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CLINICAL REPORT

Late Temporal Lobe Extensive Osteoradionecrosis Post Radiation for Nasopharyngeal Carcinoma: Case Series

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Abstract Osteoradionecrosis is one of the most serious complications of radiotherapy for nasopharyngeal carcinoma. We report three cases of osteoradionecrosis in temporal lobe who presented differently few years after completion of radiotherapy. Cranial magnetic resonance image showed lesions in temporal lobe either unilateral or bilateral with mass effect. One of the cases even showed disease progression few years after the initial diagnosis of osteoradionecrosis. Diagnosis of osteoradionecrosis for all three patients was confirmed by biopsy.

Keywords Osteoradionecrosis · Radiotherapy · Nasopharyngeal carcinoma · Complication

Introduction

Nasopharyngeal carcinoma is a common malignancy in the Asian Chinese population. Radiotherapy is the most effective means of treatment for nasopharyngeal carcinoma. A series of complication including osteoradionecrosis and non osteitic complications may follow radiotherapy. Clinical presentation may differ from asymptomatic to classical temporal lobe neurological deficits. In cases where patient presented with vague symptoms or even asymptomatic, diagnosis was often delayed. Brain abscess may develop which eventually leads to brain herniation. Tumor recurrence and cerebral metastases need to be ruled out in these cases as it affects treatment plan.

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Case Report

Case 1

A 56 years old gentleman with nasopharyngeal carcinoma diagnosed in 2010, completed one course of radiotherapy and surgery in June 2014 for initial and recurrent treatment. He presented again in November 2014 with sudden nominal aphasia, memory loss and headache. MRI brain showed an extensive heterogeneous enhancing mass 3.8 × 2.6 cm over left fronto-parieto-temporal lobe with perilesional edema and effacement of left cerebral hemisphere, suggestive of radiation necrosis (Figs. 1, 2). Nasopharyngeal spaces were cleared of tumor. Tablet dexamethasone 4 mg QID was commenced and craniotomy with excision of tumor was performed by neurosurgical team. Intraoperatively, there was evidence of tumor 2 × 2 cm with firm gliotic appearing tissue. Nasoendoscopic examination revealed clear bilateral fossa of rosenmuller with no suspicious lesion seen. Histopathology examination of brain tissue showed no malignancy but with fragments of brain tissue composed of glial cell and large areas of necrosis with prominent hyalinised blood vessels and infiltrated by macrophages and

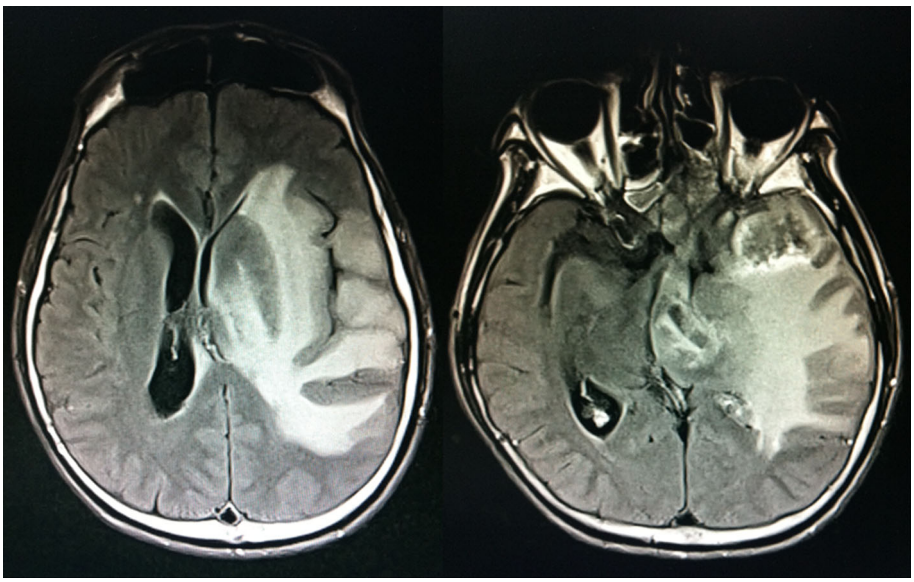

Fig. 1 Axial view of magnetic resonance of brain showing extensive deep white matter edema involving the left fronto–parieto–temporal lobe with mass effect

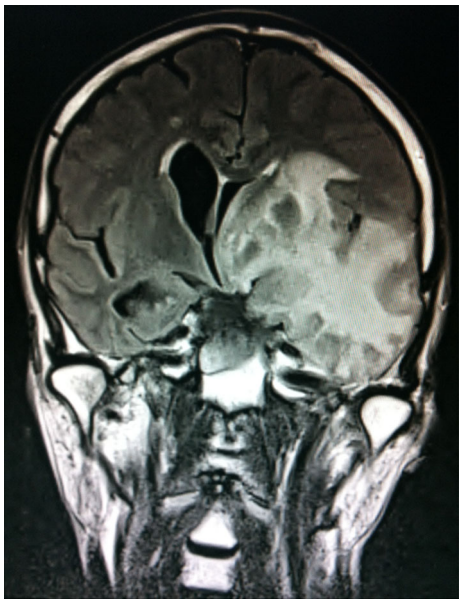

Fig. 2 Coronal view of MRI showing extensive enhancing lesion over left temporal lobe

some lymphocytes. His symptoms improved after commencement of tablet dexamethasone where he became more coherent and alert. During follow up 1 month post craniotomy, there was no evidence of neurological deficit and he was planned for a short course of oral dexamethasone if the neurological symptoms recurred.

Case 2

A 63 years old gentleman diagnosed with nasopharyngeal carcinoma in 2006, completed concurrent chemo radiation in the same year. He presented in early 2013 with 3 weeks history of severe headache, change of behavior, poor memory and altered consciousness. On physical examination, there was no evidence of neurological deficit. MRI brain however showed cystic lesion with perilesional edema of right temporal lobe. He was commenced on oral Dexamethasone 4 mg TDS and proceeded with right craniotomy for excision of tumor. Intraoperatively, there was effacement of right temporal lobe sulci with hemoserous cyst fluid and pale, yellowish, necrotic brain tissue. Diagnosis of osteoradionecrosis was made based on histopathology result. He was discharged with oral Phenytoin 100 mg OD as prophylaxis for seizures. During follow up, there was no history of fitting and neurological deficits except reduced memory. CT brain 1 week post surgery showed remnant of cystic lesion 3 $\times$3 cm at right temporal lobe with haemorrhagic component at the wall (Fig. 3).

He presented again in September 2014 with 1 day history of vomiting, headache and sudden fainting episode. He appeared disorientated but no other evidence of neurological deficits. Repeated MRI revealed new large enhancing cystic lesion measuring 6.8 $\times$ 4.8 $\times$ 5.3 cm at left temporoparietal lobe with mass effect. The right temporal region looked normal. Emergency craniotomy was performed. Xanthochromic cystic content with areas of septation and necrotic appearing brain tissue was noted. Histopathological examinations showed radiation changes of brain tissue with no evidence of malignancy. Postoperatively, he regained full conscious level and was discharged well. Repeated CT brain post craniotomy showed significant reduction in size of hypodensity at left temporal lobe. Symptomatically the patient felt better during his regular follow-up (Fig. 4).

Case 3

A 60 years old gentleman presented in December 2014 with sudden onset of headache, neck pain and vomiting. He also had personality change, emotional labiality and short term memory loss. He had intermittent expressive dysphasia but no other neurological deficits (Table 1). He had nasopharyngeal carcinoma 13 years ago and underwent radiotherapy in 2001 and 2005 for local recurrence. CT brain revealed large contrast enhancing mass lesion in the right temporal lobe and was treated as meningitis initially with antibiotic and steroids at a private hospital. MRI brain showed enhancing lobulated mass with soap bubble appearance and multiloculated cystic appearance with fluid level within the right temporal lobe. In the left temporal lobe, there is another fairly well defined cystic lesion with adjacent white matter edema. On magnetic resonance perfusion study, there was no area of increased blood volume seen within lesion at both the temporal lobes (Figs. 5, 6). Burr hole with biopsy on right temporal lobe was performed and histopathology examination confirmed radionecrosis changes with no malignancy (Fig. 7). He was later discharged well with no neurological deficit.

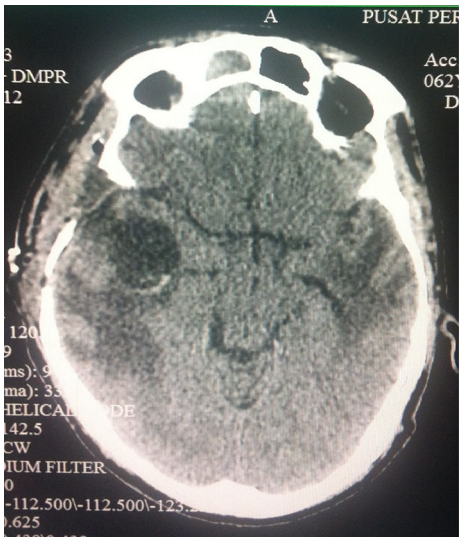

Fig. 3 Axial view of CT brain post first craniotomy in February 2013 showed cystic lesion at right temporal lobe in communication with craniotomy site

Discussion

Radiation has been the gold standard therapy for all stages of nasopharyngeal carcinoma. Patients with early stage disease who underwent radiotherapy have shown survival rates of 80–90 % [1]. However, treatment of nasopharyngeal carcinoma is difficult because of invasive nature of tumor and the anatomical proximity to critical structures. Occasionally portions of temporal lobes would have to be included within radiation portals during radiotherapy.

Risks for osteoradionecrosis related to the radiation therapy include total radiation dose, photon energy, brachytherapy, field size, fractionation [2]. Osteoradionecrosis is unlikely to occur if the radiation dose is below 60 gray, delivered by standard fractions but has a higher likelihood of occurrence if the dose is higher than 65–75 gray [2]. Total radiotherapy dosage for treatment of nasopharyngeal carcinoma usually ranges from 65 to 70 gray. A multi-institutional study showed that doses of at least 66 gray to gross disease are needed for optimal local control [3]. Hence radiation exposure of lower part of temporal lobe with conventional dose schedule would rarely be below brain tolerance unit.

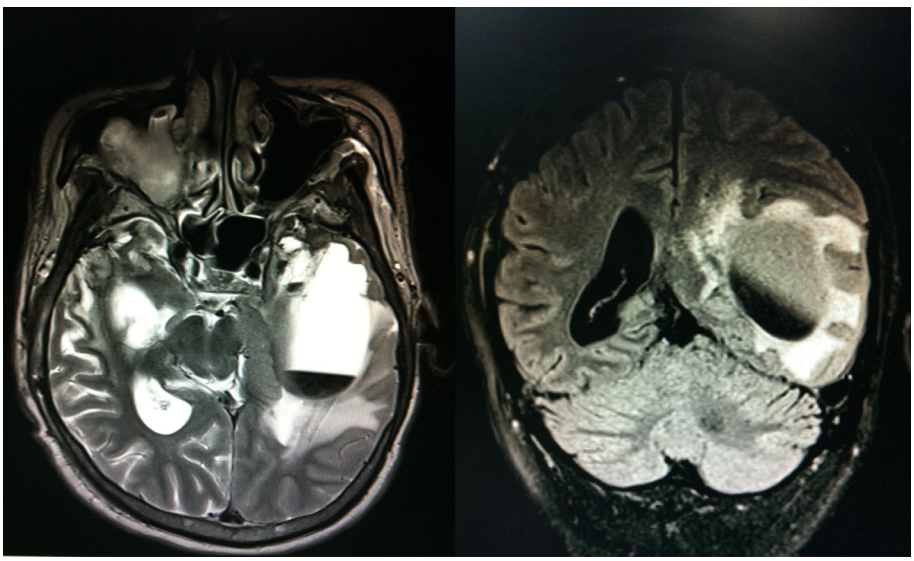

Fig. 4 MRI brain axial (*left*) and coronal (*right*) view showed large well defined left temporoparietal cystic lesion with mass effect during second presentation

Table 1 Difference of background history and clinical presentation of 3 cases

	Case 1	Case 2	Case 3
Cycles of radiotherapy	1 cycle	1 cycle	2 cycles
Interval of radiotherapy and presentation of symptoms	4 years	7 years	13 years
Symptoms on presentation	Headache	Headache	Vomiting
	Memory loss	Memory loss	Memory loss
	Nominal aphasia	Altered consciousness	Neck pain
			Emotional lability
Size of lesion	3.8 × 2.6 cm	First 3 × 3 cm	Right 4.6 × 3.3 cm
		Second 6.8 × 5.3 cm	Left 3.1 × 3.0 cm

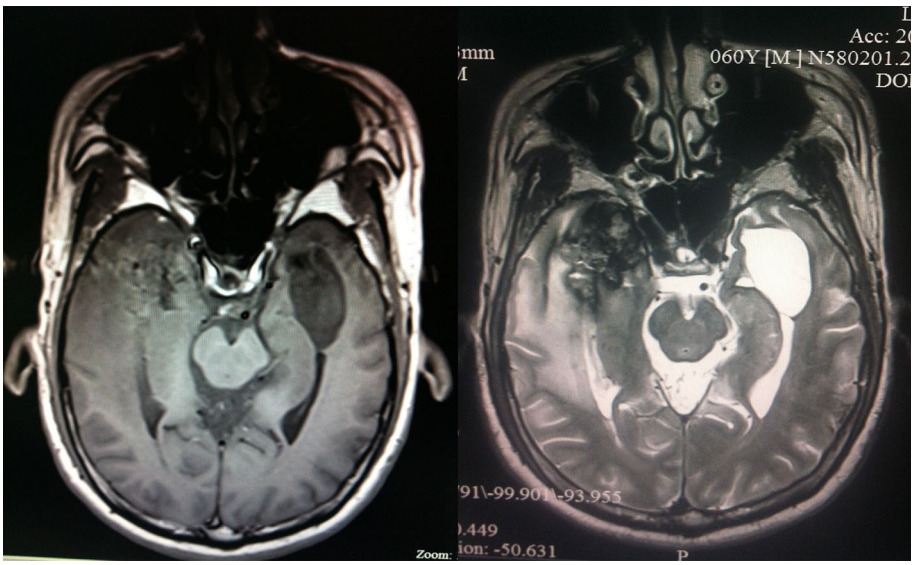

Fig. 5 Axial view of MRI brain with T1 (*left*) and T2 (*right*) showing soap bubble appearance mass in the right temporal lobe and well defined cystic lesion at left temporal lobe which appears hypointense on T1W and hypertense on T2W

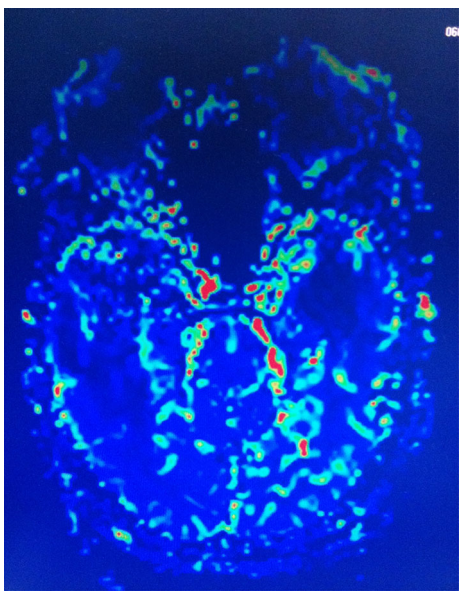

Fig. 6 MRI perfusion study showed no area of increased cerebral blood volume which is suggestive of radiation necrosis

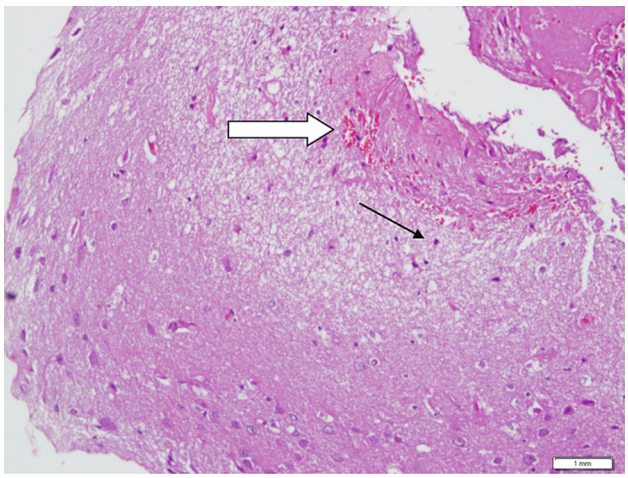

Fig. 7 Areas of necrosis with increased in lymphocytic infiltration (*thin arrow*) and small sized blood vessels (*thick arrow*) (H&E ×200)

Radiation induced cerebral injury is increasingly encountered as a result of aggressive treatment. The common sites are in the medial and inferior parts of the

temporal lobes, which lie close to skull base. It may occur in the skull base, mandible, maxilla and external auditory canal of NPC radiated patients. Acquired posterior choanal atresia in post radiation patient has been reported as well [4].

The incidence rate was reported about 7.3 % for nasopharyngeal patients treated with radical radiotherapy [5]. Late radiation effects occur from 6 months to many years post treatment. The latent interval ranged from 18 months to 11 years with median of 4 years for patients who had only one course of radiotherapy. The latent interval shortened to 7 months to 6 years for patient who had two radical courses. The incidence of temporal lobe radiation changes ranges from 3 to 20 % [6]. In this case series of three patients, the mean latent interval was 8 years.

The differential diagnosis of late temporal lobe necrosis post radiotherapy for nasopharyngeal carcinoma includes intracranial tumor extension, meningeal spread, cerebral metastases, secondary primary neoplasm and brain abscess. Four groups of clinical presentation have been observed, namely classical temporal lobe epilepsy, vague symptoms of temporal lobe damage, nonspecific features of intracranial lesions and no symptoms and signs referable to the temporal lobe [6]. Fever, drowsiness and clinical signs of sepsis are more commonly seen in patient with infective pathology.

The diagnosis of radiation necrosis on imaging has been challenging, primarily because the pattern of abnormal enhancement closely mimics that of recurrent brain tumor. Two distinctive manifestations have been observed from computerized tomography, (1) finger like hypodense shadows (finger sign) and (2) cyst like shadows (cyst sign). In deteriorating cases, the initial finger sign subsequently became cyst sign which represent a later stage in the disease process [6].

In MRI, hyperintense on Diffuse Weighted Imaging signal with a diminished signal in ADC map may point more to an abscess, while low signal intensity on Diffuse Weighted Imaging tends to indicate necrosis or tumour recurrence [7]. At perfusion weighted imaging, low values in the peripheral areas indicate an abscess, whereas high values suggest a necrotic tumour [8].

Radiation necrosis usually showed heterogeneity on Diffuse Weighted Imaging and often included spotty, marked hypointensity. There was significant difference in the maximal apparent diffusion coefficient values between radiation necrosis and tumor recurrence. Diffuse Weight Imaging is useful in differentiating recurrent neoplasm from radiation necrosis [9]. Several more advance methods for differentiation between recurrent brain tumors and post radiation necroses have been introduced including positron emission tomography, T1 single photon emission tomography, magnetic resonance spectroscopy (MRS), and stereotactic biopsy.

In case 1, patient had symptoms of temporal lobe damage which include memory lost and nominal aphasia. However, he had local recurrence of nasopharyngeal carcinoma 5 months prior to presentation. Primary or secondary spread of tumors needs to be ruled out. MRI brain and tissue biopsy later confirmed diagnosis of radiation necrosis.

In case 2, patient presented on two occasions for bilateral temporal lobe osteoradionecrosis. The disease progresses from unilateral to bilateral temporal lobe involvement in due time. However, cystic lesion of temporal lobe is highly suggestive of radiation necrotic changes. Brain abscess was ruled out as he had no fever or signs of sepsis.

In case 3, patient received two courses of radiotherapy which exposed him on higher risk of radiation necrosis. He presented with symptoms of raised intracranial pressure namely vomiting and headache and was treated as infective pathology initially despite not having fever. Further imaging showed bilateral temporal lobe lesions, suggestive of temporal lobe necrosis.

To establish an accurate diagnosis, histological diagnosis via a biopsy is mandatory. The histopathology of radiation necrosis consists of various degree of coagulative necrosis of the brain parenchyma associated with fibrinoid changes of blood vessels. Demyelination without blood vessels changes can be seen in some less severely affected vessels [8]. All 3 patients underwent craniotomy and diagnosis of osteoradionecrosis of temporal lobe were confirmed by tissue biopsy although radiological imaging was suggestive of radiation necrosis.

Medical therapy of radionecrosis consists of corticosteroids therapy. Dexamethasone treatment over 5 months produces clinical and radiological improvement in up to 34 % of patients [6]. Corticosteroid which is considered to be necessary treatment of necrosis induced by radiotherapy may increase incidence of abscess formation. In patients with significant signs of raised intracranial pressure or progressive neurological deficits despite steroid treatment, surgical resection is necessary. Surgical results are good if the lesion is focal in the temporal lobe. Other forms of treatment, includes hyperbaric oxygen and warfarin which anticoagulation, produce varying degrees of success [10].

For patients who developed temporal lobe necrosis post radiotherapy, memory, language, motor ability, and executive functions were significantly impaired, although their general intelligence remained relatively intact [11].

Conclusion

Complication of extensive latent osteoradionecrosis of temporal lobe in the radiation treatment of nasopharyngeal carcinoma is increasingly common. The diagnosis of

osteoradionecrosis versus tumor recurrence may be difficult but clinical presentation and imaging may help in distinguish between different causes. Ultimately, histological diagnosis via biopsy may become necessary to guide appropriate treatment strategy.

References

1. Bailet JW, Mark RJ, Abemayor E et al (1992) Nasopharyngeal carcinoma: treatment results with primary radiation therapy. Laryngoscope 102(9):965–972
2. Chrcanovic BR, Reher P, Sousa AA, Harris M (2010) Osteoradionecrosis of the jaws—a current overview-part 1: physiopathology and risk and predisposing factors. Oral Maxillofac Surg 14(1):3–16
3. Ozyar E, Selek U, Laskar S et al (2006) Treatment results of 165 pediatric patients with non-metastatic nasopharyngeal carcinoma: a rare cancer network study. Radiother Oncol 81(1):39–46
4. Baki MM, Gendeh BS (2006) Acquired posterior choanal atresia: post-radiotherapy. Med J Malays 61(1):94–96
5. Lee AW, Foo W, Chappell R et al (1998) Effect of time, dose, and fractionation on temporal lobe necrosis following radiotherapy for nasopharyngeal carcinoma. Int J Radiat Oncol Biol Phys 40(1):35–42
6. Lee AW, Ng SH, Ho JHC et al (1988) Clinical diagnosis of late temporal lobe necrosis following radiation therapy for nasopharyngeal carcinoma. Cancer 61(8):1535–1542
7. Leuthardt EC, Wippold FJ 2nd, Oswood MC, Rich KM (2002) Diffusion-weighted MR imaging in the preoperative assessment of brain abscesses. Surg Neurol 58(6):395–402 **(discussion 402)**
8. Muccio CF, Esposito G, Bartolini A, Cerase A (2008) Cerebral abscesses and necrotic cerebral tumours: differential diagnosis by perfusion weighted magnetic resonance imaging. Radiol Med 113(5):747–757
9. Asao C, Korogi Y, Kitajima M et al (2005) Diffusion-weighted imaging of radiation induced brain injury for differentiation from tumor recurrence. AJNR Am J Neuroradiol 26(6):1455–1460
10. Hary GB, Mainous EG (1976) The treatment of radiation necrosis with hyperbaric oxygen (OHP). Cancer 37:2580–2585
11. Cheung MC, Chan AS, Law SC, Chan JH, Tse VK (2000) Cognitive function of patients with nasopharyngeal carcinoma with and without temporal lobe radionecrosis. Arch Neurol 57:1347–1352