



Radiosurgery of Brain Metastasis – Radiologic and Histologic Consequences



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ABSTRACT

Context: Progressively enlarging encephalopathic changes, composed of necrosis and inflammatory demyelinating encephalopathy, are well-known effects of gamma knife surgery (GKS) to brain metastasis. These changes can be associated with recurrent tumor. MRI examination usually reveals variable amounts of enhancing and non-enhancing components. While radiographic differentiation between encephalopathic changes and recurrent tumor is of high clinical relevance, confident interpretation can be challenging or even impossible in some cases. We hypothesized that individual histologic analysis of gadolinium-enhancing and non-enhancing areas would reveal characteristic structural changes associated with enhancing and non-enhancing magnetic resonance imaging (MRI) properties.

Design: MRI-images of patients with progressive, etiologically ambiguous brain lesions following GKS were reviewed prior to explorative neurosurgery. Only cases in which distinct areas of enhancement and non-enhancement of at least 5mm in size could be identified (n=18) were chosen. These distinct areas were separately biopsied and histologically evaluated. Only cases with uniform histological results are presented in this study.

Results: Radiographically enhancing areas correlate either with recurrent tumor growth or inflammatory encephalopathic changes. Lack of radiographic enhancement correlates either with coagulative necrosis or brain tissue with reactive astrocytosis in the periphery of the radiation field.

Conclusions: For the first time, we performed selective neurosurgical resection of enhancing and non-enhancing areas in post-GKS encephalopathy. We show areas of radiographic enhancement to biologically represent increased metabolic activity (inflammatory demyelination or recurrent tumor) while non-enhancing areas correlate with normal or reduced metabolic activity (reactive astrocytosis or coagulation necrosis). These results may allow for more informed radiographic interpretation of GKS-induced encephalopathic changes

BACKGROUND

Gamma Knife Radiosurgery is an important component in the treatment of primary and secondary brain tumors. In comparison to external beam radiotherapy, GKS involves the administration of a much higher biological dose of radiation to a smaller amount of tissue. Progressively enlarging encephalopathic changes, composed of necrosis and inflammatory demyelinating encephalopathy, are well-known effects of gamma knife surgery to brain metastasis. Another important cause of lesion regrowth is tumor recurrence. MRI examination usually reveals variable amounts of enhancing and non-enhancing components in both scenarios. While radiographic differentiation between encephalopathic changes and recurrent tumor is of high clinical relevance, confident interpretation can be challenging or even impossible in some cases.

AIMS

In this study we tried to perform an individual histologic analysis of gadolinium-enhancing and non enhancing areas in regrowing lesions to reveal characteristic structural changes associated with enhancing non-enhancing magnetic resonance imaging (MRI) properties.

METHODS

Histological material for patients with symptomatic regrowth of brain metastasis at Yale New Haven Hospital between January 1, 2007 and June 30, 2010 was examined. These patients were chosen based on the finding on MRI-images of progressive, etiologically ambiguous brain lesions following GKS. Only cases with distinct areas of enhancement and non-enhancement of at least 5mm in size were chosen (n=18). All these patients were scheduled for an explorative neurosurgery. These distinct enhancing and non-enhancing areas were separately biopsied and histologically evaluated. Only cases with uniform histological results are presented in this study.

All these patients were initially treated with GKS at the Yale New Haven Gamma Knife Center between 2004 and 2009. According to our standards of management, these patients were followed by surveillance MRI every 6 to 12 weeks. Surgical management was considered if the patient developed focal neurological symptoms or evidence of midline shift in association with a progressive lesion seen on serial imaging.

RESULTS

In 18 cases, enhancing and non-enhancing areas of lesion regrowth after GKS for tumor metastasis were separately analyzed. The primary malignant diagnosis in these patients is variable and includes small and non-small cell lung cancer, melanoma, breast carcinoma, synovial sarcoma and testicular germ cell tumor. Ten patients had no evidence of recurrent tumor in the resection specimens. Histological examination of the MRI enhancing areas in these patients showed an inflammatory leukoencephalopathic process characterized by active demyelination and lymphocytic vasculitis. Other radiation induced effects were also observed in these areas including hyalinization and sclerosis of blood vessels. In one of these patients with a prior diagnosis of metastatic melanoma, a small area of enhancement on the MRI imaging correlated with extracellular melanin pigment with no viable tumor. The non-enhancing areas on MRI in these patients correlated with coagulative necrosis of tumor tissue or with brain tissue with reactive astrocytosis. 8 patients had viable tumor in their resection specimens consistent with recurrent tumor; these areas were consistently enhancing on MRI scans. Similar to patients with no viable tumor, the non-enhancing areas on the MRI scan corresponded to areas of tumoral necrosis or areas of brain tissue with reactive astrocytosis.

RESULTS

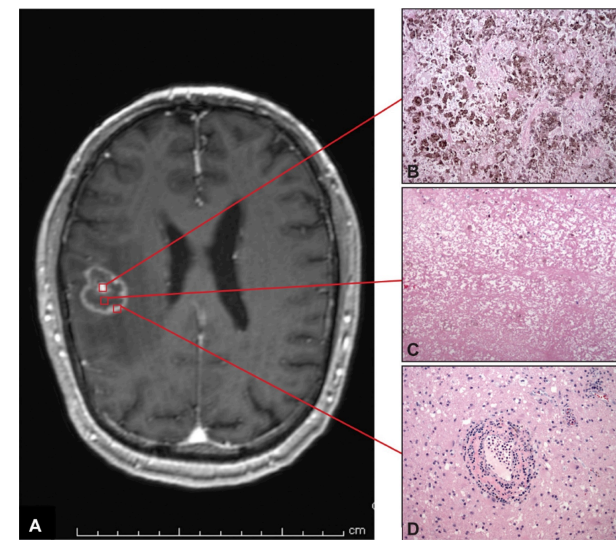


Figure 1. The MRI image of a patient with a history of metastatic melanoma status post GKS showing distinct areas of enhancing and non enhancing properties. The small central enhancing area corresponded to extracellular melanin pigment with no viable tumor. The surrounding area of non enhancing tissue showed necrotic tumor on histological examination. The external enhancing rim corresponded to an area of active inflammatory demyelination with lymphocytic vasculitis.

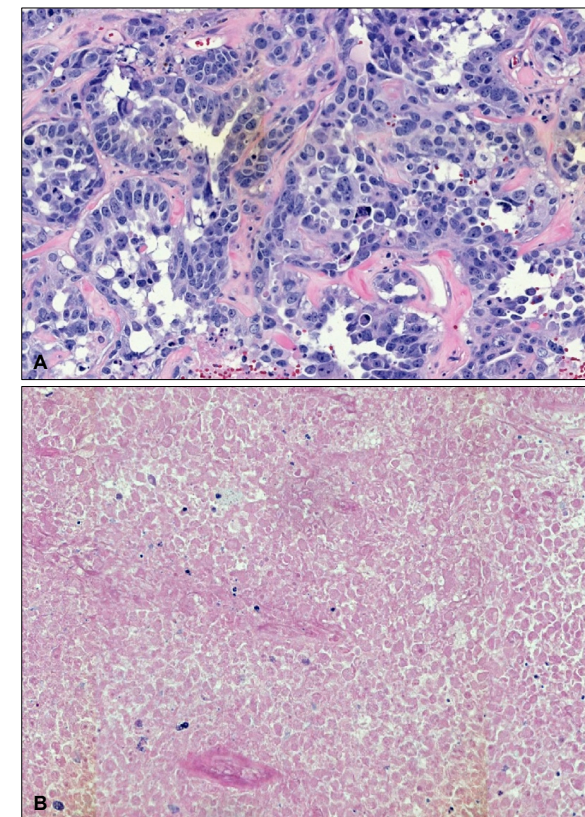


Figure 2. Histological examination of enhancing (A) and non-enhancing (B) areas in a patient with a history of metastatic breast carcinoma to the brain status post GKS showing areas of viable tumor (A) and areas of coagulative necrosis (B).

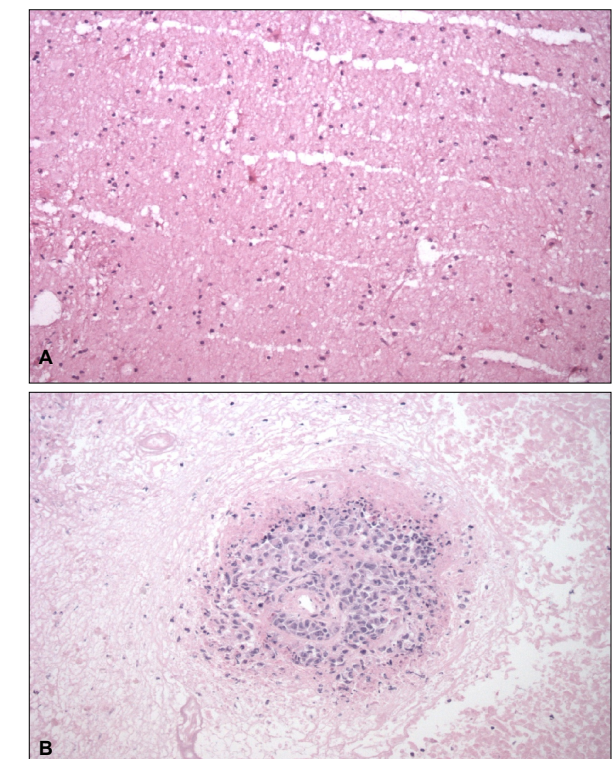


Figure 3. The histological material from a patient with a history of Non Small Cell lung cancer status post GKS. Image A was taken from an area of no enhancement and shows reactive astrocytosis. Image B was taken from an area of enhancement and corresponded to an area of residual/recurrent tumor.

CONCLUSIONS

For the first time, we performed selective histologic analysis of enhancing and non-enhancing areas in post-GKS encephalopathy. We show areas of radiographic enhancement to biologically represent increased metabolic activity (inflammatory demyelination or recurrent tumor) while non-enhancing areas correlate with normal or reduced metabolic activity (reactive astrocytosis or coagulation necrosis). These results may allow for more informed radiographic interpretation of GKS-induced encephalopathic changes.

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