



Pathology Biology Section – 2011

G60 Sudden, Unexpected Death Due to Glioblastoma: Three Fatal Cases

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The goal of this presentation is to present three cases of sudden, unexpected death due to glioblastoma, with different brain localization and expression.

This presentation will impact the forensic science community by discussing how a complete methodological forensic approach by means of autopsy, histological and immunohistochemical examinations let us to conclude for an acute central dysregulation caused by glioblastoma and relative complication with rapid increase of intracranial pressure as cause of death.

Glioblastoma is the most common malignant primary brain neoplasm, representing about 12-20% of all intracranial tumors and accounting for about 50-60% of all astrocytic gliomas. In the most European and North American countries, the incidence is approximately 2-3 new cases per 100,000 people per year. The incidence of sudden death due to undiagnosed primary intracranial tumor is low in forensic autopsy and is an uncommon event. In fact only 12% of all cases of sudden unexpected death due to primary intracranial tumors are due to glioblastomas.

Three cases of sudden unexpected death due to glioblastoma according to WHO grade IV are reported.

Case 1: a 43-year-old Polish man was found dead in a slope near the track of the railway. Death scene investigation was unremarkable. A complete autopsy was performed 48 hours after death. The external examination revealed only same abrasions and bruises on the face, and the upper and lower limbs. The internal examination revealed polyvisceral stasis, heavy lungs and reddish colored foam on trachea and the main bronchi. The skull was entire. The examination of the brain (cm 21x16x6, g 1630) after fixation in buffered formalin revealed a cerebral edema and an increase in volume of the left frontal lobe. On coronal sections, the cerebral hemispheres were asymmetrical with deviation of midline structures from left toward right. In the left frontal lobe a spherical mass (cm 3.5x3x1.5), with variegated appearance and contained regions of necrosis and hemorrhage was found. The blood alcohol concentration was 0.8 g/l.

Case 2: a 79-year-old Caucasian man, with a history of ischemic heart disease and hypertension, was brought to the hospital in the neurological unit for symptoms such as confusion, slackening, sleepiness, and tremor of the upper limbs start few days before. The brain CT scanner examination shows a large hypodense mass in the left

temporal lobe with massive oedema and compression phenomena on occipital and temporal lobe and midline shift. The patient was then referred for neurosurgical consultation, but the day before surgery he suddenly died. General autopsy performed 48 hours after death was unremarkable. The brain weighed 1600 g and measured (cm 22x16x6.5) showed diffusely swollen cerebral hemispheres and an increase in volume of the left temporal lobe. There was no herniation of the temporal lobe unci or cerebellar tonsils. On coronal section, after fixation, the left temporal lobe showed a large mass lesion, which measured 3x2.5x2.2, hemorrhagic and surrounded by necrotic and oedematous tissue.

Case 3: a 71-year-old-Caucasian man, with a past history of hyposthenia of the right arm, cervical spine surgery, chronic kidney disease, and hepatic steatosis. During his detention, showed headache, confusional state, and difficulty in walking therefore he was transferred to the local hospital. The neurological examination revealed poor general condition, marked weight loss, ataxia and ideomotor slowing, depressive syndrome, apathy, fatigue, and lack of initiative. The laboratory examination of blood and liquor was negative for infection- inflammatory disease. To diagnose a multi-infarct dementia the patient was scheduled for TC and magnetic resonance imaging of the brain and the entire spine, but suddenly died prior to the imaging. At autopsy a moderate pulmonary edema and polyvisceral stasis were observed. The brain weighed 1550 g and showed massive edema. A spherical gelatinous solid mass, measuring 1 cm in diameter was attached in the right medulla. On coronal sections, the right temporal lobe showed a reddish-rusty mass lesion, measuring 1x2 cm and the third ventricle was compressed and dislocated.

The etiopathogenetic definition was outlined by histological examinations performed on brain tissue samples using haematoxylin- eosin (H&E) and Perl's and revealed the presence of diffuse and marked cytotoxic and vasogenic brain edema, and in samples taken from left frontal lobe (case I), left temporal lobe (case II), right medulla and temporal lobe (case III) foci of central necrosis surrounded by neoplastic cells with nuclear pleomorphism, pseudopalisading, multinucleated cells ("giant cells glioblastomas") and vascular proliferation. Areas of extensive haemorrhage near tumor cells were also observed.

The immunohistochemical examination of the brain specimens revealed a positive reaction for antibodies anti-GFAP (glial fibrillary acidic protein), CD68, vimentin and S-100; NSE (neuron-specific enolase), smooth muscle actin, CD34, cytokeratins MNF 116, EMA (epithelial membrane antigen),



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synaptophysin, HMB45 (Human Melanoma Black) were negative. The positive reaction for GFAP was confirmed by Western blotting. The other organs showed signs of central dysregulation (pulmonary oedema).

The death was attributed in the first and second case to brain edema and massive hemorrhage into the glioblastoma from arrosion of vessels, with an increase in intracranial pressure and compression of cerebrospinal fluid circulation, whereas in the third case death can be explained by distortion and compression of the medulla by the tumor with consequent acute central dysregulation due to glioblastoma corresponding to WHO grade IV.

Glioblastoma, Sudden Death, Immunohistochemistry Stains and Western Blotting