Diagnostic Accuracy of Perfusion CT in Differentiating Brain Abscess from Necrotic Tumor

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Objective: *To evaluate the diagnostic accuracy of perfusion computed tomography (CTP) in differentiating between brain abscess and necrotic tumor.*
Material and Method: *Prospective study was performed in patients suspected of a space taking lesion in the brain. CTP was done at the suspected levels and post-processing measurement of cerebral blood volume (CBV), cerebral blood flow (CBF), mean transit time (MTT), and permeability surface index (PS) were evaluated at ring enhanced area, central non-enhanced area, edema and contralateral normal brain.*
Results: *Seventeen patients with 21 lesions were studied. Of the 21 lesions, 12 were abscess and nine were tumors. By comparing means, only MTT at the ring enhanced area showed statistically significant difference between brain abscess and tumor (p = 0.009, 95% CI = 1.403 to 4.900). When ratio of CBV, CBF, and MTT of the ring enhanced area and contralateral normal brain were analyzed (CBVr, CBFr, MTTr respectively), there were significant differences of CBVr and CBFr between the two groups (p = 0.003, 95% CI = -4.266 to -1.051 and p = 0.006, 95% CI = -9.934 to -1.969 respectively). With the threshold of CBVr more than or equal to 1.5 and CBFr more than or equal to 1, the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for diagnosis of tumor were 100%, 75%, 75%, 100%, and 85.7% respectively.*
Conclusion: *The CTP was shown to be useful in differentiating brain abscess from tumor. With CBVr less than 1.5, tumor can be excluded.*

Keywords: *Brain abscess, Brain neoplasms, Diagnosis, Differential, Necrosis, Tomography, X-ray computed*

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Most cerebral infection can be treated successfully without sequel as long as they are detected early. It is very unfortunate if rapidly progressive but treatable infection remains undetected until irreversible damage happens. Many patients should be referred to a surgeon earlier if the imaging had been correctly interpreted. Mortality rate of brain abscess ranges from 30-70%[1]. Differential diagnosis may be difficult because of nonspecific clinical and radiological findings[2]. The common finding such as ring-enhancing appearance can be mimicked by several other diseases especially necrotic tumor. Recently, magnetic resonance imaging (MRI) was reported to be an accurate imaging modality in this entity. Diffusion MRI and apparent diffusion coefficient (ADC) maps were suggested to be helpful in establishing a differential diagnosis between abscess and cystic/ necrotic tumor[3-7]. Proton MR spectroscopy (MRS) has shown a high potential in differentiation of these two entities[8,9]. Not only because of the low availability of the MRI machine, but also the technical difficulty in interpretation, other possible modalities have also been tried to use as a simple tool for these processes. The objective of the present study was to evaluate the usefulness and accuracy of perfusion computed tomography (CTP) in differentiating between brain abscess and necrotic tumor.

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Material and Method

The prospective study was done. Patients coming in to the authors' department of Radiology with suspected space taking lesions in the brain and requested for computed tomography (CT) brain were included in the present study. Informed consents were obtained from the patients or their relatives before the present study. The present study was approved by the institute ethical committee.

CTP scan was performed only in patients whose non-enhanced scans showed abnormal low density or mass effect. The pathological results were obtained in who patients underwent surgery. For patients treated by medical treatment, clinical outcomes and follow up were concluded to separate between brain abscess and tumor.

CT perfusion study

The locations of CTP were selected from levels that showed abnormality on non-enhanced scan. With the 64-multidetector CT scanner (Lightspeed; GE Medical Systems, Milwaukee, Wisconsin), 4 cm coverage was achieved with 5 mm slice thickness and interval. The 40-ml non-ionic contrast media was injected during the scan with a rate of injection 4 ml/second. Post processing measurement was done using commercial work station (Advantage Windows; GE Medical System). With the deconvolution algorithm, cerebral blood volume, blood flow, mean transit time, and permeability surface index (CBV, CBF, MTT, and PS respectively) were measured at the enhancing rim, non-enhancing central lesion, surrounding edema area, and contralateral normal brain. All lesions were measured with the same amount of area of region of interest (ROI) at the same level (Fig. 1). All measurements were done by a more than 10 years experienced neuroradiologist blindly from clinical data. The values of each parameter are shown on the screen of the work station collected.

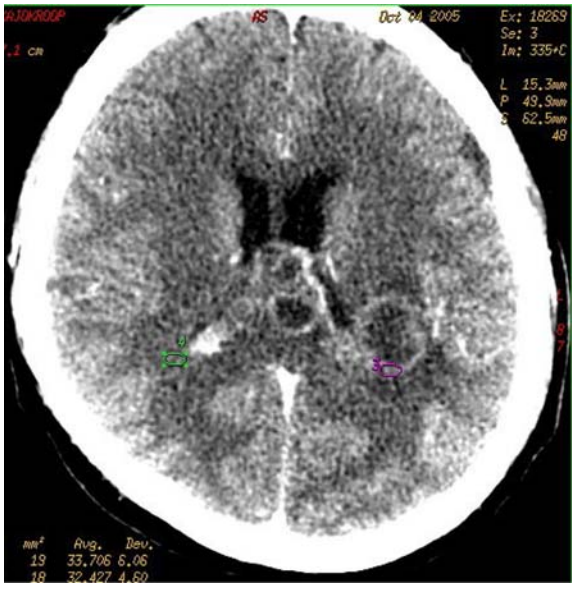

Fig. 1 Axial scan of source image of CTP shows the way to place ROI (circles) of ring-enhanced lesion on the left and contralateral normal brain on the right. The value of each measurement will appear on each functional map

Statistical analysis

By using Student t-test (SPSS 11.5), the mean $\pm$ SD and 95% confidence interval (95% CI) of CBV, CBF, MTT and PS were calculated and compared between brain abscess and necrotic/cystic tumor. Statistically significant difference was determined at $p < 0.05$. The ROC curve was calculated to obtain threshold to separate and calculate diagnostic accuracy of CTP.

Results

Between May 2005 and May 2006, 17 patients were included into the present study, nine males and eight females. The mean age was 43.5 years old with range between 18-67 years. Twenty-one lesions were analyzed. Fourteen patients had one lesion, two had two lesions, and one had three lesions. The locations of lesions were frontal lobe (9 lesions), temporal lobe (3 lesions), parietal lobe (2 lesions), thalamus (1 lesion), basal ganglion (3 lesions), periventricular white matter (1 lesion), and cerebellar hemisphere (2 lesions).

Ten patients were proven to be brain abscess; four cases by tissue biopsy, four cases by responding to anti-toxoplasmosis drug, one case by blood chemistry as positive IgG for toxoplasmosis, and one case by positive hemoculture for tuberculosis. Seven patients were proven to have tumor by biopsy (4 cases) and known primary malignancy (3 cases). The detail of diseases is shown in Table 1. Of the 21 lesions, 13 were abscess and 8 were tumors.

CT findings

All lesions were shown on CT as ring enhancing mass with perilesional edema. No hemorrhage or calcification was found. By comparing means, only MTT at the ring enhanced area showed statistically significant difference between brain abscess and

Table 1. Detail of final diagnosis of each patient

	Patient number	Number of lesions	Final diagnosis and mode of conclusion
Tumors	1	1	Glioblastoma maltiforme (biopsy)
	2	1	Lymphomas (biopsy)
	3	1	Metastasis, moderately differentiate adenocarcinoma (biopsy)
	4	2	Metastasis (known case of CA lung)
	5	1	Glioblastoma maltiforme (biopsy)
	6	1	Metastasis (known CA ovary)
	7	1	Metastasis (known CA cervix)
Brain abscess	8	1	Toxoplasmosis (positive IgG for *toxoplasma* spp.)
	9	1	Toxoplasmosis (improved after antibiotics)
	10	1	Toxoplasmosis (improved after antibiotics)
	11	1	Toxoplasmosis (improved after antibiotics)
	12	1	Toxoplasmosis (improved after antibiotics)
	13	1	Tuberculosis (hemoculture)
	14	3	*Cladophialophora Bantianum* (biopsy)
	15	1	*Nocardia* spp. (biopsy)
	16	1	*Taenia* spp. (biopsy)
	17	2	Bacterial abscess (biopsy)

Table 2. Statistical results of the CTP comparing between abscess and tumor

CTP		Means	SD	p-value	95% CI
MTT	- Abscess (12)	6.27	2.37	0.009	1.403 to 4.900
	- Tumor (9)	3.12	0.88		
CBVr	- Abscess	1.21	0.78	0.003	-4.266 to -1.051
	- Tumor	3.87	2.52		
CBFr	- Abscess	0.96	0.94	0.006	-9.934 to -1.969
	- Tumor	6.91	6.56		

95% CI = 95% confidence interval

tumor (p= 0.009). When ratio of CBV, CBF, and MTT of the ring enhanced area and contralateral normal brain were analyzed (CBVr, CBFr, MTTr), there were significant differences of CBVr and CBFr between the two groups (p = 0.003 and 0.006 respectively). With the threshold of CBVr more than or equal to 1.6 and CBFr more than or equal to1.3, the sensitivity for diagnosis of tumor was 88.9%, specificity was 83.3% and accuracy 85.7%. For the CBVr more than or equal to 1.5 and CBFr more than or equal to 1, the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for diagnosis of tumor were 100%, 75%, 75%, 100%, and 85.7% respectively. The statistical results are concluded in Table 2.

Discussion

The transition of cerebral infection from cerebritis stage to capsular stage has been known to be the reason of different CT findings at different stages. Enzmann et al studied brain abscess evolution in dogs by correlating the CT appearance with the neuropathological findings[10]. They found that at the late cerebritis stage (4-9 days) and early capsular stage (10-13 days), vascular proliferation at the abscess periphery became more evident. This finding corresponded to within 1 mm of the inflamed periphery of the necrotic center and of ring enhanced area on CT. In late capsular stage, the complete collagen capsule is responsible for the enhancing ring.

In the present study, when considering timing of performing CTP after clinical onset, most of brain abscess cases underwent CTP in late capsular stage. With the threshold of CBVr 1.5 and CBFr 1, three cases showed hyperperfusion: one toxoplasmosis (late capsular stage), one nocardial brain abscess (late cerebritis to early capsular stage) and one

toxoplasmosis (late cerebritis stage). According to Enzmann's study, the later two cases given false positive (hyperperfusion) is possible from vascular proliferation of the inflamed tissue. However, the authors cannot conclude the reason for false positive result of the first case.

The angiogenesis effect of tumor induces neovascularization and increasing vascular space manifesting as increased CBV as well as CBF. This effect has been shown clearly by perfusion MRI in many studies[11,12]. With the same concept, the authors have shown clearly here that all tumor cases had increasing CBVr (≥ 1.5) and CBFr (≥ 1). By observation, the authors also found that the entire cerebral hemisphere containing tumors had increased cerebral perfusion but containing abscess had decreased perfusion. These may be from angiogenetic-induced effect of the tumor and vasospasm of the infective process (Fig. 2).

In the practical point of view, treatment of brain abscess is medical treatment. Surgical drainage is recommended to decrease the mortality[13]. It is generally accepted that surgical aspiration and/or excision is optimally utilized after capsular formation has taken place. Unfortunately, the greatest mass effect may occur in the cerebritis stage. However, successful treatment of brain abscess in its early stage by medical management alone suggested that treatment could be tailored to a specific stage of abscess evolution. In the clinical setting of nonspecific sign and symptom, it is reasonable to try treatment with antibiotics and corticosteroids in the acute phase (cerebritis stage). After 1-2 weeks, if clinical symptoms have not improved, repeated CT scan with CTP is recommended. After 10 days, most of cerebritis evolutes to be capsular stage and is appropriate for CTP to differentiating from tumor. With the threshold of CBV 1.5, no tumor was missing in the present study, leaving only a few cases of infection that needed to undergo surgical procedure. Diffusion MRI and ADC maps have been reported useful in separating brain abscess and tumor. In immunocompetent hosts, brain abscess showed decreased ADC and brain tumor increased ADC. However, in immunocompromised hosts, the reversed result was reported between toxoplasmosis and lymphomas[6,7].

Because of the complicated technique of measuring ADC and the low availability of MRI machine when compared with MDCT in this country, an alternative modality was investigated. The present study showed the simple method of measuring CBV and CBF value with either 16 or 64-MDCT machine. Although the authors used deconvolution algorithm, comparing values of CBV and CBF between lesion and normal brain to get the ratio, analyst may get comparable result using single compartment algorithm.

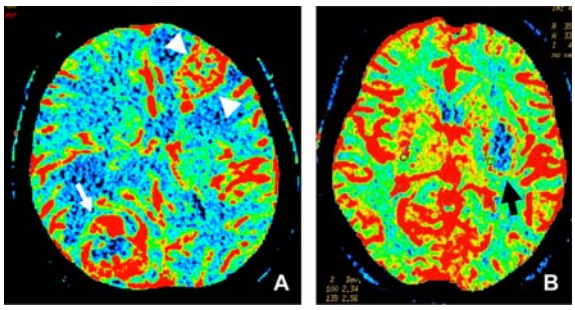

Fig. 2 Cerebral blood volume maps of (A) metastasis and (B) toxoplasmosis demonstrate hyperperfusion of left frontal (arrow heads in A) and right occipital lobes (white arrow in A) in metastatic cerebrum but none in left basal ganglion abscess (black arrow in B). Note the increased perfusion of regional brain in (A) and decreased perfusion of left cerebral hemisphere (especially left frontal lobe) in (B)

Conclusion

The CTP was shown to be useful in differentiating brain abscess from tumor. With CBVr less than 1.5, tumor can be excluded.

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การแยกฝีหนองในสมองออกจากเนื้องอกสมองโดยใช้เอกซเรย์คอมพิวเตอร์ตรวจเลือดที่หล่อเลี้ยงสมอง

อรสา ชวาลภาฤทธิ์, เจนจิรา อาจแก้ว, ถนอมศักดิ์ อเนกธนานนท์, นันทศักดิ์ ทิศาวิพาต, พนิดา ชาญเชาว์วานิช, ตุ้มทิพย์ แสงรุจิ

วัตถุประสงค์: *เพื่อศึกษาความแม่นยำของการวินิจฉัยแยกรอยโรคฝีหนองในสมองออกจากเนื้องอกสมองโดยใช้เอกซเรย์คอมพิวเตอร์ตรวจเลือดที่หล่อเลี้ยงสมอง*

วัสดุและวิธีการ: *ได้ทำการศึกษาผู้ป่วยจำนวน 17 รายที่มาตรวจเอกซเรย์คอมพิวเตอร์สมองด้วยภาวะสงสัยว่ามีก้อนทูมในสมอง โดยทำการตรวจเพิ่มด้วย CT perfusion ซึ่งเป็นการตรวจภาวะเลือดที่เลี้ยงสมอง จากนั้นนำข้อมูลมาสร้างภาพ และวัดค่า cerebral blood flow, blood volume, mean transit time ของบริเวณที่เห็นขาวขึ้น หลังฉีดสารทึบรังสี บริเวณเนื้อตายตรงกลางรอยโรค บริเวณสมองที่บวม และบริเวณสมองที่ปกติด้านตรงข้าม*

ผลการศึกษา: *จากการศึกษา รอยโรค 21 รอยโรคจากผู้ป่วย 17 ราย เป็นฝีหนอง 12 รอยโรค และเป็นเนื้องอก 9 รอยโรคพบว่า เมื่อเปรียบเทียบค่าเฉลี่ยของทั้งสองกลุ่ม มีเพียงค่า mean transit time ของบริเวณที่มีความทึบรังสีเพิ่มขึ้นหลังฉีดสารปรับความเปรียบต่างที่ต่างกันในสองกลุ่มอย่างมีนัยสำคัญทางสถิติ (p = 0.009, 95% CI = 1.403 ถึง 4.900) และเมื่อเปรียบเทียบค่าสัดส่วนระหว่าง cerebral blood flow ของบริเวณทึบรังสีกับบริเวณที่ปกติ และค่าสัดส่วนระหว่าง cerebral blood volume ของบริเวณทึบรังสีกับบริเวณที่ปกติ ในรอยโรคที่เป็นฝีหนองและเนื้องอกมีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ (p = 0.003, 95% CI = -4.266 ถึง -1.051 และ p = 0.006, 95% CI = -9.934 ถึง -1.969 ตามลำดับ) โดยถ้าใช้สัดส่วน cerebral blood volume มากกว่า 1.5 หรือ cerebral blood flow มากกว่า 1 ในการทำนายเนื้องอกสมองจะมีความไวร้อยละ 100 ความจำเพาะร้อยละ 75 การทำนายผลบวกถูกต้อง ร้อยละ 75 การทำนายผลลบถูกต้องร้อยละ 100 และความแม่นยำร้อยละ 85.7 จากการศึกษาครั้งนี้พบว่ามีความเป็นไปได้ที่เอกซเรย์คอมพิวเตอร์ตรวจเลือดที่หล่อเลี้ยงสมองสามารถใช้แยกรอยโรคที่เป็นเนื้องอกออกจากฝีหนองสมองได้*