In India rabies still remains a major public health problem and has high risk of mortality associated with it. Two types of antirabies vaccines are in current use in humans as prophylaxis against rabies, i) nervous tissue vaccine (BPL inactivated vaccine) and ii) duck embryo vaccine. Severe neuroparalytic reactions have been described following use of each type of vaccine (Toro et al 1977, Rubin et al 1973, Kaiser et al 1965, Shiraki et al 1962). These reports have described in detail neurological complications of the vaccine. However, no report has mentioned any specific psychiatric sequelae or behavioural abnormality associated with its use. In this paper we describe two cases who presented predominantly with behavioral disturbances following administration of antirabies vaccine.

Case No. 1.

R.S., 25 years old single male was admitted to the psychiatry ward with complaints of acute excitement and disorientation of one week duration. He was bitten by a stray dog on right leg two months earlier. The dog was subsequently killed by people. The patient received 14 injections of antirabies vaccine (BPL inactivated) and remained well for next one month. At this point, he developed acute abnormal behaviour characterized by marked restlessness and agitation, abusive and aggressive behaviour and urinary incontinence. He became completely disoriented to time, place and person and started running around naked. At times he was seen to be talking and muttering to himself. There was no history of any suspiciousness or paranoid behaviour. There was no history of any drug or alcohol abuse, fever or trauma. There was no past or family history of mental illness.

On examination, patient was very restless and showed grossly abnormal behaviour. He was confused and disoriented but had no neurological deficit or any evidence of raised intracranial tension. Because of the nature of symptoms, the illness was diagnosed as acute confusional state due to antirabies vaccine. Investigations of biochemical, C.S.F. radiographic and electroencephalographic parameters showed no abnormality.

In the ward, patient was put on phenothiazines but inspite of high doses of chlorpromazine upto 1200 mg/day, he did not respond satisfactorily. His symptoms waxed and waned during the day and he continued to be agitated, confused and disoriented. After two weeks of trial with drugs, it was
decided to treat him with electroconvulsive therapy. He received one modified ECT from which he recovered uneventfully. However, next evening he had two tonic-clonic seizures in quick succession which were not of focal onset. Following these seizures, detailed neurological examination showed no abnormality. Due to this development drugs and ECT were stopped and patient was put on anti-epileptic treatment, viz., diphenylhydantoin 100 mg T.I.D. and phenobarbitone 60 mg B.I.D. Haloperidol was added in doses of 15-20 mg per day to control his agitation and aggressiveness. Gradually he showed some improvement in his aggressiveness and agitation. However, he continued to be restless and mildly confused during his two months stay in the ward. Following his discharge he came for follow-up four times. He had not recovered completely and had not resumed his job as rickshaw puller even four months after the onset of psychiatric symptoms.

Case No. 2

P.D., a 23 year old married male, unskilled labourer by occupation was referred from a district hospital for the management of acute excitement. Four months earlier, patient was bitten by a stray dog on the left arm. There is no information about dog's fate subsequently. From third day of dog bite he started receiving antirabies vaccine daily. After seventh injection patient complained of fever, headache and generalized body rash and discontinued the injection. He complained of gradual diminution of vision for which no medical treatment was sought. One week prior to his contact with the clinic, the patient developed acute excitement, disinhibition and disorientation. He showed marked impairment of memory and judgement. His fundi showed bilateral optic atrophy, otherwise neurological examination was essentially normal.

There was no family or past history of mental illness. His haemogram, blood chemistry, radiological examination of chest and skull were normal. EEG showed generalized slowing. He was treated with oral phenothiazines but showed no response. Gradually his physical and mental condition deteriorated further. He remained confused and disoriented and started developing bilateral pyramidal signs. After four weeks of inpatient stay, patient's relatives took him home against medical advice. After two months of discharge, one family member visited our clinic in response to a postal enquiry and informed about further deterioration in patient's mental and physical condition. He was totally bed-ridden and had developed bed-sores. He did not communicate his needs nor did he respond to verbal stimuli. He was maintained on spoon-feeding.

Discussion

Incidence of neuroparalytic reactions of antirabies vaccine is 1.2-2.4/100,000 vaccines from nervous tissue vaccine and 0.3/100,000 from duck embryo vaccine (Park and Park, 1979). In India, at present only nervous tissue vaccine is available having 4 to 10 times more risk than duck embryo vaccine. Three main neuroparalytic reactions have been described, (i) peripheral neuritis, (ii) acute encephalomyelitis with ascending paralysis and (iii) dorsolumbar myelitis (Briggs and Brown 1960, Prussin and Katabi 1964). Toro et al (1977) have comprehensively studied neuroparalytic reactions of antirabies vaccine derived from suckling mouse brain. They found one major reaction in 4615 vaccinations, with a fatality rate of 52%. Symptoms usually occurred, on the average, after 13
doses with a latent period of 14 days. Seventy-six percent of their cases manifested symptoms pertaining to peripheral nervous system (Guillain Barre syndrome, ascending polyradiculoneuropathy) with a mortality rate of 37.5%. Central nervous system manifestations included encephalopathy, myelopathy and encephalomyelopathy. Acute encephalopathy was characterized by fever, headache, vomiting, changes in mental state, seizures, neck rigidity, stupor, coma and death. Hemiparesis, ataxia, blurred vision, papilloedema, diplopia, opthalmoplegia, hyperreflexia and evidence of brain stem herniation were other manifestations. The mechanism of these reactions is not clear. It is probably due to an immune reaction induced by nervous tissue used in the vaccine. That is why the rate of neurologic reactions to duck embryo vaccine, the first non-neural rabies vaccine for human use, is only 0.3/100,000 vaccines. However, the antigenic responses of this vaccine are poor (Toro et al 1977).

Both the cases described in this paper developed delirium or acute confusional state following antirabies vaccine. On detail history and examination, it was noted that there were no contributory factors other than the vaccine. The predominant picture in both the cases was of behavioural abnormality. Case 1 manifested symptoms after one month of last injection. Along with acute delirium, he also manifested generalised seizures when he was already on phenothiazines and ECT. This patient improved with treatment but very slowly. Case 2 showed a poorer outcome. Though he showed acute behavioural disturbances nearly four months after the last injection, the reaction had probably set in soon after the 7th dose when he complained of fever, headache and dimunition of vision. Case 1 showed no specific neurological deficit but in case 2 optic atrophy and bilateral pyramidal signs with progressive downhill course were chief complications.

There is an urgent need for increasing public awareness against rabies and making effective and stringent laws regarding stray animals to decrease mortality and morbidity associated with rabies and antirabies vaccine. A new human diploid cell rabies vaccine has been developed and has shown very good results. With its increasing use, neuroparalytic reactions will probably disappear (Aoki et al 1975, Bahnanyar et al 1976). India should also take adequate steps in preparing and using this new vaccine.

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