Late Neurological Sequelae due to Brainstem Irradiation for an Assumed Glioma

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Abstract

Purpose: There is ongoing discussion whether radiotherapy might be beneficial in the treatment of intracranial cavernomas, however long-term sequelae due to brainstem irradiation may exist.

Case Report: The case of a 72-year-old female is reported who received radiotherapy in the pre-MRI era due to a suspected intra-axial pontine lesion. Later on she developed severe trigeminal neuropathy and an MRI was performed 27 years after irradiation of the brainstem. On these images a large cavernous malformation with signs of multiple haemorrhages instead of the pontine glioma was seen accompanied by a substantial atrophy of brainstem structures.

Conclusion: This case impressively demonstrates the long-term outcome of brainstem irradiation and reflects that cavernomas do not respond to radiotherapy.

Key Words: brainstem cavernoma, radiotherapy, complications, trigeminal neuropathy

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INTRODUCTION

Radio-oncologic treatment protocols are intended to avoid irradiation of brainstem structures as they are known to cause several early and delayed neurological deficits[1,2]. Radiation therapy of the brainstem itself in cases of intra-axial tumours is planned with reduced dosages to diminish these complications[3,4]. We report about a patient who received a radiation dosage for a presumed brainstem glioma in the pre-MRI era where the differential diagnosis of brainstem lesions was limited. As a very late sequelae, severe trigeminal neuropathy occurred and treatment with balloon-compression of the gasserian ganglion was required.

CASE REPORT

This 72-year-old female patient first presented to the neurological department in 1977 with diffuse persisting headaches and dizziness. Subsequently several cranial nerve deficits, brainstem symptoms and cerebellar signs occurred. Due to the diffuse symptoms and an initially acquired regular computed tomography scan, the patient was diagnosed and treated for multiple sclerosis. The

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symptoms improved, but in 1978 and 1981 again clinical deterioration with a spastic left-sided hemiparesis occurred. This time the CT-scan revealed a large brainstem lesion, with peripheral enhancement of contrast-agents (Figure 1A-C). An angiography showed signs of brainstem expansion, no neo-vascularisation in relation to the tumour, suggesting a pontine glioma.

The patient received palliative radiation therapy in 1978 with 60 Gy applied by an 8 MV linear accelerator at 1.0-2.0 Gy per fraction. The final 20 Gy were applied on a focused field. Some brainstem related symptoms improved over the years but the patient remained with several deficits including a spastic hemiparesis.

She survived but twenty years after radiotherapy she developed a severe right-sided drug-resistant trigeminal neuropathy. The patients described to experience persistent burning sensations, triggered by several conditions. For the first time an MRI was performed in 2005 demonstrating a large pontine cavernoma with signs of several previous but no recent haemorrhages (Figure 1D-E). No signs of brainstem oedema or extra-axial lesions could be seen, however a marked atrophy of the irradiated brainstem and cerebellum was striking. Comparing the MRI with the CT scans from 1978, the cavernoma was situated exactly at the site of the suggested brainstem glioma. As the limited medical condition of the patient did not allow a trigeminal nucleotractotomy (Karnofsky-Score <60), she underwent balloon-compression of the trigeminal nerve in local anaesthesia and was pain free after treatment.

DISCUSSION

The success of radiation oncology has led to longer patient survival. This provides a greater opportunity for radiation injuries of the peripheral and/or cranial nerves to develop. With a high frequency of radiotherapy related sequelae in long-term survivors of brainstem gliomas (50%) white matter changes consistent with leukoencephalopathy, cerebral atrophy, multiple teleangiectasia, diffuse microhaemorrhages and dystrophic calcification in the radiation field have been shown[2,5]. Radiation-induced neuropathy is an uncommon but serious complication of radiotherapy. Treatment protocols in the beginning of radiosurgery (before 1994) for vestibular schwannoma describe an incidence of facial and trigeminal neuropathy in 29% due to a maximum dose to the brainstem of more than 12.5 Gy[6,7]. Although the patient did not receive radiosurgery but radiotherapy, a cumulative dose of 60 Gy to the brainstem did exceed the limits set recently[18]. This may cause delayed motor and sensitive impairment associated with severe treatment-resistant pain. However, as radiosurgery and radiotherapy treatment plans evolved over time, incidences of facial and trigeminal neuropathies decreased markedly from the investigated time period before 1994 and since then (5% and 2% respectively)[6]. However patients having had stereotactic radiotherapy for trigeminal neuralgia therefore should be followed carefully for possible delayed ischemic events secondary to the radiation-induced vascular injury as radiation exposure can also result in vascular injury presenting as focal atheromatous changes within skull-based arteries[9]. If we presume the lesion in the presented case may have been a self-limiting inflammatory process or a radiosensitive tumour, instead of a cavernoma in the beginning, the cavernoma might then have been induced by the radiation therapy as it is well described in the literature[9].

Various therapeutic approaches to control radiation-induced neuropathy-pain have been reported, all demonstrating poor outcomes. Trigeminal nucleotractotomy and dorsal root entry zone lesions in cervical spinal cord have been shown to be effective for the treatment of pain associated with actinic peripheral neuropathy[10,11]. Thermocoagulation or balloon-compression of the gasserian ganglion are useful as well, if the condition of the patient does not permit more invasive treatment forms[12,13].

The patient presented here "survived" an irradiated brainstem cavernoma but experienced repeated haemorrhages with clinical deterioration and development of a severe trigeminal neuropathy. With this report we want to emphasize the potential late-term sequelae due to radiotherapy of the brainstem and near-by structures. Treating benign pathologies like trigeminal neuralgia, vestibular schwannoma or related lesions, the initial morbidity might be low compared to microsurgical approaches[14]. But one has to bear in mind that with a normal life expectancy of these patients, a clinically devastating long-term morbidity can develop. Secondly radiotherapy or radiosurgery does not apply for cavernous

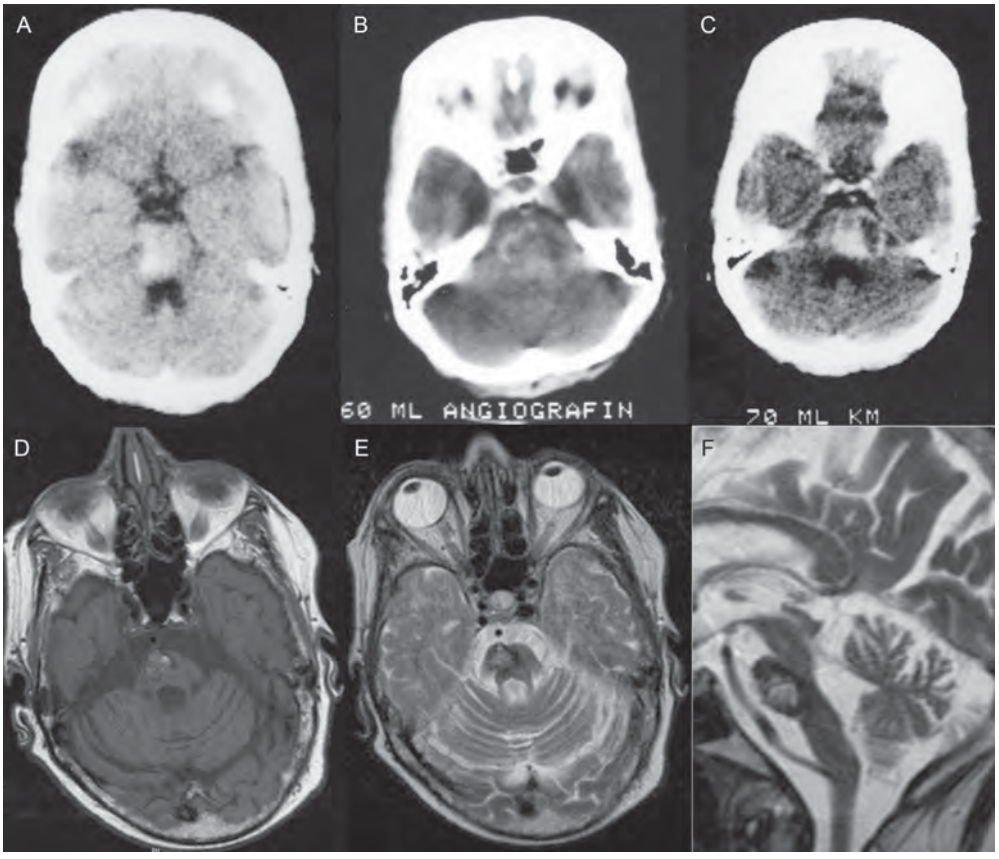

Figure 1. Axial CT-scan of the patient in 1978 without (A) and with contrast-enhancement (B). Repeated CT-scan in 1981 (C). Axial T1-, and T2-weighted (D, E) MRI scan in 2005 showing the brainstem cavernoma. Note the marked atrophy of the irradiated field on the sagittal T2-image (F).

malformations although some reports suggest a positive value[15-17]. This case clearly demonstrates that despite radiation therapy of the assumed brainstem cavernoma repeated haemorrhages occurred, leading to subsequent neurological deterioration of the patient. Thirdly MRI again proved evidence of the superiority in the differential diagnosis of brainstem lesions especially in cavernous hemangiomas, where adapted sequences can be used[18]. As radiation therapy in sensitive areas like the brainstem improved markedly and lessons learned from previously encountered severe events, the new protocols have been adopted by the radiation oncology society leading to excellent long-term results in patients[19].

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