G6 Gliomatosis Cerebri as a Cause of Sudden Death in a Young Woman

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After attending this presentation, attendees will be made aware of gliomatosis cerebri as a rare yet potential cause of sudden natural death.

This presentation will impact the forensic community and/or humanity by providing a well-illustrated example of an uncommon disease entity that can be a cause of sudden death that has not heretofore been well described in the forensic science case literature.

This central nervous system (CNS) neoplasm is briefly reviewed, which follows a typical premortem course, demonstrated in this case. The report is richly illustrated with premortem neuroradiographic images, postmortem images of whole and cut brain, and photomicrographs. In particular, the gross and microscopic postmortem findings provide an excellent example of the kind of subtle changes one may encounter in the postmortem neuropathologic evaluation of cases of gliomatosis cerebri. The pathogenesis of sudden death in the context of gliomatosis cerebri is discussed vis-à-vis changes in the permeability of the blood-brain barrier.

Sudden death due to undiagnosed primary intracranial neoplasm is uncommonly encountered by the forensic pathologist. In a recent review [1] of nearly 55,000 autopsies performed over a twenty year period at the Chief Medical Examiner of Maryland, undiagnosed primary CNS tumors comprised 0.02-0.05% of sudden deaths. Glial tumors, particularly astrocytomas and glioblastoma multiforme, were the most frequent tumor types in these cases, and mechanisms of death included seizure, acute hemorrhage, and herniation. In all of the reviewed cases, discrete CNS tumor masses were identified at the time of autopsy.

Gliomatosis cerebri is a rare brain neoplasm characterized macroscopically by enlargement, often subtle, of affected brain regions with preservation of native CNS architecture and absence of a discrete tumor mass. Microscopically, the tumor consists of proliferating malignant glial cells which diffusely infiltrate large areas of the CNS, involving more than two lobes [2], and often involving both supratentorial and infratentorial brain regions. The majority of patients diagnosed with gliomatosis cerebri are relatively young (median age 44 [3]), and experience insidiously progressive symptoms, which can include headaches, alteration of mental status and cognition, dysphasia, visual deficits, hemiparesis, and seizures. Often these cases present significant diagnostic challenges to clinicians, and final diagnoses are not made until postmortem examination. Invariably the mechanism of death in cases of gliomatosis cerebri is compressive sequelae from expanding intracranial mass.

This presentation describes a case of sudden death in a young woman due to previously undiagnosed gliomatosis cerebri. The patient, 40 years old, had a several month history of intermittent headaches that were gradually increasing in frequency and severity. Over this period the patient underwent multiple clinical evaluations, which were unremarkable, apart from nonspecific white matter enhancement and mass effects by magnetic resonance brain imaging. The patient's headaches were effectively controlled with mild analgesia and she remained fully active up until her death. This witnessed event occurred suddenly, shortly after the characteristic onset of episodic headache. General autopsy was unremarkable.

Neuropathologic examination showed changes consistent with acute transtentorial herniation as a mechanism of death. Subtle mass effects and white matter expansion were noted on gross and cut brain examinations. Histologic evaluation revealed malignant glial infiltration diagnostic of gliomatosis cerebri. Immunohistochemical staining of lesion tissue suggests the pathogenesis of sudden death in cases of gliomatosis cerebri may be related to catastrophic failure of the blood-brain barrier vis-à-vis its permeability regulatory function.

References:

1. Eberhart CG, et al. Decreasing incidence of sudden death due to undiagnosed primary central nervous system tumors. *Arch Pathol Lab Med*. Aug, 2001; 125: 1024-30.
2. Vates GE, et al. Gliomatosis cerebri: A review of 22 cases. *Neurosurgery*. Aug, 2003; 53(2): 261-71.
3. Chamberlin MC.Gliomatosis cerebri:Better definition, better treatment. *Neurology*. July, 2004; 63: 204-5.

Gliomatosis Cerebri, Tumor, Death

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