



Bacterial brain abscess formation in post-irradiated patients: What is the possible pathogenesis?



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ABSTRACT

Background: Until recently, post-radiotherapy brain abscess was considered rare, but it has become an increasingly important aetiology. Discussions of the relationship between bacterial brain abscess and radiotherapy (RT) are rare in the literature. Our clinical study was conducted to analyse the role of RT in the pathogenesis of bacterial brain abscess.

Methods: For our retrospective study, 146 patients with bacterial brain abscess were recruited. Ten patients with a history of RT before brain abscess formation were reviewed.

Results: Eight of these patients underwent RT treatment for nasopharyngeal carcinoma, one for olfactory neuroblastoma, and another for nasal plasmacytoma. Three showed presence of temporal lobe radiation necrosis neighbouring abscess. Eight patients were shown to have the evidence of tumour invasion. Seven had evidence of nasal infection or otitis media. Statistically significant differences between the RT and non-RT patients were observed for radionecrosis, bone defects between the middle fossa/sphenoid sinus, and the presence of nasal infection/otitis media. The mortality rate was 30%.

Conclusion: This study shows possible pathogenesis of bacterial brain abscess formation in post-irradiated patients, which is complicated by both radiation effects and tumour effects. Skull base deficits (either from tumour erosion or osteonecrosis) and nasal/ear infection were significantly different in patients who received radiation vs. those who did not. Radiation-related temporal lobe necrosis was also a predisposing factor. Further study based on a proper patient cohort is warranted.

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1. Introduction

Post-radiotherapy brain abscess was considered rare, but it has become an increasingly important aetiology for the past few years [1,2]. Reports of brain abscess formation in post-irradiated patients have increased, especially in nasopharyngeal carcinoma (NPC) population. In Taiwan, the frequency of reported cases is estimated at 1–4% [2–4]. Infection of the central nervous system (CNS) is an adverse prognostic factor in post-irradiated patients [2]. Clinical research reports on bacterial brain abscess following radiotherapy

(RT) are rare, and the pathogenesis and pathophysiology are unclear [1].

Our retrospective study investigated the clinical characteristics, underlying disease, dose schedules, imaging findings, causative pathogens, and therapeutic outcomes in patients with bacterial brain abscess following RT. We compared the differences between bacterial brain abscess patients who received RT and those who had not to clarify the clinical characteristics of such infections and improve therapeutic strategies for this potentially fatal CNS infection.

2. Patients and methods

Our retrospective study reviewed the medical records of cases with the International Classification of Diseases, Ninth Revision

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code of 324.0 (intracranial abscess). The medical records of all patients who were diagnosed with bacterial brain abscess at Kaohsiung Chang Gung Memorial Hospital from January 1994 to December 2007 were reviewed. The diagnosis of brain abscess was defined based on the criteria associated with at least one of the following characteristics: (1) characteristic computerised tomography (CT) and/or magnetic resonance imaging (MRI) findings; (2) evidence of a brain abscess seen during surgery or histopathological examination; or (3) classical clinical manifestations including headache, fever, localised neurological signs, and/or consciousness disturbance [5,6]. Patients with subdural or epidural abscess, fungal abscess, or tuberculosis abscess were excluded from our study. The study protocol was approved by Chang Gung Memorial Hospital's Institutional Review Committee on Human Research.

2.1. Clinical assessment

We retrospectively reviewed the microbiological records for abscess, CSF and blood cultures, medical records, and neuroimaging findings. Patients with a history of RT before brain abscess formation were reviewed. The dose schedule of their previous RT was obtained. All brain images were reviewed. A radiologist experienced in the interpretation of images and blinded to the patients' clinical and biochemical data analysed the images to conduct volumetric measurements of brain abscesses. Nasal infection or otitis media were also recognised from radiological evidence or clinical assessment of nasal cavity and eardrum. All images were processed with the use of Vitrea version 3.9.0.1 image-processing software (Vital Images, Minnesota, USA) running on an offline workstation. Evidence of temporal lobe radionecrosis and skull bone defect or erosion, especially between the middle fossa and sphenoid sinus, was recorded [7–10].

A combination of surgical intervention and antibiotic therapy is the primary treatment for bacterial brain abscesses. In our institution, the surgical management of brain abscesses consists of

image-guided stereotactic aspiration or craniotomy with complete excision, and the combination of third-generation cephalosporins and metronidazole is the primary choice for initially empirical antimicrobial treatments. The Glasgow Outcome Score was used to evaluate therapeutic outcomes after discharge. The follow-up period was terminated at death or at the end of the study (December 2007). Recovery was evaluated 1 year after patient discharge. Follow-up appointments for most patients were conducted at the outpatient department. Others were interviewed by telephone to identify neurologic outcomes. Mortality was defined as death by any cause occurring during hospitalisation.

2.2. Statistical analysis

The demographic data of the post-RT and non-RT groups were compared. Categorical variables were compared using Fisher's exact test. Continuous variables within the two groups were compared using the Mann–Whitney U test for nonparametric data. Any imbalance between the post-RT and non-RT groups in baseline prognostic variables was considered. *P* values less than 0.05 were considered statistically significant. Variables found to be associated with RT-related bacterial brain abscess were entered into a forward stepwise logistic regression analysis model that allowed simultaneous control of multiple factors. All statistical tests were two-tailed. All statistical analyses were conducted using the Statistical Product and Service Solution software package, version 13.0 (IBM Corporation, New York, USA).

3. Results

The 146 patients reviewed for this study included 113 men (77.4%) and 33 women (22.6%). Nine men and one woman had histories of RT before brain abscess formation. The clinical features and dose schedules of their previous RT are shown in Table 1. Clinical characteristics, imaging findings, and causative pathogens are

Table 1
Clinical characteristics and dose schedules of 10 patients with post-radiotherapy bacterial brain abscess formation.

Case no.	Age/sex	Initial presentation	Primary pathology	First dose (cGy/fraction)	Second dose (cGy/fraction)	Latent period ^a (months)	Treatment	Outcome
1	55/F	Fever for 2 days	NPC (T4N3) ^b (anaplastic carcinoma)	7560/42	Nil	168	Medical treatment only	Moderate disability
2	48/M	Fever, headache and consciousness change for 2 days	NPC (T4N1) (undifferentiated carcinoma)	7020/39	Nil	31	Medical treatment only	Moderate disability
3	48/M	Fever, headache and consciousness change for 1 day	NPC (T4N2b) (undifferentiated carcinoma)	8100/45	5400/30	8	Surgical drainage	Expired 80 days later
4	51/M	Fever for 2 days	NPC (T2N2) (undifferentiated carcinoma)	7020/39	Nil	7	Surgical excision	Good recovery
5	48/M	Headache and consciousness change for 1 week	NPC (T2N1) (undifferentiated carcinoma)	Unknown	Unknown	82	Surgical excision	Good recovery
6	45/M	Right hemiparesis for 4 days	Olfactory neuroblastoma	Unknown	Unknown	42	Medical treatment only	Good recovery
7	53/M	Headache, nausea, and right hemiparesis for 2 days	NPC (T2N1) (undifferentiated carcinoma)	7200/40	Nil	35	Surgical excision	Good recovery
8	36/M	Fever and consciousness change for 2 days	NPC (T4N2) (poor differentiated SCC)	Unknown	Unknown	432	Surgical drainage	Moderate disability
9	59/M	Fever for 2 days	NPC (T4N1) (poor differentiated SCC)	Unknown	1980/11	83	Medical treatment only	Expired 2 days later
10	58/M	Seizure and consciousness change for 1 day	Left nasal plasmacytoma	Unknown	1980/11	1.2	Medical treatment only	Expired 19 days later

NPC, nasopharyngeal carcinoma; SCC, squamous cell carcinoma.

^a The time period between the end dose of radiotherapy and the onset of clinical presentation.

^b The American Joint Committee on Cancer defined TNM classification for nasopharyngeal cancer.

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