Combined neuroleptic malignant syndrome and the central anticholinergic syndrome

The neuroleptic malignant syndrome (NMS) is an idiosyncratic reaction to neuroleptic drugs characterised by encapselopathy, rigidity, dysautonoma and hyperthermia. Dopamine receptor blockade appears central to the pathogenesis of NMS, rather than possibly the encapselopathy. Because cholinergic receptor blockade can also cause encapselopathy, the differential diagnosis of NMS includes the central anticholinergic syndrome (CAS). Neuroleptics, anticholinergics, which are used to treat Parkinsonism associated with neuroleptic use, are often used to treat the rigidity in NMS. However, anticholinergics could theoretically exacerbate the encapselopathy of NMS, possibly sparing the development of combined NMS and CAS. We report the first case of combined NMS and CAS.

After four months of lithium therapy, a 28 year old man with a severe affective disorder was given 15 mg of daily haloperidol. One week later he was brought to the emergency room confused, agitated and hallucinated. Neurological examination disclosed a fever of 101°F, cogwheel rigidity, resting tremor, and dysmetria. Serum glutamic oxaloacetic transaminase 128 IU/I (normal 5–35), serum glutamic pyruvate transaminase 65 IU/I (normal 5–30), lactic dehydrogenase 373 IU/I (normal 90–220) were all increased in concentration. His creatinine phosphokinase was 7700 IU/I (normal 25–145). All other laboratory studies, including computed tomography, were normal. The haloperidol and lithium were stopped.

Treatment included leurodopa/carbidopa 25/250, and 4 mg of intramuscular benztropine two hours later. Several hours after receiving the benzotropine, his mental status deteriorated from being agitated and confused to comatose, and his temperature increased from 101°F to 104°F. The rigidity was unchanged, but he developed urinary retention, decreased bowel sounds and large pupils, suggesting anticholinergic toxicity. Six mg of intravenous physostigmine was administered. Within minutes he was able to follow simple commands. His temperature decreased from 102°F to 99.5°F over the next hour.

The differential diagnosis of NMS includes CAS. In a recent review, Guze and Baxter state that a response to physostigmine is sufficient to differentiate between NMS and CAS. However, this case suggests that the two disorders can coexist in the same patient. Furthermore, since drugs that cause NMS have anticholinergic properties, cholinergic blockade by neuroleptic drugs may make patients more susceptible to CAS from even low doses of anticholinergic agents.

Two points are illustrated by this unusual case. First, anticholinergic agents, which do not have demonstrable efficacy in NMS are probably contraindicated in NMS. Second, when NMS should be carefully monitored for signs of anticholinergic toxicity. DAVID A BENNETT Rush Alzheimer’s Disease Center, and Department of Neurology, Rush Presbyterian-St Luke’s Medical Center, 710 S Paulina Street, Chicago, Illinois, 60612.

Intraoperative aneurysm rupture during the predissease stage

Much has been written about intracranial aneurysms which rupture as they are being dissected, probably because of the frequency of this event (24%, in one well known series). Less has been written about rupture of aneurysms during the period before the craniotomy is started and before the aneurysm is exposed, the predissease stage, discussed by Batjer and Samson. Fortunately, this is uncommon. (Yasargil 1964; Sooy 1967; John L, personal communications). Batjer and Samson encountered it four times in a series of 307 consecutive aneurysm operations and questioned whether the operations should have been aborted. I report an experience of rupture of an aneurysm before dissection.

A 59 year old right handed white woman experienced the acute onset of severe headache 48 hours before admission. She had no neurological symptoms and the only abnormal finding was neck stiffness. Computerised tomography (CT) of the head was normal but lumbar puncture disclosed grossly bloody fluid under an opening pressure of 210 cmH2O. Left carotid angiogram showed an anterior communicating artery aneurysm 3 mm in diameter pointing forward and down. During opening the patient was given 50 cc of 20% mannitol, but spinal fluid was not drained. A slow drip of nitroprusside was started. As the chiasmatic cistern was opened, and before the aneurysm was displayed, the brain herniated massively into the craniotomy opening. A hand held brain retractor was left in place to allow escape of blood. At the time of rupture the patient’s blood pressure was 100/80 mm Hg. Following an abrupt rise to 120/95 mm Hg. Immediately after rupture the patient was given 40 mg of nitroprusside and 20 mg of dexamethasone intravenously. Five minutes after rupture nitroprusside was stopped and a nitroglycerin drip (40 mg in 50 cc of 5% dextrose and water) was started. Within two minutes, that is seven minutes after rupture, the brain suddenly returned to its pre-rupture position and the BP fell to 60/40 mm Hg. Frontal lobe amputation, which had removed only 5 cc of brain, was terminated and the BP was allowed to rise slowly over the next 45 minutes. No further attempt to

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