



G136 A Rare Case of a Large and Bilateral Acute Cerebral Necrosis Following a Very Low Total Dose of Conventional Radiotherapy Treatment for Anaplastic Oligoastrocytoma

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The goal of this presentation is to examine the histopathological aspects of an acute cerebral radionecrosis following conventional radiotherapy at subtherapeutic dosages associated with adjuvant chemotherapy. The adoption of adjuvant chemotherapy may therefore increase the incidence of radionecrosis due to its radiosensitization effect.

This presentation will impact the forensic science community by showing the necessity of a complete methodological forensic approach by means of autopsy, histological, and immunohistochemical examinations to diagnose an unusual early cerebral radionecrosis, due to a very low dosage of conventional radiotherapy and to differentiate from tumor recurrence.

Malignant gliomas are the most common primary brain tumors, and glioblastoma multiforme and anaplastic oligoastrocytoma comprise the greatest part of these. The actual standard protocol of treatment for these patients consists in maximal safe resection followed by radiotherapy and concomitant and adjuvant chemotherapy (temozolomide). However, even with treatment, outcomes are poor. The median survival for patients with glioblastoma multiforme is 10 – 12 months, whereas two-year survival rates for glioblastoma multiforme and anaplastic astrocytoma are only 9% and 44%, respectively.

Radiation doses in the region of 46 – 50 Gy are as efficacious as higher doses in the treatment of low-grade glioma, but doses of 60 Gy provide better outcomes for high-grade gliomas and are commonly prescribed for these tumors.

Radiation therapy for the brain, however, may often result in several episodes of acute and chronic damage, even if the total dose of radiation appears to be the most important risk factor for subsequent necrosis. Three distinct periods of radiation effect may be identified: acute (during the radiation itself), early delayed (at around 1.5 months after the radiation), and late delayed (between 4.7 and 7.6 months and for more than two years). More simply, radiation-induced effects are considered late effects if they occur after 90 days from the first day of radiotherapy. However, necrosis has been reported as early as three months and as late as 47 years after radiotherapy.

Reported is a rare case of large and bilateral acute cerebral necrosis following a very low total dose of conventional radiotherapy.

A 56-year-old female first presented epileptic attack associated with aphasia and paralysis. Magnetic Resonance (MR) imaging showed a lesion of 2cm in diameter in the left temporal lobe, without perilesional edema and gadolinium enhancement after perfusion. The tumor was totally excised via a left fronto-temporal approach. The histological examination of the mass confirmed the typical Anaplastic Oligoastrocytoma. Following the operation, a treatment with a total dose of 60 Gy conventional radiotherapy was programmed, in 1.80 Gy daily fractions, associated with steroids (desamethasone, 8mg each day) and chemotherapy (temozolomide, 100mg each day). After the twentieth dose (a total dose of 36 Gy), she presented an epileptic attack associated with fever, tremor, confusion, aphasia, and recurrent focal deficit. MR imaging showed a mass with edema in the fronto-temporal lobes which suggested radiation-induced necrosis, without enhancement by gadolinium. In the following month, the woman died and the autopsy was effectuated.

The external examination was unremarkable. The examination of the brain, regular in size and weight, after fixation in buffered formalin revealed diffusely swollen cerebral hemispheres. On coronal sections, the cerebral frontal and temporal lobes revealed regions of necrosis and cortical hemorrhages.

The etiopathogenetic definition was outlined by histological examinations performed on brain tissue samples using Haematoxylin-Eosin (H&E) and Masson and it revealed the presence of diffuse and marked cytotoxic and vasogenic brain edema, and in samples taken from right and left fronto-temporal lobes foci of central necrosis and extensive cortical hemorrhages, marked stasis, and cerebral vessels surrounded by inflammatory cells, above all granulocytes. The immunohistochemical examination of the brain specimens was also conducted for antibodies anti-GFAP (glial fibrillary acidic protein), CD68, CD15, TNF- α , fibrinogen, HSP, cytokeratins, and TUNEL. The other organs showed signs of central dysregulation (pulmonary edema).

The exitus was attributed to an acute central dysregulation caused by edema and necrosis radiation-induced and relative complication with rapid increase of intracranial pressure.

In conclusion, according to scientific literature, the cerebral necrosis could appear in areas radiated to less than 50 Gy, but with daily fractions of 2.25 Gy. In this case, the cerebral necrosis was very large and it was caused by inferior dosage (36 Gy), so it corroborates that the adjuvant chemotherapy, temozolomide in particular, significantly increases the risk of cerebral necrosis by approximately fivefold. A review of the literature is presented



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