

## Sudden Death, Epilepsy and Cerebral Cortical Heterotopia

### To the Editor:

Recently, Matschke et al<sup>1</sup> reported a case of sudden death in a 35-year-old man related to a lethal epileptic seizure. Neuropathologic examination revealed a neuronal heterotopia and a discrete lymphocytic meningitis. The authors concluded that the death was “probably” caused by the combination of the 2 lesions, leading to a lowered seizure threshold and lethal seizure.

We found this article particularly interesting because we have been recently confronted with a similar case. A 36-year-old man presented at the university hospital emergency care unit because he thought he had possibly been exposed to helium intoxication at a research laboratory. He complained of dizziness and smelling a strange strong odor. As no abnormalities were observed, he returned home. The next day, he was found dead at his residence on his bed at 2:30 PM. In the neurologic patient file, we found a refractory epilepsy with no cerebral CT scan or magnetic resonance imaging (MRI) abnormalities. A video-EEG performed 2 months before demonstrated complex partial seizures with discharges localized in right anterior temporal area. Autopsy revealed pulmonary congestion and edema, a slight brain edema, and a small quantity of bloody liquid in the trachea and the bronchi. Neuropathologic examination confirmed heterotopia lesions in this region, which is known to be a frequent cause of a refractory epilepsy. The examination also revealed cortical lamination with clusters of small ectopic pyramidal neurons in the first layer of the neocortex, isolated large pyramidal neurons in the white matter, and axonal “retraction balls” distant from the limit between cortex and the white matter. No pathologic cardiac abnormalities were observed. Toxicologic

screening revealed only a blood concentration of Gabapentin of 4.8 mg/L (therapeutic range: 10–20 mg/L).

In the literature, heterotopia is described as neuron clusters and glia that form unusual locations of gray matter in an inappropriate location. They may be single or multiple and may be found lining the ventricles<sup>1</sup> or in the deep white matter, in the subcortical white matter (our case), or in the leptomeninges. The overlying cerebral cortex can be normal or show a disruption of cortical layers or cellular organization.<sup>2</sup> The mechanism involved in the formation of the heterotopias remains uncertain, but it may be related to mutations in filamin-1.<sup>3</sup> Clinically, heterotopias may be associated with refractory epilepsy, normal findings on neurologic examination, and normal intelligence.<sup>2</sup> The mean age of epilepsy onset is late childhood to early adolescence. Complex partial seizures are the most common type, with generalized tonic-clonic seizures, simple partial seizures, and infantile spasms being less common.<sup>4</sup>

These 2 cases confirm the link between sudden death in epilepsy (SUDEP or not) and pathologic changes in the brain, as previously reported.<sup>1,3–7</sup> They underline that neuropathologic studies are necessary to study unexplained death.

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## Response to the National Association of Medical Examiners Position Paper on the Certification of Cocaine-Related Deaths

### To the Editor:

The members of the special committee appointed by NAME to review cocaine-related deaths and make recommendations for investigative guidelines are to be commended for devoting their time and professional expertise to this important subject.<sup>1</sup>

There is a critical aspect of these deaths that needs to be emphasized and clarified. While the committee mentions “supervening causes” and “a readily identifiable mechanism or disease,” these references do not take into account the most important and controversial feature of such cases, namely, physical altercations with multiple police officers.

The committee refers to “cocaine-induced excited delirium,” which is almost always the diagnosis and explana-

tion rendered by forensic pathologists and other medical experts in rejecting allegations of suffocation, mechanical or positional asphyxiation, and cardiac arrhythmia precipitated by hypoxia as alternative explanations for sudden death. I believe this is a serious and significant omission in the committee's overall discussion and specific recommendations.

Experienced forensic pathologists recognize and appreciate the fact that each and every death case involving cocaine must be reviewed and analyzed on the basis of its own specific set of facts and

circumstances, resulting in differences of opinion from one case to another as to etiology. However, the adamant refusal of some of our colleagues to even consider police misconduct and brutality as the underlying feature of such cases is most regrettable and, in my opinion, morally and ethically indefensible.

Sincerely yours,

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1. Stephens BG, Jentzen JM, Karch S, et al. National Association of Medical Examiners position paper on the certification of cocaine-related deaths. *Am J Forensic Med Pathol.* 2004;25:11-13.