

CEREBRAL RADIONECROSIS WITH CYSTIC DEGENERATION FOLLOWING RADIOTHERAPY FOR NASAL CAVITY SQUAMOUS CELL CARCINOMA: A CASE REPORT

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A 31-year-old man with nasal cavity squamous cell carcinoma was treated in our hospital with two courses of radiotherapy (120 Gy total dose) followed by surgical tumor resection. Three years after the last irradiation, he developed seizures as well as changes in behavior and consciousness. Medical therapy with diphenylhydantoin (Dilantin[®]) terminated the seizures. Dysphagia, unsteady gait, and right-side limb weakness developed 37 months after the onset of seizures. Magnetic resonance imaging showed a large, cystic mass in the left temporal lobe with left to right midline shift. Following craniotomy with decompression of the cystic mass, the patient improved clinically. No malignant cells were found in the specimen. No further progression of neurologic symptoms was noted after a 1-year follow-up. Cerebral radionecrosis is an uncommon late complication of radiotherapy and needs to be differentiated from tumor recurrence or metastasis if the irradiation field covers the cerebral region in patients with head and neck malignancies.

Key Words: radionecrosis, brain
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Malignant tumors of the sinonasal tract constitute less than 1% of all malignancies and about 3% of those arising in the upper respiratory tract [1]. Treatment includes surgical resection, radiotherapy, or a combination of both. Radiotherapy is not without morbidity, and damage to the neighboring structures may lead to long-term complications. Delayed radionecrosis is rare and needs to be differentiated from tumor metastasis or recurrence. Once malignant disease has been excluded, initial conservative treatment with corticosteroids has been suggested in many articles. We report a rare case of cerebral cystic radionecrosis following radiotherapy for sinonasal tract malignancy.

CASE PRESENTATION

In June 1995, a 31-year-old male presented with the complaints of painful nasal congestion, especially on the left side, for 6 months, and blood-tinged sputum. A nasal mass involving the anterior and middle parts of the nasal septum and left inferior turbinate was biopsied at a local hospital. Pathology was positive for poorly differentiated squamous cell carcinoma, so the patient was referred to our hospital for further evaluation and treatment. Treatment was initiated with a total of 60 Gy of radiotherapy administered from 3 July to 25 August 1995. A small portion of normal brain was included within the two radiation portals (anterior and left side). The tumor had a partial response to radiation. The nasal septum and left inferior turbinate were resected in September 1995.

Six months after surgery, outpatient biopsy demonstrated recurrent tumor. The patient received another 60 Gy

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of radiotherapy followed by lateral rhinotomy with Denker's operation (medial maxillectomy). Regular follow-up was unremarkable, without evidence of recurrent disease, until November 1999.

At this time, there was sudden onset of seizures, behavioral changes, and consciousness disturbances. Magnetic resonance imaging (MRI) demonstrated bilateral digitiform lesions in the frontal and temporal lobes, especially in the left temporal lobe (Figure 1). Cerebral lesions were thought to be secondary to radionecrosis. The patient was treated with diphenylhydantoin (Dilantin®; Parke-Davis Corp, Taoyuan, Taiwan) and ginkgo biloba extract (Cerenin®; Dr Willmar Schwabe Co, Karlsruhe, Germany). For the next 3 years during routine follow-up examinations, the patient had only minor complaints of memory impairment without any recurrence of seizures.

In December 2002, 37 months later, the patient developed an unsteady gait with right-side weakness and experienced memory loss and difficulties in speaking. MRI showed a large cystic left temporal lobe mass with midline shift from left to right (Figure 2). During craniotomy with decompression of the cystic mass, yellowish fluid was found within the cystic lesion. Pathology showed hemosiderin-laden macrophages associated with reactive glial cells and focal lymphoid tissue aggregated around sclerotic vessels. No tumor cells were found. Neurologic symptoms subsided after surgery and no further progression of neurologic symptoms was seen after 1 year of follow-up.

DISCUSSION

Cerebral radionecrosis is a late complication of radiotherapy, and the reported latency period from the end of radiotherapy

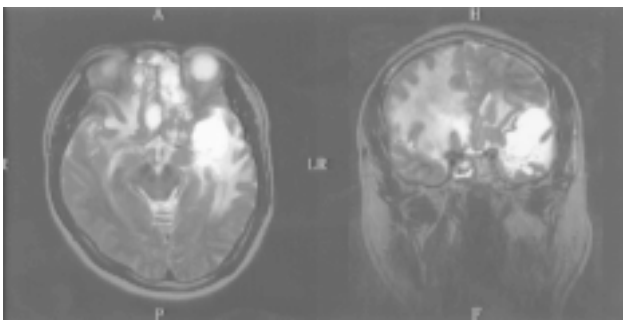


Figure 1. Magnetic resonance image shows a digitiform hyperintense lesion at bilateral frontotemporal lobes with interposed irregular enhancement after contrast administration.

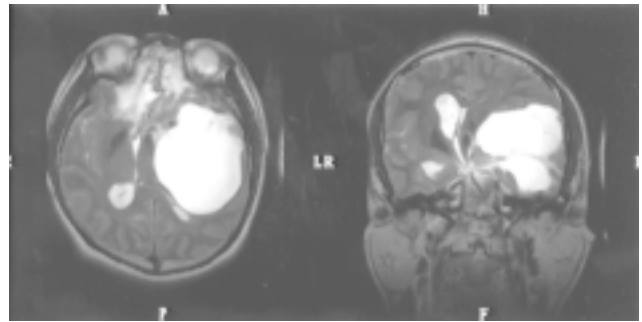


Figure 2. Magnetic resonance image 37 months later. The brain parenchyma, left thalamus, and basal ganglion are displaced to the right, and the left lateral ventricle is severely compressed.

to the time of diagnosis ranges from 3 months to 19 years in extracranial malignancies [2]. Clinical symptoms vary and may include major symptoms such as consciousness changes and seizures, as well as minor complaints of vertigo, headache, or memory impairment. If a patient has neurologic or psychiatric symptoms following radiation, delayed radiation encephalopathy or brain metastases should be considered. Several authors have emphasized that, if left untreated, delayed cerebral radionecrosis is usually irreversible, progressive, and often fatal [3,4].

In our case, a radiotherapist administered a total of 120 Gy within a 12-month period in two divided 60 Gy doses, each delivered in 30 fractions over 42 days. Our patient received a much higher radiation dose than is normally administered because of the need for irradiation for tumor recurrence. The radiotherapy portal lower limit for the nasal cavity was set just below the level of the zygoma and the upper limit could have included a portion of the temporal lobe.

A 60 Gy dose delivered in 1.8–2.0 Gy fractions represents the upper limit of the safe dose of irradiation to brain tissue [5]. If the dose exceeds the limit, the incidence of radionecrosis increases. In 1984, Glass et al reported nine cases of cerebral radionecrosis with extracranial malignancies and reviewed another 65 cases in the literature [6]. Only 14 sinonasal malignancies developed cerebral radionecrosis, and few cases have been reported otherwise. Out of a total of 74 cases of cerebral radionecrosis, 36 of 68 (53%) reviewed cases received a radiation dose of more than 60 Gy; the remaining six cases were not included as the dosage was unknown. Hawkins et al reported their results with primary and adjuvant radiotherapy for nasal cavity carcinoma [7]. Twenty-three of 56 (41%) cases received more than 65 Gy; however, no patient developed cerebral radionecrosis. The exact incidence of cerebral radionecrosis

in extracranial malignancies is not clear because it occurs sporadically and depends on tumor location and type.

Lee et al reported the incidence of cerebral radionecrosis following nasopharyngeal carcinoma as 1.03% in a large series [8]. In another study of 1,008 consecutive patients with nasopharyngeal carcinoma who were treated with radiotherapy, 74 patients had a clinical diagnosis of temporal lobe radionecrosis. Analysis of irradiation regimens led them to conclude that fractional dose was the most important factor causing late radiation necrosis, and that prolonging the treatment time offered little protective effect [9]. Lee et al estimated that 64 Gy at the conventional fractional dose of 2 Gy daily would result in a 5% necrotic rate after 10 years [9].

The most commonly accepted etiology of cerebral radionecrosis is radiation-induced endothelial cell damage followed by long-term ischemic changes in affected cerebral tissue [10]. The gold standard for diagnosis of radiation necrosis is pathologic proof by surgical exploration or autopsy. However, a clinical diagnosis can be made without pathology, and imaging findings of radionecrosis have been discussed in the literature. Computed tomography (CT) can show digitiform or round hypodense lesions. On MRI images, radionecrosis manifests as low signal areas in T1-weighted and high-signal areas in T2-weighted images, with irregular or cystic shapes. MRI is superior to CT in sensitivity, and lesions are best shown on T2-weighted scans [11]. Differentiation of radionecrosis from tumor is difficult based on CT or MRI findings alone because both lesions have similar imaging characteristics and can show contrast enhancement. Scintigraphic studies such as ¹⁸F-fluorodeoxyglucose positron emission tomography (FDG-PET) and ²⁰¹Tl chloride single-photon emission CT (SPECT) can distinguish tumor from radionecrosis, and both techniques are sensitive to tumor recurrence [12]. There are no significant differences in sensitivity or specificity for FDG-PET and ²⁰¹Tl SPECT, and either can provide important diagnostic information.

MRI findings in our patient in November 1999 showed a digitiform hyperintense lesion in bilateral frontotemporal lobes, with interposed irregular enhancement after contrast administration, and these findings need to be differentiated from tumor recurrence. In this case, there was no evidence of metastatic disease elsewhere in the body or in the brain. Fiberscopic examination with repeat nasal cavity biopsy was negative for tumor. All changes in the base of the skull and the nasal cavity seen on imaging studies were consistent with postsurgical changes without osseous destruction or other obvious evidence of recurrent neoplasm.

Although treatment of cerebral radionecrosis includes surgical exploration, such as necrotomy and cerebral lobectomy, medical therapy with corticosteroids is more often recommended in the recent literature. Studies have reported using 4–16 mg of dexamethasone daily for 4 to 6 weeks, and gradually tapering the dose over the next 2 months [8,13]. The changes of radionecrosis are irreversible, although some effects caused by pressure or edema can be relieved by surgical decompression or corticosteroid treatment. In our case, we found that the disease progressed slowly over several years without corticosteroid treatment. However, long-term use of corticosteroids for cerebral radionecrosis is not without significant risks. Lee et al reported that 44% of cerebral radionecrosis patients on corticosteroids experienced associated side effects, and that the mortality rate was 8% due to uncontrolled sepsis [8]. In addition, the use of corticosteroids is a predisposing factor for brain abscess formation in patients with cerebral necrotic tissue [14]. Lee et al also used MRI to survey temporal lobe radionecrosis in patients with nasopharyngeal carcinoma. They assumed that irregular lesions consisted mainly of reactive white matter edema, and that rounded lesions were mainly central liquefactive necrosis with surrounding gliosis [11]. Only patients with marked reactive edema and minimal liquefactive necrosis were likely to show a durable objective response to conservative treatment with corticosteroids [11]. In our experience, an obviously liquefactive lesion with mass effect should be treated with surgical intent, followed by postoperative corticosteroids. Mildly symptomatic or asymptomatic patients can be initially treated with corticosteroids.

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鼻腔上皮癌放射治療後之 腦部放射性壞死併囊狀退化 — 病例報告

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一位 31 歲鼻腔上皮癌男性病患於本院接受 2 個療程放射線治療之後接受手術切除腫瘤。於最後一次照射 3 年後，病患發生癲癇，意識以及行為改變。經由核磁共振造影診斷為放射線腦部壞死。以 diphenylhydantoin (Dilantin[®]) 治療終止了癲癇發作。37 個月後，病患產生吞嚥困難，步態不穩以及右側肢體麻痺等症狀。再一次核磁共振造影顯示左側顳葉有一巨大囊狀腫塊，腦部中線向右側偏移。經由開顳手術對腫塊減壓之後，病患臨床症狀改善。病理檢驗並無發現惡性細胞。病患經追蹤 1 年無神經學症狀之惡化。放射線腦部壞死是放射治療後少見的晚期併發症，必須與腫瘤復發或轉移做鑑別診斷。在頭頸癌病患如果放射治療有包含腦部區域，臨床醫師必須要小心是否有此併發症的產生。

關鍵詞：放射性壞死，腦

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