Status Epilepticus Following Withdrawal of Allopurinol

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Allopurinol has proven to be a highly effective agent in the treatment of primary and secondary hyperuricemia. Some reports have suggested that allopurinol may have an anticonvulsant effect [1, 2] although there have been no systematic controlled trials for this indication. We report a case of convulsive status epilepticus (CSE) occurring after allopurinol withdrawal. The patient had previously been therapy resistant but demonstrated a dramatic reduction in seizure frequency with the addition of allopurinol to his previous drug regimen. Allopurinol was chosen because of previous reports [2] and its putative mechanisms of action.

A 26-year-old man with therapy-resistant seizures since age 3 was placed on allopurinol. He continued to suffer 35 nocturnal left-sided simple partial seizures with motor signs per month despite a primidone dose of 1,500 mg per day (blood level 20 μg/ml) and a simultaneous carbamazepine dose of 1,800 mg per day (blood level, 11 μg/ml). He demonstrated some clinical toxicity at these dosages. His antiepileptic drugs were therefore reduced to primidone 1,000 mg per day (blood level, 11 μg/ml) and carbamazepine 1,800 mg per day (blood level, 8 μg/ml). These levels were maintained for two months with a seizure frequency of 60 to 90 unilateral focal motor seizures per month and 3 partial seizures with secondary generalization per month. Interictal electroencephalogram demonstrated consistent focal slowing in the right frontal temporal area with frequent spikes in the posterior frontal area. Allopurinol was started as adjunctive therapy at a dose of 100 mg three times a day. In one week he became essentially seizure free. He had but one generalized seizure in the ensuing six weeks and reported only a few 2- to 3-second simple partial seizures with motor signs in the left cheek and arm. Allopurinol rapidly tapered inadvertently over a six-day period with maintenance of his other medications. On the fifth day, he developed increasingly frequent generalized seizures and subsequent CSE despite carbamazepine (blood level, 12 μg/ml), phenobarbital (blood level, 29 μg/ml), and primidone (blood level, 11 μg/ml). The CSE was controlled with diazepam and allopurinol was reinstituted. His generalized seizures stopped and he experienced a steady decline in the frequency of partial seizures during the next week. Prewithdrawal seizure control was established. This had continued for over sixteen weeks. He has had no generalized seizures and his partial seizures have consisted of brief "twitches" of the left arm and cheek.

The clinical evolution of this case suggests a distinct relationship between the withdrawal of allopurinol and the subsequent development of CSE. The patient maintained consistent dosages and blood levels of his baseline anticonvulsants throughout the time reported. Previously he had become essentially seizure free with adjunctive allopurinol therapy after years of therapy-resistant seizures. The relatively rapid withdrawal of allopurinol, we believe, induced his status epilepticus.

The induction of CSE is a well-known effect of acute anticonvulsant withdrawal in both pediatric [3] and adult populations [4]. We suggest that patients who are treated with allopurinol, especially those with previous seizure histories, be withdrawn from this agent gradually. This patient's response coupled with previous reports suggests that allopurinol may have some efficacy as an adjunctive anticonvulsant.

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Altered Glucose Metabolism in Alzheimer's Disease

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The recent study by Marcus and coworkers [1] provides potentially important evidence for reduced activity of hexokinase in Alzheimer's disease (AD), based on activities measured in microvessels isolated from postmortem brain and the rate constant (K_3) for phosphorylation by hexokinase calculated from positron emission tomographic studies. It seems premature, however, to accept the authors' claim to have "demonstrated that one of the defects in AD is the decreased ability, via decreased hexokinase activity, of the brain to utilize glucose as an energy source."

A number of previous studies have shown that homogenates prepared from postmortem AD brain exhibit reductions in the activity of various enzymes involved in glucose metabolism [e.g., 2, 3]. In one of these studies [2], however, several enzymes including hexokinase and phosphofructokinase were affected by aging or agonal state of the patient differently in the control and AD groups, making interpretation difficult, even with very large changes as were seen for phosphofructokinase. Subsequent determination of phosphofructokinase in biopsied samples of neocortex, which