ABSTRACT

Context: Progressively enlarging encephalopathic changes, composed of necrosis and inflammatory demyelination, are well-known effects of gamma knife surgery (GKS) to brain metastases. 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.

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.

RESULTS

In 18 cases, enhancing and non-enhancing areas of lesion regrowth after GKS for tumor metastases 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 specimen. 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 correlated with extracellular melanin pigment with no viable tumor. The surrounding area of non-enhancing tissue showed necrotic tumor on histological examination. The etiological ambiguous brain lesions following GKS were resected and histologically evaluated. 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.

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 astrogliosis or coagulation necrosis). These results may allow for more informed radiographic interpretation of GKS-induced encephalopathic changes.

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