Late DWI abnormality after febrile seizures

Takanashi et al. report an encephalopathy syndrome in young children heralded by a prolonged seizure, followed by additional seizures between 4 and 6 days. MRI showed no abnormality within 2 days; subcortical white matter lesions on DWI between 3 and 9 days; and cerebral atrophy after 2 weeks.

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Diffusion-weighted imaging: A crystal ball for febrile seizures?

Commentary by Nina Felice Schor, MD, PhD

The outcome of prolonged febrile seizures is excellent in 97% of patients. In those children who have a less benign outcome, the most common sequela is the development of complex partial seizures. The pathogenesis of such complex partial seizures in children with antecedent febrile seizures is thought to involve hippocampal sclerosis, cytokine-induced tissue injury, glutamatergic excitotoxicity, and, perhaps, failure of endogenous neuroprotective mechanisms.[1,2] Studies in rats induced to sustain febrile seizures demonstrate T2-weighted MRI signal hyperintensity in the limbic system, most notably the dorsal hippocampus and piriform cortex, and pathologic examination of these animals indicates that the lesion that produces these MRI changes does not involve subacute cell death.[3] Long-term studies of patients with repeated episodes of prolonged febrile seizures demonstrate reduced hippocampal volume. In patients who develop complex partial seizures after prolonged febrile seizures, the duration of the epileptic diathesis, and not the duration or occurrence of febrile seizures, correlates with the degree of hippocampal hypometabolism found on FDG-PET studies.[4] This is consistent with the absence of cell death subsequent to the initial prolonged febrile seizures induced in rats.

The patients described by Takanashi et al. are clearly different from both the patients and the animals previously described. The location of their MRI abnormalities and the type and severity of their sequelae differentiate these patients from those whose course is primarily an epileptic one. The latency to development of their MRI abnormalities perhaps relates to an indirect, chemical mechanism, such as a cytokine-mediated inflammatory response or a glutamatergic or oxidative insult or both.

The importance of this report lies in its suggestion that there is a subset of patients identifiable by diffusion-weighted MRI who present with prolonged febrile seizures and then go on to develop severe long-term neurologic sequelae. Whether the sequelae are the consequence of the seizures in this somehow biologically unusual host or, more likely, of an unusual proximate etiology responsible for both the seizures and the subsequent neurologic impairment is not yet clear.

References

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