Clinical Neurology and Neurosurgery 148 (2016) 67–71

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Role of mass effect, tumor volume and peritumoral edema volume in the differential diagnosis of primary brain tumor and metastasis

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ARTICLE INFO

Article history:
Received 2 May 2016
Received in revised form 1 July 2016
Accepted 2 July 2016
Available online 4 July 2016

Keywords:
Brain neoplasms
Magnetic resonance imaging
Metastasis
Volume measurement

ABSTRACT

Introduction: The differentiation of metastatic and primary brain tumors with certainty is important since clinical management and treatment of these two types of tumors are radically different.

The purpose of the present study was to evaluate the effect of peritumoral edema volume, tumor volume and mass effect of tumor on differential diagnosis of metastatic and primary brain tumors. Also we have planned to investigate if the relationship between edema volume and mass affect can contribute to the differential diagnosis.

Material and methods: We retrospectively reviewed MR images of patients with primary (n = 40) and metastatic (n = 40) intra-axial supratentorial brain tumor. Supratentorial primary solitary brain tumor group was also subdivided as GBM subgroup (n = 24) and other than GBM subgroup (n = 16) for statistical analysis. Metastasis at suitable localization which can lead to midline shift (due to mass effect) were selected. Tumor volume, peritumoral edema volume and mass-edema index (peritumoral edema volume/tumor volume) were calculated. Displacement of the midline structures (subfalcian herniation) was measured.

Metastasis, GBM and other than GBM groups were evaluated for subfalcian shift, shift grade, tumor volume, peritumoral edema volume and mass-edema index by using Kruskal-Wallis test after Bonferroni correction. Mann-Whitney *U* test was used to analise subfalcian shift, tumor volume, peritumoral edema volume and mass-edema index of primary tumor and methastasis groups since the data was not normally distributed. Shift grade of the two groups was analised with chi-square test.

Results: Midline shift, tumor volume and mass-edema index were significantly different between metastasis and primary tumor groups ($p = 0.001$, $p < 0.001$, $p = 0.001$ respectively). Midline shift and tumor volume of the primary tumor group were greater than metastasis group while mass-edema index was less. Shift grade of metastasis and primary tumor groups was also significant ($p = 0.041$). A midline shift more than 5 mm (grade 2) was more common in primary tumors. There was no significant difference between GBM and other than GBM groups.

Conclusion: Measurement of midline shift, tumor volume and mass-edema index may contribute to the differential diagnosis of brain metastasis from primary brain tumors. Also mass-edema index can be a useful tool for differential diagnosis in the future. But further studies with larger series are needed.

1. Introduction

The differentiation of metastatic and primary brain tumors with certainty is important since clinical management and treatment of these two types of tumors are radically different [1,2]. Yet, it is often difficult to differentiate a solitary brain metastasis from glioblastoma multiforme (GBM) based on conventional magnetic resonance (MR) imaging characteristics such as signal-intensity and contrast enhancement patterns alone [3–6].

Metastatic and primary brain tumors are both surrounded by extensive peritumoral edema [7]. In previous studies, it is reported that pathophysiology of peritumoral edema is different in brain metastasis than it is in primary brain tumors [2]. Metastasis is expansive and displaces the surrounding brain tissues rather than invading them [8–12]. Thus peritumoral edema area of metastatic

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http://dx.doi.org/10.1016/j.clineuro.2016.07.008
0303-8467/

brain tumors consists of vasogenic edema essentially [13–15]. On the other hand, GBM typically grows infiltratively and invades the surrounding tissues [7]. For this reason peritumoral edema area of metastatic brain tumors also contains peritumoural infiltrating neoplastic cells localized along the perivascular spaces [13–15]. Furthermore, Ludwig et al. found that peritumoral edema extension in metastatic and primary brain tumors is associated with different nitric oxide synthase (NOS) isoenzymes [16].

The purpose of the present study is to evaluate the effect of peritumoral edema volume, tumor volume and mass effect of tumor on differential diagnosis of metastatic and primary brain tumors. Also we planned to investigate if the relationship between edema volume and mass affect can contribute to the differential diagnosis.

To the best of our knowledge, ours is the first study in English literature that compares the peritumoral edema volume of metastatic and primary brain tumors.

2. Material and methods

2.1. Patients

This study was conducted with institutional review board approval. We retrospectively searched the imaging database of our radiology department for cranial magnetic resonance (MR) images of the patients with metastatic or primary brain tumor. The patients who had only CT investigation before treatment without MR examination were not included in the study. Posterior fossa tumors and extra-axials masses were excluded from the study. Hemorrhagic tumors were also not included in the study since peritumoral edema would indirectly be affected. Solitary primary tumors were selected. In the other group metastasis at suitable localization (such as frontal, parietal, parieto-occipital or parietotemporal lobe) which can lead to midline shift (due to mass effect) were selected. We stopped to search the database when the number of patients reached fourty in both groups (primary brain tumor group and metastasis group). Forty patients with intra-axial supratentorial primary brain tumor and forty patients with intra-axial supratentorial metastatic brain tumor constituted the study group. Supratentorial primary brain tumor group was subdivided as GBM subgroup and other than GBM subgroup. Information on histopathological type of tumor was obtained from pathology reports.

2.2. MRI protocol

MR examinations were performed on a 1.5T scanner (Gyroscan Achieva or Intera, Philips, Best, the Netherlands) equipped with a head coil in the axial plane. All of the examinations were acquired by using our standard protocol for the assessment of brain tumors. The images included axial proton-density and T2-weighted turbo spin-echo (TSE) (dual-echo spinecho) (slice thickness: 5 mm; intersection gap: 1 mm; field of view: 230 mm; matrix: 320 × 512; TR: 4000 ms; TE: 20/120 ms; NEX: 2; flip angle: 90), axial fluid-attenuated inversion-recovery (FLAIR) (slice thickness: 5 mm; intersection gap: 1 mm; field of view: 230 mm; matrix: 256 × 256; TR: 6000 ms; TI:2000 ms; TE:120 ms; NEX: 2), sagittal T1-weighted (slice thickness: 5 mm; intersection gap: 1 mm; field of view: 250 mm; matrix: 256 × 256; TR: 596 ms; TE:15 ms; NEX: 2; flip angle; 69) and post contrast sagittal and axial T1-weighted sequences (slice thickness: 5 mm; intersection gap: 1 mm; field of view: 230 mm; matrix: 256 × 256; TR: 650 ms; TE:15 ms; NEX: 2; flip angle: 69).

2.3. Measurement

Tumor volume and peritumoral edema volume were measured using Lesion Annotation & Volume Assessment (LAVA) software (Medical Image Mining Laboratories, Llc 400 Columbus Avenue, Valhalla, New York, United States). Tumors were annotated slice by slice on axial post contrast T1-weighted images and total volume was calculated automatically by the software. FLAIR and T2-weighted TSE sequence images were used for peritumoral edema volume measurement by the same method (Fig. 1). "Mass-edema index" was calculated according to the equation of "mass-edema index = peritumoral edema volume/tumor volume".

Axial FLAIR sequence was used to measure subfalcian herniation. The degree of midline shift was categorized as grade 1 herniation when the displacement from midline was absent or less than 5 mm and as grade 2 herniation when the displacement was 5 mm or more.

2.4. Statistical analysis

Statistical analysis was performed using statistical package for social sciences version 15.0 (SPSS, Chicago, IL, USA). Metastasis, GBM and other than GBM groups were evaluated for subfalcian shift length, shift grade, tumor volume, edema volume and mass-edema index by using Kruskal-Wallis test after Bonferroni correction. Mann-Whitney *U* test was used to analise subfalcian shift, tumor volume, edema volume and mass-edema index of primary tumor and methastasis groups since the data was not normally distributed. Shift grade of the two groups was analised with chi-square test. A p-value less than 0.05 was considered significant.

3. Results

3.1. Findings

There were 21 female, 19 male patients in metastasis group. Primary tumor group consisted of 24 female and 16 male patients. The mean age of metastasis and primary tumor groups were 59 (29–81 years) and 55 (14 and 82) respectively.

In metastasis group, 40 lesions of 40 patients were evaluated. Brain lesions were the metastasis of lung cancer (n = 20), breast cancer (n = 10), renal cell cancer (n = 2), colon cancer (n = 2), pancreas cancer (n = 1), malignant fibrous histiocytoma (n = 1), bladder cancer (n = 1), adenocarcinoma of lung (n = 1), and adenocarcinoma of unknown origin (n = 2). In primary tumor group 40 lesions of 40 patients were measured. Pathological diagnoses were glioblastoma multiforme (GBM) (n = 24), oligodendroglioma (n = 4), anaplastic oligoastrocytoma (n = 4), gliosarcoma (n = 3), hemangiopericytoma (n = 1), astrocytoma (n = 1), primary lymphoma of CNS (n = 1), pleomorphic xanthoastrocytoma (n = 1) and dysembryoplastic neuroectodermal tumor (n = 1).

Metastases were at the parietal lobe in 15 patients, at the frontal lobe in 16 patients, at the temporal lobe in 1 patient, at the parieto-occipital lobe in 7 patients and at the frontoparietal lobes in 1 patient. Primary tumors were at the parietal lobe in 10 patients, at the frontal lobe in 17 patients, at the temporal lobe in 3 patients, at the frontoparietal lobes in 4 patients and at the frontotemoral lobes in 2 patients.

The mean tumor volume and peritumoral edema volume of metastases were 12.0 cm^3 and 38.6 cm^3 respectively. In primary tumor group, mean tumor volume and peritumoral edema volume were 26.1 cm^3 and 37.9 cm^3 respectively. When GBM and other than GBM subgroups were evaluated, the mean tumor volume was 26,2 cm3 and peritumoral edema volume was 37.7 cm^3 in GBM subgroup. In other than GBM subgroup, the mean tumor volume