Opsonoclus in hyperosmolar nonketotic coma

Sir: Opsonoclus is the term used to describe rapid, irregular and chaotic eye movements that occur in all directions. This phenomenon has been associated with encephalitis, neuroblastoma, remote carcinomas, demyelinating disease, intoxications, thalamic haemorrhage, hemispheric glioblastoma, Friedrich ataxia and hydrocephalus.1 We describe a patient in hyperosmolar nonketotic coma with opsonoclus. We believe that this is the first report of opsonoclus in metabolic disorders.

A 64-year-old woman was admitted for evaluation of right upper abdominal pain and fever. On admission, neurological examination was normal. Vital signs were normal except for body temperature 38-4°C. The fever of unknown cause persisted after admission. A CT scan of the liver revealed multiple space occupying lesions. The patient was treated with antibiotics and steroid hormone. Four weeks after admission she became obtunded. Her skin was dry. The next day she was semicomatose. She showed appropriate withdrawal of the limbs to painful stimuli but was unresponsive to verbal commands. The pupils were of normal size and responded briskly to light. A striking finding was the presence of opsonoclus. Continuous, rapid and chaotic ocular saccades were noted with irregular myoclonic jerks in the face and four limbs. The eye movements were conjugate and mainly in the horizontal plane but with rotary and vertical components. Ice water caloric stimuli transiently produced conjugated deviation of both eyes toward the irrigated ear and opsonoclus stopped during the deviation. The eye movements persisted unchanged with lids open and closed. Deep tendon reflexes were hypoactive in the four limbs. Plantar responses were flexor.

Laboratory values at the time of semicomma included: serum osmolality, 410 mosmol/kg; blood glucose, 827 mg/dl; serum sodium, 172 mmol/l; serum potassium, 4.1 mmol/l; serum calcium, 11.3 mg/dl; serum chloride, 115 mmol/l; BUN, 66 mg/dl; creatinine, 1.2 mg/dl; arterial blood pH, 7.49; PaO2, 49 mm Hg; PaCO2, 45 mm Hg; SGOT, 194 IU (normal, 12 to 34 IU); SGPT, 228 IU (normal, 5 to 29 IU); alkaline phosphatase, 190 U (normal, 3 to 13 U); and serum ammonia, normal. Urine showed glucoseuria without ketones. An EEG demonstrated diffuse slowing in the delta and theta range.

Treatment with insulin and intravenous fluid replacement was instituted. The patient soon became responsive to verbal stimuli. Opsonoclus and myoclonus disappeared within 24 hours of the therapy, which brought the serum osmolality level to 362 mosmol/kg, blood glucose value to 340 mg/dl and serum sodium level to 164 mg/dl. Four days after initiation of the therapy, her mental state was almost normal and the osmolality was controlled between 310 and 340 mosmol/kg. The blood sugar was between 100 and 200 mg/dl and serum electrolytes were normal. However, renal and liver function deteriorated acutely. Seven days after initiation of the therapy, the patient became comatose and died. Postmortem examination was performed. She was found to have an adenocarcinoma in the tail of the pancreas with multiple metastasis to the liver. The microscopic and microscopic examination failed to reveal any structural lesion in the brain.

Our case with carcinoma of pancreas developed opsonoclus and unresponsiveness when the patient had nonketotic hyperglycaemic hyperosmolality. The eye movements and alteration in consciousness resolved with correction of the hyperosmolar state. No structural lesion could be demonstrated in the brain at necropsy. Although opsonoclus may occur with remote effects of carcinomas,2 its appearance is not transient as in our case. This indicates that the opsonoclus was due to the hyperosmolar nonketotic coma.

This appears to be the first report of a patient with opsonoclus in metabolic disorders. However, Keane et al2 reported opsonoclus in a case with a unilateral glioblastoma who had greatly elevated serum glucose and urea nitrogen values. The author3 also described transient opsonoclus in two cases with thalamic haemorrhage complicated by metabolic disorders. One patient had azotaemia and hypernatraemia. Another showed hyperglycaemia. These three cases suggest the possibility that the metabolic disorders might cause or play a part in opsonoclus.

The anatomic basis of opsonoclus has not yet been determined. The frequent association of opsonoclus with ataxia and occasional necropsy findings in the cerebellum support the suggestion that opsonoclus is a sign of cerebellar involvement.2 Evidence from a limited number of cases suggests, however, the involvement of brainstem in at least some cases of opsonoclus.2 Our case revealed no pathologic changes in the brain, including cerebellum and brainstem.

Many mechanisms may be responsible for opsonoclus.2 A metabolic basis seems most likely in our case. Histochemical studies of brain have been performed rarely with opsonoclus4 and hyperosmolar coma. Ross and Zeman5 carried out histochemical study in a patient with opsonoclus and bronchogenic carcinoma. The authors described definitely decreased sucrose dehydrogenase activity in the dentate nucleus. They suggested a possible relation between the opsonoclus and this biochemical change in the dentate nucleus.

Ziegels6 reported that plasma hyperosmolality diminished the same enzyme activity in the ependymal epithelium of the rat but did not investigate the activity in the dentate nucleus. Although no conclusion can be drawn from these two reports, we speculate that hyperosmolality may induce a biochemical alteration in the dentate nucleus which causes opsonoclus.

References

4 Keane JR. Transient opsonoclus with thalamic

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Successful treatment of migraine attacks with intravenous injection of aspirin

Sir: Aspirin is occasionally used for prophylaxis1 and treatment2 of migraine attacks. Ross-Lee et al2 reported that oral administration of aspirin was usually or sometimes effective in aborting acute attacks in 42 of 61 patients with migraine. They also studied plasma levels in patients treated with aspirin and indicated that there was a general correlation between better relief from pain and higher plasma aspirin levels.3

Intravenous aspirin (DL-lysine-acetylsalicylate; Venopiran®) has been available in Japan since 1983. One vial of the agent contains 497 mg of aspirin. We used the aspirin in three patients and succeeded in promptly terminating migraine attacks.

Patient 1 was a 23-year-old male with classical migraine. His grandfather and mother had recurrent headache. The patient's throbbing headache began at the age of 19. Attacks were preceded by scintillating scotoma which were severe, on the left side, lasting about 12 hours, occurring approximately once per month. Associated symptoms were nausea and vomiting. He was referred to our clinic 4 hours after an attack started because ergotamine tartrate was of little help. The pain was severe and required bed rest. One vial of the aspirin was injected. About 15 minutes after the injection, the headache disappeared completely without any side-effect.

Patient 2 was a 56-year-old female with common migraine. Her parents and brother had recurrent headache. The patient's throbbing headaches began at the age of 20, and were moderate, on the right side, lasting about 12 hours, occurring approximately once per month. Oral administration of aspirin and dimate had beneficial effect. She was referred to our clinic 2 hours after an attack started, because oral aspirin and dimate were of no help. The pain was severe and required bed rest. One vial of the aspirin was injected. About 15 minutes after the injection, the headache disappeared completely without any side-effect. Patient 3 was a 21-year-old female with common migraine. There was no family history of headache. The patient's throbbing headache began at the age of 13, were moderate, on the right side, lasting about 12 hours, occurring approximately once per month. Associated symptoms were nausea and photophobia. She was referred to our clinic 3 hours after an attack started. One vial of the aspirin was injected. About 10 minutes after the injection, the headache disappeared completely with mild light-headedness.

Aspirin is a potent inhibitor of platelet aggregation4 and prostaglandin synthesis.5 If taken in the early stage of migraine attacks, it may be of benefit by inhibiting platelet aggregation which is thought to be the initial biochemical event of the attacks.6 At a later stage in the attacks, aspirin may inhibit prostaglandin formation and help relieve pain. Prostaglandin appears to play a part in migraine headache.7 The pain of migraine attacks in our three patients disappeared within 15 minutes after the intravenous administration of aspirin. The pain persisted in Ross-Lee's patients for about 2 hours following oral administration of aspirin before there was beneficial effect. The rapid effect of our treatment was remarkable. The effect may be attributed to the prompt inhibition of prostaglandin because the severe headache was established when the agent was used.

Zuker et al8 studied effect of different concentrations of aspirin on human platelets. They indicated that over 28 μg/ml of aspirin was required to inhibit the platelet aggregation promptly. Intravenous injection of 497 mg of aspirin in humans produced high concentration in plasma of 80 μg/ml within one minute; after 5 minutes the concentration was 37 μg/ml. While peak plasma concentration of about 14 μg/ml was reached 20 minutes following oral administration of the same dose of aspirin. Cyclooxygenase is an enzyme in the synthesis of prostaglandin. Inhibition of the enzyme activity was studied in animals after intravenous and oral administration of aspirin (10 mg/kg).9 Marked inhibition was observed 5 minutes after the injection. However, the inhibition was not detected until 30 minutes after the oral administration. These findings seem to be the basis of the rapid relief.

Side-effects were slight and mainly restricted to nausea and perspiration in 5 of 75 patients who were treated with the intravenous aspirin for postoperative pain.10 Although our experience is limited, it suggests that the agent may be safe and effective in rapidly aborting migraine attacks.

References


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