

RESEARCH ARTICLE

Application of Computed Tomography for Differential Diagnosis of Glioma Stroke and Simple Cerebral Hemorrhage

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Abstract

Objective: To explore the value of computed tomography (CT) in the differential diagnosis of glioma stroke and simple cerebral hemorrhage. **Materials and Methods:** A total of 45 patients with glioma stroke and stroke as the initial symptom in our hospital from Jun., 2009 to Oct., 2013 were selected along with 50 individuals with simple cerebral hemorrhage in the same period randomly collected as a control group. The CT results in both groups were analyzed and compared. **Results:** In the observation group, there were 25 patients with astrocytoma (55.6%), 11 with oligodendroglioma (24.4%), 8 with ependymoma (17.2%) and 1 with glioblastoma multiforma (GBM, 2.22%). Additionally, the major CT manifestation was coexistence of hemorrhage and tumor signs. By comparison, it could be found that the proportions of patients respectively with peripheral edema and space-occupying effect in the observation group were significantly higher than in the control group ($P<0.01$). **Conclusions:** Application of CT examination combined with medical history in patients has very important clinical value in the differential diagnosis of glioma stroke and simple cerebral hemorrhage.

Keywords: Glioma - simple cerebral hemorrhage - computed tomography - differential diagnosis

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Introduction

Glioma, approximately accounting for 50% in primary stroke, has high-grade malignancy, various environmental and genetic risk factors, rapid progression and a large of tumor vessels with immature structures formed in the process of growth (Das et al., 2013; Doroudchi et al., 2013; Yilmaz et al., 2013; Wang et al., 2013; Yu et al., 2013). Its weak and thin wall easily ruptures to cause bleeding, consequently leading to the stroke, also called glioma stroke. The patients with small amount of bleeding may have no symptoms and signs, whereas those with large amount usually manifest acute intracranial hypertension or aggravated disturbance of neurologic function, even coma, which is frequently misdiagnosed as cerebrovascular stroke or cerebral traumatic hemorrhage so as to cause the delayed treatment (Cervera et al., 2008). Except for medical history and clinical manifestations in clinical diagnosis, computed tomography (CT) examination can provide a very important diagnostic reference for identifying glioma stroke and simple cerebral hemorrhage, and is conducive to avoiding misdiagnosis. The CT results of 48 patients with glioma stroke and 50 with simple cerebral hemorrhage were compared in this study to try to investigate the CT clinical significance in the differential diagnoses of both diseases.

Materials and Methods

General data

A total of 45 patients with glioma stroke and stroke as the initial symptom in our hospital from Jun., 2009 to Oct., 2013 were selected as observation group, and meanwhile 50 ones with simple cerebral hemorrhage at the same term were randomly collected as control group. The diagnosis of all patients was confirmed by pathological examination or surgery. In observation group, the males and females were respectively 26 and 19 cases, with the mean age of 50.62 ± 6.81 . On admission to hospital, 25 patients encountered sudden severe headache and vomiting, 19 from disturbance of consciousness to coma, 10 hemiplegia and 6 papilledema. In control group, the males and females were respectively 28 and 22 cases, with the mean age of 52.19 ± 8.23 . On admission to hospital, 32 patients encountered sudden severe headache and vomiting, 13 from disturbance of consciousness to coma, 10 hemiplegia and 8 papilledema. There was no statistical significance between two groups by comparison to the gender, age and symptoms on admission to hospital ($P>0.05$), with better compatibility.

Methods

Siemens SOMATOM Emotion16-layer spiral CT

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machine was applied. The patients in both groups were given skull CT examination in 24 h after hospitalization, and took routine decubitus. Routine spiral CT scan (120 KV and 250 mA) with 5 mm thickness of layer and 5 mm thread pitch for 2 s were performed from orbitomental line as the baseline to the vertex. The reinforced scan of patients in observation group was conducted after the residual tumor focus was found. Non-ionic iohexol (omnipaque, made in China) contrast agent was given cubital venous bolus by bolus method. Besides, the patients allergic to contrast agents and with vital organ insufficiency such as heart, liver and kidney were all excluded.

Statistical data analysis

SPSS17.0 software package was used to analyze the data. The measurement data and enumeration data were managed respectively with *t* and χ^2 tests. $P < 0.05$ was considered to be statistically significant.

Results

Pathological examination results

In observation group, there were 25 patients with astrocytoma (55.56%), 11 with oligodendroglioma (24.44%), 8 with ependymoma (17.18%) and 1 with glioblastoma multiforms (GBM, 2.22%).

CT signs of patients in both groups

CT signs of patients in observation group mainly manifested coexistence of hemorrhage and tumor signs. a. CT density: 37 patients with clear-boundary high-density hematoma, 34 with visible solid tumors and 11 with invisible tumor focus; b. Distribution of tumor and hemorrhage focuses: the focuses of 15 patients were located in temporal lobe, 10 in frontal lobe, 12 in frontal-parietal lobe and 8 in basal ganglia; c. Hemorrhagic forms: 18 patients with nodal hematoma edge or cloddy space-occupying focuses, 6 with cystic focuses, and others with irregular hemorrhagic forms and different sizes; d. Peripheral edema: 25 patients with peripheral edema zone like finger press, 13 with more extensive zonal edema and 7 with inconspicuous edema zone; e. Space-occupying effect: 27 and 18 patients respectively with obvious and unobvious space-occupying effects; f. CT value: CT value was 60~80 Hu, averagely (67.38±5.12) Hu. Space-occupying effect was intensified when CT scan was reinforced, in which 15 patients showed uniform intensity, 18 annular intensity and 7 irregular intensity without non-intensified hematoma (Figure 1).

CT signs of patients in control group: a. CT density: Significantly-increased density shadow was presented in all patients. b. Hemorrhage focuses and forms: Most patients suffered from irregular basal ganglion hemorrhage, in which nephroid patients with medial conspicuous sunk and lateral distension were more, and only 9 had mild edema zone. c. CT value: CT value was 60~70 Hu, averagely (68.47±1.75) Hu. d. Space-occupying effect: The patients with bleeding >30 mL and medial ones had more significant space-occupying effect. In this study, significant space-occupying effect

was shown in 12 cases (Figure 2).

By comparison to the CT signs in both groups, it could be found that the proportions of patients respectively with peripheral edema and space-occupying effect in observation group were significantly higher than in control group, and there was statistical significance ($P < 0.01$) (Table 1).

Discussion

The overwhelming majority of gliomas characterized by high-grade malignancy, rapid progression and a large amount of immature new vessels belong to primary tumors, and angiorrhexis easily occur in the process of tumor growth, consequently leading to the stroke. The studies demonstrated that about 5% patients with gliomas can encounter apoplectic hemorrhage, especially those with glioblastoma (Barkovich et al., 1998; Fiveash et al., 2003; Pina et al., 2014; Ryken et al., 2014; Wang et al., 2014). Glioma hemorrhage is mainly caused by the following factors: a. tumor vascular occlusion and distal vascular necrosis caused by vascular endothelial proliferation, hemangiectasis and vascular distension due to tumor growth as well as invasion of tumor on blood vessels; b. degeneration and necrosis of adjacent tissue structures resulted from tumor infiltration and oppression as well as extended tumor vessels; c. local blood stasis and increased press caused by tumors oppressing adjacent regurgitant vessels; d. changes of tumor haemodynamics due to head trauma and radiotherapy (Fraum et al., 2011; Jo et al., 2014).

In terms of clinical symptoms between glioma stroke and simple cerebral hemorrhage, there are a great many similarities like headache, vomiting, disturbance of consciousness and blurred vision, which easily lead to misdiagnosis. Hence, the patients with glioma stroke and stroke as the initial symptom are very easy to be misdiagnosed as simple cerebral hemorrhage (Choi et al., 2013). The diagnostic evidences for glioma stroke primarily include the signs of primary intracranial tumors or systemic metastatic brain tumors, clinical manifestation of stroke onset and several factors like intracranial tumors and metastatic tumors accompanied by imaging changes of cerebral hemorrhage displayed by CT or MRI. The auxiliary examination such as CT and MRI plays extremely crucial roles in the differential diagnosis of glioma stroke and simple cerebral hemorrhage (Fatterpekar et al., 2012), especially CT diagnosis for supratentorial glioma (Beppu et al., 2011). Pathologically, gliomas include astrocytoma, oligodendroglioma, ependymoma and GBM, all of which have significant characteristics in CT signs. Astrocytoma, originating from astroglia, is the most commonly-encountered tumor in nervous system, usually occupying over 70% in gliomas. Uneven density, unclear edge, much annular intensity, different degrees of edema and space-occupying effect are presented in its CT signs (Gielen et al., 2013; Skogen et al., 2013). Oligodendroglioma, accounting for 5% in brain-derived tumors, frequently manifests slightly low density, calcification and mild space-occupying effect, and part of them can encounter cystic change. Besides,

Table 1. Comparison of CT Signs in Two Groups (x±s)

Groups	n	CT value (Hu)	Peripheral edema [n(%)]	Space-occupying effect [n(%)]
Observation group	45	67.38±5.12	38 (84.44)**	27 (60.00)**
Control group	50	68.47±1.75	9 (18.00)	12 (24.00)

Compared with control group, ** $P < 0.01$

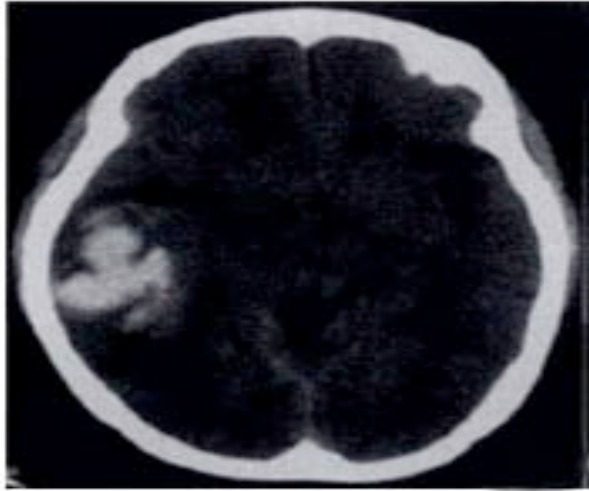


Figure 1. CT Imaging of Glioma Stroke: Peripheral Edema Like Finger Press

reinforced scanning intensity, characterized by large and irregular calcification within focuses like non-strings or clumps, is insignificant and usually uniform intensity (Narang et al., 2011). The manifestations of ependymoma are diversified. By comparison to the adjacent brain tissue, low, moderate, high or mixed density can be presented in plain scan. Calcified focuses can be found in about half pathological tumors, and most tumors show uniform intensity by reinforced CT scan (Iwamoto et al., 2013). Under CT, GBM usually displays mixed density, edema zone, significant space-occupying effect and cystic change area. Additionally, irregular annular intensity can be found by reinforced scan (Park et al., 2011). In this study, there were 25 patients with astrocytoma, 11 with oligodendroglioma, 8 with ependymoma and 1 with GBM in observation group. Its characteristics of general CT signs are in accordance with the previous reports (Berberat et al., 2014).

By comparison to the CT signs in both groups, it could be found that the CT signs of patients with glioma stroke usually manifested coexistence of hemorrhage and tumor signs. High-density shadow is usually shown when tumor volume is bigger and not covered by hematoma, which is very easy to diagnose. However, the tumor volume is the same as the hematoma density when it is smaller or covered by hematoma, which makes the diagnosis more difficult. Hence, edema zone has a greater reference value. As the typical characteristic of tumor edema, the edema zone of glioma stroke is usually not in accordance with hematoma age. With its growing and increasing, the mechanistic oppression of tumor volume to peripheral brain tissue or broken degree of blood brain barrier is aggravated, and brain tissue edema surrounding the tumor volume also becomes conspicuous gradually. A lot of studies demonstrated that the space-occupying effect after cerebral hemorrhage was primarily affected

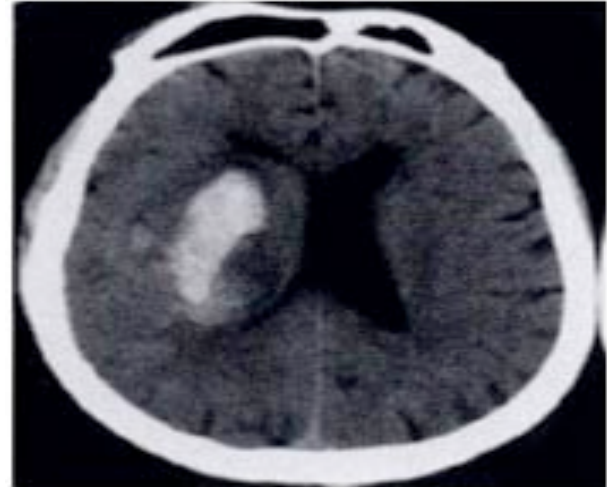


Figure 2. CT Imaging of Simple Cerebral Hemorrhage: Insignificant Peripheral Edema Zone

by hematoma volume and its peripheral edema volume, whereas it was mainly influenced by edema severity when except for rehaemorrhagia (Brott et al., 1992; Lee et al., 1995; Wagner et al., 1996). The brain edema in patients with glioma stroke due to prominent tumor edema is obviously more severe than in those with simple cerebral hemorrhage. Hence, more significant space-occupying effect is shown in CT signs. Besides, irregular hemorrhage forms, conspicuous peripheral edema zone and space-occupying effect as well as intensified tumor volume when reinforced scan is used are all notably different from simple cerebral hemorrhage. The results in this study revealed that the proportions of patients respectively with peripheral edema and space-occupying effect in observation group were significantly higher than in control group.

To sum up, glioma stroke has much common with simple cerebral hemorrhage in clinical manifestations, but their CT signs are greatly different. Hence, timely skull CT examination is conducive to clinicians to accurately identify and diagnose glioma stroke and simple cerebral hemorrhage in clinical diagnosis except for inquiring medical history and conducting strict neurological examination.

References

- Barkovich AJ, Atlas SW (1988). Magnetic resonance imaging of intracranial hemorrhage. *Radiol Clin North Am*, 26, 801-20.
- Beppu T, Sasaki M, Kudo K, et al (2011). Prediction of malignancy grading using computed tomography perfusion imaging in nonenhancing supratentorial gliomas. *J Neurooncol*, 103, 619-27.
- Berberat J, Grobholz R, Boxheimer L, et al (2014). Differentiation between calcification and hemorrhage in brain tumors using susceptibility-weighted imaging: a pilot study. *AJR Am Roentgenol*, 202, 847-50.

- Brott T, Broderic J, Barsan W, et al (1992). Hyper-acute clot retraction in spontaneous intracerebral hemorrhage. *Stroke*, 23, 141.
- Cervera V, Mai W, Vite CH, et al (2008). A case of glioblastoma misdiagnosed initially due to positive finding of anti-glutamate receptor antibody. *Rinsho Shinkeigaku*, 48, 497-500.
- Choi G, Park DH, Kang SH, et al (2013). Glioma mimicking a hypertensive intracerebral hemorrhage. *J Korean Neurosurg Soc*, 54, 125-7.
- Das BR, Tangri R, Ahmad F, et al (2013). Molecular investigation of isocitrate dehydrogenase gene (IDH) mutations in gliomas: first report of IDH2 mutations in Indian patients. *Asian Pac J Cancer Prev*, 14, 7261-4.
- Doroudchi M, Pish ZG, Malekzadeh M, et al (2013). Elevated serum IL-17A but not IL-6 in glioma versus meningioma and schwannoma. *Asian Pac J Cancer Prev*, 14, 5225-30.
- Fatterpekar GM, Galheigo D, Narayana A, et al (2012). Treatment-related change versus tumor recurrence in high-grade gliomas: a diagnostic conundrum--use of dynamic susceptibility contrast-enhanced (DSC) perfusion MRI. *AJR Am J Roentgenol*, 198, 19-26.
- Fiveash JB, Spencer SA (2003). Role of radiation therapy and radiosurgery in glioblastoma multiforme. *Cancer J*, 3, 222-9.
- Fraum TJ, Kreisl TN, Sul J, et al (2011). Ischemic stroke and intracranial hemorrhage in glioma patients on antiangiogenic therapy. *J Neurooncol*, 105, 281-9.
- Gielen I, Kromhout K, Gavin P (2013). Agreement between low-field MRI and CT for the detection of suspected intracranial lesions in dogs and cats. *J Am Vet Med Assoc*, 243, 367-75.
- Iwamoto N, Murai Y, Yamamoto Y, et al (2013). Supratentorial extraventricular anaplastic ependymoma in an adult with repeated intratumoral hemorrhage. *Brain Tumor Pathol*, 31, 138-43.
- Jo JT, Schiff D, Perry JR (2014). Thrombosis in brain tumors. *Semin Thromb Hemost*, 40, 325-31.
- Lee KR, Betz AL, Keep RF, et al (1995). Intracerebral infusion of thrombin as a cause of brain edema. *J Neurosurg*, 83, 1045-50.
- Narang J, Jain R, Scarpace L, et al (2011). Tumor vascular leakiness and blood volume estimates in oligodendrogliomas using perfusion CT: an analysis of perfusion parameters helping further characterize genetic subtypes as well as differentiate from astroglial tumors. *J Neurooncol*, 102, 287-93.
- Park SS, Chunta JL, Robertson JM, et al (2011). MicroPET/CT imaging of an orthotopic model of human glioblastoma multiforme and evaluation of pulsed low-dose irradiation. *Int J Radiat Oncol Biol Phys*, 80, 885-92.
- Pina S, Carneiro A, Rodrigues T, et al (2014). Acute ischemic stroke secondary to glioblastoma. A case report. *Neuroradiol J*, 27, 85-90.
- Ryken TC, Aygun N, Morris J, et al (2014). The role of imaging in the management of progressive glioblastoma: A systematic review and evidence-based clinical practice guideline. *J Neurooncol*, [Epub ahead of print].
- Skogen K, Ganeshan B, Good C, et al (2013). Measurements of heterogeneity in gliomas on computed tomography relationship to tumour grade. *J Neurooncol*, 111, 213-9.
- Wagner KR, Xi G, Hua Y, et al (1996). Lobar intracerebral hemorrhage model in pigs: rapid edema development in perihematomal white matter. *Stroke*, 27, 490-7.
- Wang L, Wu XY, Liu J, et al (2014). Evidence of Shenmai and cantharides injection for patients with breast cancer. *Int J Med Res Clin Oncol*, 1, 11-5.
- Wang YX, Fan K, Tao DB, et al (2013). Association between genetic polymorphism of xrccl gene and risk of glioma in ? Chinese population. *Asian Pac J Cancer Prev*, 14, 5957-60.
- Yilmaz U, Zeybek U, Kahraman OT, et al (2013). Investigation of ICAM-1 and β 3 integrin gene variations in patients with brain tumors. *Asian Pac J Cancer Prev*, 14, 5929-34.
- Yu CY, Liang GB, Du P, et al (2013). Lgr4 promotes glioma cell proliferation through activation of Wnt signaling. *Asian Pac J Cancer Prev*, 14, 4907-11.