EPILEPTIC EFFECTS OF INTRACISTERNAL ALUMINA CREAM IN MONKEYS*

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APPLICATION of alumina cream by disc or injection into a cerebral hemisphere is an effective method for the production of chronic experimental epilepsy in monkeys. The present study was undertaken to determine the comparative effectiveness of alumina cream injected into the cerebrospinal fluid of the cisterna magna.

METHOD

Alumina cream prepared in the laboratory was centrifuged and the sediment was injected into the cisterna magna of 5 young healthy Macaca mulatta (3.4–4.4 kg.). Approximately 0.2 to 0.5 ml. of cisternal cerebrospinal fluid was withdrawn through a 21 gauge hypodermic needle, mixed with 0.2 to 0.3 ml. of alumina cream sediment and slowly reinjected. The injection procedure was performed on animals under Nembutal anesthesia, seated with head and neck flexed. Immediately following the intracisternal injections, the monkeys were placed prone on a flat surface and allowed to recover from the effects of anesthesia without further positioning or restraints. In 1 animal (#811) a second intracisternal injection of alumina cream sediment was made 9 months after the first injection. Intracerebral multiple injections of saline had been made 20 months earlier in 1 monkey (#761). In another monkey (#701) ligation of the right middle cerebral artery had been made (2 years before), followed by contralateral multiple intracerebral Aquaphor injections (1 year before) without significant clinical residuals at the time of intracisternal injection. Clinical observations and electroencephalographic studies were made on all animals. Activation of clinical convulsions by injection of intramuscular pentamethylenetetrazole (Metrazol) was sometimes employed. The brains and spinal cords were removed for gross and histologic examination in 4 of the monkeys; the remaining animal (#812) still survives (12+ months following intracisternal injection).

RESULTS

Epileptic seizures occurred in 4 of the 5 monkeys 15 to 27 days after intracisternal injection of alumina cream. Two of the animals (#806, #761) died in status epilepticus on the 2nd and 6th days respectively following onset of their clinical seizures (Table 1). Two others (#812, #701) exhibited spontaneous epileptic seizures or could be readily provoked to seizure by prodding or intramuscular Metrazol (8–24 mg./kg.) for 9 and 10 months.

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TABLE 1

Effect of intracisternal alumina cream in Macaca mulatta

<table>
<thead>
<tr>
<th>Monkey No.</th>
<th>Previous Treatment</th>
<th>Intracisternal Alumina Cream, ml.</th>
<th>Clinical Features</th>
<th>EEG Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>806</td>
<td>—</td>
<td>.2</td>
<td>Convulsions 23 days later with status epilepticus and death in 48 hrs.</td>
<td>Status. Spike and wave pattern</td>
</tr>
<tr>
<td>812</td>
<td>—</td>
<td>.2</td>
<td>Convulsions 25 days later. Clinical activation by photic stimulation. Spontaneous seizures. Survived 12 mos. to date</td>
<td>Diffuse spiking; increased slow background</td>
</tr>
<tr>
<td>811</td>
<td>Intracisternal alumina 9 mos. prior</td>
<td>.2</td>
<td>No change Onset 16 days later: weakness, alteration of consciousness and body jerks. Sacrificed 4 days later</td>
<td>Slight slowing Slowing on 15th day</td>
</tr>
<tr>
<td>761</td>
<td>Multiple intracerebral saline inj. 21 mos. prior</td>
<td>.25</td>
<td>Convulsions 15 days later. Died in status on 20th day</td>
<td>Status</td>
</tr>
<tr>
<td>701</td>
<td>Multiple intracerebral Aquaphor (Lt.) inj. and middle cerebral ligation (Rt.) 12 mos. prior</td>
<td>.3</td>
<td>Convulsive response to i.m. Metrazol (16 mg./kg.) 29 days later and thereafter. Survived 9 mos.</td>
<td>Mild slowing</td>
</tr>
</tbody>
</table>

respectively. One animal (#811) showed no spontaneous clinical seizures or epileptic response to intramuscular Metrazol (32 mg./kg.) for 9 months. Sixteen days following a second intracisternal injection of alumina cream sediment an abrupt change in clinical status occurred, characterized by debility, staggering gait, intermittent jerks of body and extremities, and impaired level of consciousness up to time of sacrifice 4 days later.

Convulsive seizures were usually tonic-clonic generalized motor in type, although focal motor seizures with Jacksonian spread and myoclonic jerks were also noted. In one monkey (#812) seizures featured by salivation, twitching of face, turning of head to the side, chewing mouth movements and irregular jerking of the extremities occurred during the first month following onset of epileptic seizures. When seizures were frequent or the animal appeared to be in status epilepticus, monkeys appeared dazed, incoordinate and weak between clinical episodes.

The electroencephalograms in 2 monkeys (#806, #761) that died in status epilepticus, showed diffuse rapid spike, and spike and slow wave convulsive discharges of varying intensity often followed by isoelectric periods (Fig. 1). The principal changes noted in the resting patterns of the other animals was