg. tablets, 2 tablets, three times a day, (2) liver extract, 2 c.c.m. intramuscularly on alternate days, and (3) fersolate tablets, one tablet, three times a day after meals. His diarrhoea disappeared on the third day of this treatment and his skin condition completely cleared up in a fortnight. The mental condition of the patient, however, showed no improvement, though he took the drug for about 2 months.

Mental symptoms in nicotinic acid deficiency

Recently, American authors have drawn attention to the occurrence of neurotic and neurasthenic manifestations in sub-clinical states of vitamin deficiency (Jolliffe, 1941; Ruffin, 1941). Spies *et al.* (1938) studied 60 patients with mental symptoms but without the characteristic skin and gastro-intestinal manifestations of pellagra. Their patients showed loss of memory, delirium, mania, depression, and many of them presented symptoms of a neurasthenic nature, *viz.*, fatigue, insomnia, anorexia, vertigo, palpitation, headache, nervousness, unrest, apprehension, anxiety, forgetfulness and paræsthesia. Some of them showed paranoic reactions with fears of relatives and delusions of persecution. Treatment with nicotinic acid led to recovery in all cases within 6 days. Sydenstricker and Cleckley (1941) studied 29 such patients with symptoms of active psychosis but with no signs of pellagra.

They showed some of the following signs : manic excitement, delirium, hallucinations, disorientations and delirium tremens. It was possible to show that in 22 of them, symptoms were due to nicotinic acid deficiency while in others it was probably due to psychoneurosis, arteriosclerosis, senility and other factors. Cleckley *et al.* (1939) found remarkable improvement with this drug in 19 stuporous patients, and Evans (1939) in a case showing schizophrenia-like psychoses. A similar case has been reported by Slater (1942) in England. His patients showed symptoms suggestive of a melancholic, a schizophrenic and an organic state. This case made dramatic recovery with nicotinic acid.

Two such cases came under the author's observation recently :—

Case 2.—A Hindu male, aged 18 years, of Moughyr district, came under the author's observation on the 28th February, 1942, with the following complaints : (1) restlessness, getting worse every day for the last 10 days, (2) insomnia for the last 5 days, and (3) diarrhoea for the last 10 days.

He was the second of four children of over-indulgent parents. Both the parents were healthy and so were the other children. There was no history of psychosis in the family. The patient was a man of temperate habits and was not addicted to alcohol, toddy or any other intoxicant. He was considered to be social and well behaved. He took part in sports. He was an average boy in school. He was unmarried. His diet consisted of rice, pulse, and ordinary vegetables. He occasionally took meat. He had typhoid at the age of 10 and dysentery at 12.

About 6 months ago, the patient received the news of his failure at the supplementary matriculation examination. This gave him a shock, but he was not broken-hearted, and started his studies in earnest. It is said that he read for about 6 to 8 hours at night in addition to his studies during the day. During this period, he paid little attention to his food and often went without it at night. Even when he was not at work, he remained alone and took no interest in his family or friends. He gave up sports. During this period, he would frequently have loose motions, several times a day, and would then often pass 2 or 3 days without any. He continued in this way for about 3 months. Then he started getting headache which was very annoying as it disturbed his studies. Often he was seen tossing in bed and on enquiry he would say that he had a mild attack of headache. His father advised him to stop his studies for the time being, and start again after he was well. He paid no attention to his father's advice, and his father says that he was getting more irritable every day. Twice during the last 3 months he had colicky pains in his abdomen but he refused treatment. He was having loose motions, 5 to 6 times a day for the last 10 days, which was attended with griping. He could not sleep for the last 5 days and was very restless. He often spoke at random for 2 to 3 hours at a time. He often made attempts to run away from the house and was calm and quiet at times.

Mental examination revealed flight of ideas, elation and a sense of grandeur. He appeared also to be suffering from hallucinations and delusions of persecution but refused to say anything about them. He refused to answer questions and believed that every one was either a fool or his enemy. At times he was violent, particularly on the night he was seen by the author. He was making attempts to leave the bed, and 5 persons found it difficult to keep him under control. Orientation in place, person and time was good. Memory could not be tested.

The patient was lean, thin and emaciated. His height was 5 feet 5 inches and weight 100 lb. His tongue was pale and flabby. His abdomen was distended and tympanitic. There was no obvious skin disease. Examination of the central nervous system revealed no abnormality. Repeated examination of the stool showed nothing.

The patient was treated with hydrotherapy and sedatives combined with nicotinic acid, 50 mg. tablets, 2 tablets three times a day. The presence of vague abdominal symptoms suggested nicotinic acid deficiency, and nicotinic acid was given in the hope that it would ameliorate abdominal symptoms. Curiously enough the patient recovered completely on the third day of the treatment. He had good sleep on the second night and was perfectly sane on the third day.

Case 3.—A Hindu boy, aged 8 years, of Patna district was bitten by a street dog on the 13th March, 1943. He came for treatment to the out-patient department of the Pasteur Institute, Medical College Hospital, Patna, 2 days later. He is the only child of his parents, who were healthy. There is no history of mental illness in the family. Treatment was started on 15th March, 1943, and he was given seven injections of anti-rabic vaccine. He got an attack of delirium at 4 p.m. on 21st March, 1943. He became very apprehensive and restless. He cried at the top of his voice but gave no reasons for it. He tried to throttle himself and was prevented from doing so. His father poured a bucketful of water over his head but to no effect. He became quiet in about an hour and went to sleep. His sleep was disturbed. Next day when an enquiry was made about his fear and cry, he said that a little before the attack he felt that something like air had entered his neck and was throttling him. He saw monkeys and dogs coming to attack him. No vaccine was given on 22nd March, 1943 and 23rd March, 1943, as the anti-rabic treatment was suspected to be responsible for it. The attacks of delirium, however, recurred again on 22nd March, 1943 and 23rd March, 1943, at the same time. Vaccine was restarted and the patient was given nicotinic acid, 50 mg. tablets, one tablet three times a day. There was no further attack and the patient was given a full course of 14 injections.

Comments

The first case is a typical case of pellagra with gastro-intestinal, dermal and mental manifestations characteristic of the disease. It is interesting to note that while the gastro-intestinal and dermal lesions disappeared readily with nicotinic acid, mental symptoms remained stationary. The patient developed mental symptoms in the course of the disease. He had already suffered from vague abdominal disturbances for 3 years before his uncle noticed a change in his character. The mental symptoms were probably a manifestation of pellagra. Cases of this nature, where mental symptoms have proved resistant to treatment, have already been reported by Mody (1935), Jersild (1941) and Petri *et al.* (1937). In the present state of our knowledge it is difficult to give any definite explanation. The possibility of certain organic changes having taken place in the brain, incapable of repair on supplying the deficiency, should not be lost sight of, and post-mortem evidence of this nature have been found by Dunlap and Watson (Henderson and Gillespie, 1940). On the other hand Bogart (1938) has reported a case of dementia which was promptly cured by nicotinic acid.

The mental condition of the patient formed the prominent feature of the last two cases. The

second case was seen in a maniacal condition and had no skin lesions. The third case was in a delirious state, and both the skin and gastrointestinal manifestations were conspicuous by their absence. Both of them made a dramatic response to nicotinic acid and thus appeared to be cases of nicotinic acid deficiency. Cases of this nature have already been studied by Spies *et al.* (1938), Cleckley *et al.* (1939), Sydenstricker and Cleckley (1941), Jolliffe (1941) and Ruffin (1941) in America and Slater (1942) in England. No such case appears to have been reported so far in this country. Cases of nicotinic acid deficiency are quite common here, and it is likely that many more cases of this nature may come to light if a note is made of their existence.

Conclusions

Mental symptoms in pellagra are legion, and we find that pellagra can simulate any one of the psychoses or psycho-neuroses met with in practice. At present it is difficult to associate any one in mental state with this syndrome, but depression is the usual effect seen in such patients. Mental symptoms without any other signs of pellagra occur in cases of nicotinic acid deficiency and show dramatic improvement when the deficiency is supplied.

Summary.

1. A review of the recent articles on the subject has been given.

2. Attention has been drawn to the occurrence of only mental symptoms in cases of nicotinic acid deficiency, and two such cases have been reported.

3. One case of typical pellagra has been reported in which the mental symptoms proved resistant to nicotinic acid therapy.

Acknowledgments

The author is indebted to Dr. B. P. Varma, F.R.C.S.E., Superintendent, Medical College Hospital, and Dr. S. A. Imam, Superintendent, Pasteur Institute, Patna, for permission to report the last case.

REFERENCES

- AHMED, N. (1942) .. *Indian Med. Gaz.*, **77**, 140.
Idem (1942a) .. *J. Indian Med. Assoc.*, **12**, 1.
 BATRA, B. L. (1942) .. *Indian Med. Gaz.*, **77**, 269.
 BOGART, C. N. (1938) .. *J. Amer. Med. Assoc.*, **111**, 613.
Idem., **112**, 2107.
 CLECKLEY, H. M., SYDENSTRICKER, V. P., and GEESLIN, L. F. (1939).
 DAS, P. C. (1942) .. *Ann. Rep. Indian Mental Hosp., Kanke, 1940.* Supdt., Govt. Printing, Bihar, Patna.
 DEY, N. C. (1943) .. *Indian Med. Gaz.*, **78**, 200.
 DHUNJIBHOY, J. E. (1938). *Ann. Rep. Indian Mental Hosp., Kanke, 1936.* Supdt., Govt. Printing, Bihar, Patna.
 DHUNJIBHOY, J. E. (1939). *Ann. Rep. Indian Mental Hosp., Kanke, 1937.* Supdt., Govt. Printing, Bihar, Patna.
Idem (1940). *Ibid.*, 1938.
Idem (1940a). *Ibid.*, 1939.
 DHYAGUDE, R. G., and KHADILKAR, V. N. (1939).
 EVANS, V. L. (1939) .. *J. Amer. Med. Assoc.*, **112**, 1249.
 FOUTS, P. J., HELMER, O. M., LEPKOVSKY, S., and JUKES, T. H. (1937).
 GOODALL, J. W. D. (1940). *Indian Med. Gaz.*, **75**, 147.
 GUPTA, S. N. (1935) .. *Ibid.*, **70**, 148.
 HEILIG, R. (1943) .. *Ibid.*, **78**, 129.
 HENDERSON, D. K., and GILLESPIE, R. D. (1940). *A Textbook of Psychiatry.* Oxford University Press, London.
 JERSILD, M. (1941) .. *Nordisk Med.*, **9**, 426. (Abstract—*Trop. Dis. Bull.*, **38**, 398.)
 JOLLIFFE, N. (1941) .. *J. Amer. Med. Assoc.*, **117**, 1496.
 LOWE, J. (1931) .. *Indian Med. Gaz.*, **66**, 491.
 MANSON-BAHR, P. (1940). *Manson's Tropical Diseases.* Cassell & Co., Ltd., London.
 MATTHEWS, R. S. (1938). *J. Amer. Med. Assoc.*, **111**, 1148.
 MILLER, R. S., and ISMAIL, A. C. (1920). *Lancet*, *ii*, 788.
 MODY, M. S. H. (1935). *Indian Med. Gaz.*, **70**, 625.
 NAPIER, L. E., and CHAUDHURI, R. N. (1943).
 PANJA, G. (1935) .. *Arch. Dermat. and Syph.*, **31**, 213.
 PATEL, N. D., and SHAH, P. A. (1942). *Indian Physician*, **1**, 78.
 PATEL, V. J., and MOTASHAW, M. D. (1942). *Ibid.*, **1**, 85.
 PETRI, S., WANSCHER, O., STUBBE TEGLEJAERG, E., and STUBBE TEGLEJAERG, H. P. (1937). *Hospitalstidende*, **80**, 817. (Abstract—*Trop. Dis. Bull.*, 1938, **35**, 73.)
 RACHMILEWITZ, M., and GLUECK, H. I. (1938). *Brit. Med. J.*, *ii*, 353.
 RAMAN, T. K. (1933) .. *Indian Med. Gaz.*, **68**, 381.
Idem (1940) .. *Indian J. Med. Res.*, **27**, 743.
 RUFFIN, J. M. (1941) .. *J. Amer. Med. Assoc.*, **117**, 1493.
 SLATER, E. (1942) .. *Brit. Med. J.*, *i*, 257.
 SMITH, D. T., RUFFING, J. M., and SMITH, S. G. (1937). *J. Amer. Med. Assoc.*, **109**, 2054.
 SPIES, T. D., AIRING, C. D., GELPERIN, J., and BEAN, W. B. (1938). *Amer. J. Med. Sci.*, **196**, 461.
 SPIES, T. D., BEAN, W. B., and ASHE, W. F. (1939). *Ann. Intern. Med.*, **12**, 1830.
Idem (1939a). *J. Amer. Med. Assoc.*, **112**, 2414.
 STRECKER, E. A., and EBAUGH, F. G. (1935). *Practical Clinical Psychiatry.* P. Blakistons Son & Co., Philadelphia.
 SYDENSTRICKER, V. P., and CLECKLEY, H. M. (1941). *Amer. J. Psychiat.*, **98**, 83.