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Clinical Study

Differentiation of tumor recurrence from radiation necrosis in high-grade gliomas using ^{201}Tl-SPECT

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Abstract

MRI is routinely performed to detect recurrence in patients with primary brain tumors, but it may not differentiate recurrent tumor from radiation-induced necrosis reliably. Thallium-201 single-photon emission computed tomography (^{201}Tl-SPECT) might be useful in distinguishing between these two clinical entities. In a retrospective study ^{201}Tl-SPECT studies with corresponding MRI studies in 19 patients with clinical or radiological suspicion of high-grade tumor recurrence were reviewed. The diagnostic accuracies of both modalities were based on the subsequent histology or clinical course where biopsy was not performed. Post-scan histology was available in nine patients (43%) who underwent re-resection. The SPECT result determined management in six patients (29%). Post-SPECT survival was significantly better in patients with negative ^{201}Tl-SPECT studies compared to patients with positive studies (median survival 15 + vs. 6 months) ($p = 0.04$, log-rank test). The sensitivity and specificity of ^{201}Tl-SPECT in diagnosing tumor recurrence were 83% and 100%, respectively. ^{201}Tl-SPECT can accurately differentiate tumor recurrence from radiation necrosis in patients with high-grade gliomas and abnormal MRI findings post irradiation. This is reflected in a significantly longer post-scan survival time in patients with a negative ^{201}Tl-SPECT result.

Keywords: ^{201}Tl-SPECT; Radiation necrosis; High-grade gliomas

1. Introduction

Management of high-grade gliomas remains one of the greatest challenges in oncology, requiring a multidisciplinary approach, which consists of cytoreductive surgery, radiation therapy and chemotherapy. Nonetheless, these tumors recur almost invariably, with a median survival of 14.6 months in patients with glioblastoma multiforme treated with concurrent radiotherapy and temozolomide followed by 6 months of adjuvant temozolomide.[1]

Serial MRI is routinely performed in these patients after primary treatment to detect tumor recurrence. However, conventional contrast-enhanced CT scans or MRI cannot reliably distinguish radiation necrosis from recurrent tumor. Both entities can cause extensive edema and blood–brain barrier disruption that result in mass effect and abnormal contrast enhancement.[2,3] Radiation-induced necrosis often occurs within 2 years after radiation therapy, the same time frame during which tumor recurrence is most frequent.[4]

Differentiation between tumor progression and radiation necrosis carries obvious prognostic and therapeutic implications. To overcome this problem, several functional and physiological imaging techniques, such as MR spectroscopy (MRS), perfusion-weighted MRI, positron emission tomography (PET), and thallium-201 single-photon emission computed tomography (^{201}Tl-SPECT) have been examined for clinical use.[5–12] Radiothallium (^{201}Tl) is a monovalent cationic radioisotope with biological properties similar to potassium.[13] Experimental evidence suggests that the ionic movement of thallium and potassium are

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related to active transport through an adenosine triphosphate (ATP) cell membrane pump, and that ^{201}Tl uptake is related to cell growth rates.[14] Previous studies showed substantial ^{201}Tl uptake in brain tumors with little uptake in normal brain.[15,16] In the mid-1980s, noting the disparity between clinical status and CT scan results in patients with gliomas, Kaplan et al. found ^{201}Tl to be superior to CT scans, gallium-67 citrate and technetium-99m gluceptate in identifying viable tumors.[11] Subsequently, other studies suggest that ^{201}Tl-SPECT may be a useful method to differentiate between tumor recurrence and radiation necrosis.[12,17–20]

We use ^{201}Tl-SPECT in our centre to clarify equivocal MRI findings in patients with post-irradiated brain tumors. Although previous studies have examined the accuracy of ^{201}Tl-SPECT in differentiating radiation necrosis from recurrent tumor, its impact on clinical decision making has not been explored. The aim of this study was to establish the value of ^{201}Tl-SPECT in differentiating radiation necrosis from recurrent tumor, and its influence on therapeutic decision making in a cohort of patients with post-irradiated high-grade gliomas and abnormal MRI findings.

2. Patients and methods

2.1. Patients

We identified 19 consecutive patients with primary brain tumors who underwent ^{201}Tl-SPECT at the Royal Melbourne Hospital between March 2004 and May 2007. Two patients had two ^{201}Tl-SPECTs during this time. Therefore, a total of 21 SPECT scans from 19 patients were included in this retrospective analysis. MRIs were performed as routine follow-up evaluation of treated brain tumors, or when there was clinical suspicion of disease recurrence. In all patients, ^{201}Tl-SPECT was prompted either by an inconclusive MRI finding showing abnormality compatible with tumor progression and radiation necrosis, or if the treating neuro-oncologist wished to confirm the MRI findings. All patient characteristics, treatment history, clinical status at the time of scan, MRI and ^{201}Tl-SPECT reports, post-scan histology, post-scan clinical course and survival data were extracted from clinical records.

2.2. Imaging

2.2.1. MRI

MRIs were performed with a 1.5-T imaging system (Signa Echospeed Plus or Signa Horizon; GE Medical Systems, Milwaukee, WI, USA) at our institution, using a standard protocol including multisequence, multiplanar transverse T2-weighted and T1-weighted images before and after administration of 15 mL of gadolinium (Magnevist, Bayer HealthCare, Pymble, NSW, Australia). Axial fluid-attenuated inversion-recovery (FLAIR) images were also obtained. MRI interpretations were based on our radiologists' reports and were classified into 3 categories: progressive disease, radiation necrosis or equivocal. MRI findings were considered equivocal if the reporting radiologist believed that the area of abnormality could be due to either tumor recurrence or radiation damage.

2.3. SPECT

Thallium-201 at a dose of 125 MBq was administered intravenously and SPECT imaging was performed 15 minutes later. Triple head (MultiSPECT, Siemens, Munich, Germany) or dual head (Symbia T2, Siemens, Munich, Germany) gamma cameras were used for image acquisition. Projection data were acquired with a 128×128 matrix, 40 s per projection. Iterative reconstruction without attenuation correction was performed. SPECT-CT studies were acquired in a few patients, with low dose non-contrast CT scan (130 kV, 120 mAs, 3 mm slice thickness) performed on the Symbia camera for the purposes of anatomical correlation. The nuclear medicine specialist reported SPECT studies as positive or negative based on a qualitative assessment of uptake in the area of interest compared to background brain uptake.

2.4. Clinicopathologic follow-up

We made the final differentiation between recurrent tumor and radiation necrosis based on subsequent histological or, in cases where biopsies were not available, on subsequent clinical and/or radiological findings. Histological confirmation within 4 months of the ^{201}Tl-SPECT was available in 9 cases. In the remaining patients, a clinical diagnosis of tumor recurrence or radiation necrosis was made on the basis of the patient's clinical course 6 months after the ^{201}Tl-SPECT. Tumor recurrence was defined by progressive clinical deterioration or an increase in size of the suspicious brain lesion on serial MRI. Radiation necrosis was defined by stabilization or improvement in both the clinical condition and the abnormal finding on MRI.

2.5. Influence on management

^{201}Tl-SPECT was said to have correctly determined management if the ^{201}Tl-SPECT finding was consistent with the final outcome of tumor recurrence or radiation necrosis but was inconsistent with the MRI report. ^{201}Tl-SPECT was considered to have assisted management when both the imaging findings were consistent with the final outcome.

2.6. Statistical methods

Follow-up was complete through to June 2007. Sensitivities, specificities, positive and negative predictive values, and accuracies were calculated for ^{201}Tl-SPECT and MRI. For the purpose of calculating diagnostic accuracies and post-scan survival, both "equivocal" and "radiation necrosis" MRI reports were considered negative for tumor