Journal of Clinical Neuroscience 22 (2015) 296–302

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

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

Clinical Study

Clinical presentation and imaging characteristics of occult lung cancer associated ischemic stroke

Hui Mai [a,1], Jun Xia [b,1], Yongjun Wu [b], Junlong Ke [a], Junliang Li [a], Jiangang Pan [a], Wubiao Chen [b], Yiming Shao [c], Zhi Yang [d], Saihua Luo [e], Yonghua Sun [f], Bin Zhao [a], Longxuan Li [a,g,*]

[a] Department of Neurology, Guangdong Medical College Affiliated Hospital, 57 South Renmin Road, Zhanjiang 524001, Guangdong, PR China
[b] Department of Radiology, Guangdong Medical College Affiliated Hospital, Zhanjiang, PR China
[c] Department of Critical Care Medicine, Guangdong Medical College Affiliated Hospital, Zhanjiang, PR China
[d] Department of Neurology, Maoming People's Hospital, Maoming, PR China
[e] Department of Neurosurgery, Lianjiang People's Hospital, Lianjiang, PR China
[f] Department of Radiology, Lianjiang People's Hospital, Lianjiang, PR China
[g] Department of Neurology, Gongli Hospital, Pudong New Area, Shanghai, PR China

ARTICLE INFO

Article history:
Received 14 September 2013
Accepted 18 May 2014

Keywords:
Clinical presentation
Diffusion-weighted magnetic resonance imaging
Ischemic stroke
Lung cancer
Recurrence

ABSTRACT

We investigated the clinical and imaging characteristics of initial and recurrent strokes in patients with occult lung cancer associated ischemic stroke (OLCA-stroke). A retrospective review of all ischemic stroke patients with occult lung cancer in the absence of conventional stroke etiologies between 2005 and 2013 was conducted. We compared the initial and recurrent lesion patterns on diffusion-weighted MRI in patients with OLCA-stroke, with respect to vascular territory involved, number and size of lesions, clinical presentation, cancer subtypes, recurrences and fatalities, and outcome of survivors. Thirteen patients with confirmed OLCA-stroke were identified. All had elevated D-dimer levels, six had central lung cancer and seven had peripheral lung cancer. Eight (62%) had adenocarcinoma, and nine (69%) had metastasis. Ten (77%) patients had multiple lesions in multiple vascular territories. Twelve (92%) patients suffered recurrent strokes. Multiple small and large disseminated lesions in multiple vascular territories were more frequent in recurrent strokes in comparison with initial strokes. The middle cerebral artery was most frequently involved in recurrent strokes, followed by the posterior circulation territory and anterior cerebral artery, which were of similar frequency as initial strokes. Overall, 58% of patients had their first recurrent stroke within the first month, and 69% had a poor outcome, especially for those with multiple recurrent strokes and metastases. Occult cancer should be considered in the setting of multiple and recurrent embolic strokes within the short term in the absence of conventional stroke etiologies. The severity of malignancy and cancer treatments and stroke influenced the recurrences and outcome.

1. Introduction

Cancer and stroke are the leading causes of death in China [1,2]. In cancer patients, cerebrovascular disease is recognized as the second most common central nervous system complication after metastases [3]. Approximately 15% of patients with cancer have cerebrovascular disease [4]. Lung cancer has been reported to be the most common primary tumor in stroke patients with cancer, occurring in 30% of patients with ischemic stroke [5] and in 14% of patients with intracranial hemorrhage [6]. A population-based cohort study showed that lung cancer is associated with increased risk of subsequent stroke within 1 year after diagnosis for men and 2 years after diagnosis for women [7]. Moreover, lung cancer is well known to be associated with an increased risk of thromboembolic events [8]. Yet undiagnosed malignancy, including lung cancer, seldom presents as stroke. Only a few cases of occult cancer-associated stroke have been reported [9–11]. In these patients, stroke may precede a diagnosis of cancer and be the first clinical evidence of a hidden malignancy, but these studies only reported the initial manifestations of the stroke.

In the current study we report data obtained in a retrospective chart review of ischemic stroke patients with occult lung cancer in the absence of conventional stroke etiologies. We report the clinical presentation and imaging characteristics of initial and

* Corresponding author. Tel.: +86 75 9238 7322; fax: +86 75 9223 1754.
E-mail address: Longxuanlee2006@yahoo.com (L. Li).
[1] These authors have contributed equally to the manuscript.

http://dx.doi.org/10.1016/j.jocn.2014.05.039
0967-5868/

recurrent strokes of patients with occult lung cancer associated ischemic stroke (OLCA-stroke), which may provide a better understanding of the diagnosis and treatment of this subtype of stroke.

2. Methods and patients

We reviewed the clinical presentation, pathologic and radiologic records of ischemic stroke patients with occult lung cancer at our stroke center between January 2005 and April 2013.

The inclusion criteria for this study were (1) subjects presented with neurologic symptoms, (2) subjects had acute ischemic lesions identified on diffusion-weighted MRI (DWI), and (3) subjects had primary occult lung cancer, which was defined as undiagnosed lung cancer found and diagnosed during hospitalization at the time of stroke. The diagnosis of lung cancer was confirmed by radiological and histological evidence.

For all patients, age, sex, cancer diagnosis and types, vascular risk factors, treatments, and frequency of stroke and mortality in the first 3 months after initial stroke were recorded. Neurological imaging reports of relevant CT or MRI scans were reviewed, and all data relevant to stroke evaluation were identified and recorded. This included physical and neurological examinations such as National Institutes of Health Stroke Scale (NIHSS) scores, modified Rankin Scale scores, ultrasound of the extracranial vessels, cerebral MRI, including DWI, T1-weighted, T2-weighted, contrast enhanced sequences and fluid attenuated inversion recovery MRI, three-dimensional time-of-flight magnetic resonance angiography (MRA), contrast-enhanced MRA, Holter monitoring, echocardiography, and laboratory data (basic chemistries, complete blood count, coagulation studies, prothrombin time, activated partial thromboplastin time, fibrinogen, D-dimer, and screening for vasculitis).

The following patients were excluded from the study: (1) those who had one or more conventional stroke etiologies using the Stop Stroke Study Trial of Org 10172 in Acute Stroke Treatment (SSS-TOAST) classification [12]; (2) those who had not undergone MRI including DWI or these scans did not show acute ischemic lesions; (3) those who had primary or metastatic brain tumors; (4) those who had diagnosed malignancy treated or untreated before stroke; and (5) those who had any other primary occult cancers (not lung cancer) found and diagnosed during hospitalization at the time of stroke.

The Ethics Committee of Guangdong Medical College Affiliated Hospital approved our study. All patients gave their informed consent.

Descriptive statistics were used to summarize the clinical profiles of eligible patients.

3. Results

3.1. Patient profiles

Twenty-five patients were diagnosed with OLCA-stroke between January 2005 and April 2013. Twelve patients were excluded from the study. Ten patients had one or more conventional stroke etiologies (six patients had severe large artery atherosclerosis, three had atrial fibrillation, and one had large artery atherosclerosis and atrial fibrillation) and two patients didn't undergo MRI for individual reasons. The included patients (five men, eight women) were aged 44 to 70 years (mean ± standard deviation [SD]: 58.54 ± 8.72 years). The primary lung cancer was first discovered between 3 days and 2 months after stroke. Patient characteristics are presented in Table 1. Of the 13 patients, one had deep vein thrombosis, and one had splenic infarction. Regarding the location of the primary lung cancer, six were central and seven were peripheral. According to histological subtypes, there were eight (62%) adenocarcinoma, four (31%) squamous cell carcinoma and one (8%) adenosquamous carcinoma. Additionally, nine (69%) patients had systemic metastasis. Four patients received surgery, eight chemotherapy, and four radiotherapy, but three refused surgery, chemotherapy or radiotherapy. At admission, D-dimer levels ranged from 1.92 to 8.95 μg/mL (mean 5.69 ± SD 2.42 μg/mL, normal range: 0–0.25 μg/mL).

3.2. Symptoms at presentation

The symptoms of the first-ever ischemic stroke depended on the part of the brain involved. Overall, hemiparesis was the most common symptom (8/13 patients, 62%), followed by hypesthesia in five (38%) patients; visual disturbances were reported in 23%. At neurologic examination on admission, the mean NIHSS score was 5.23 ± SD 3.32 (median 5; range 1–15). Within 3 months of initial stroke, 12 of 13 (92%) patients suffered recurrent stroke, with four (31%) suffering one recurrent stroke, and eight (62%), two or more recurrent strokes (Table 1). Twenty-five percent of patients had their first recurrent stroke within 7 days of a first-ever stroke, 33% occurred from the second week to 1 month, 25% within the second month, and 17% over 2 months after the first-ever stroke.

In the 24 recurrent strokes, hemiparesis was observed in 10 (42%) patients, hemiplegia in nine (38%), dysphasia/dysarthria in eight (33%), and two (8%) were silent, confirmed by follow-up DWI. The mean NIHSS score at the time of first recurrent stroke (8.83 ± 4.38, median 7; range 4–17) was significantly higher than at admission ($p < 0.05$).

3.3. MRI and sonogram/ultrasound findings

MRI was performed between 3 hours and 7 days after onset, depending on the time of admission. The initial DWI lesion patterns of first-ever stroke are listed in Table 1. Overall, one patient (8%) had multiple small lesions defined as infarction <2 cm in diameter (MSS) in a single vascular territory, two (15%) patients had multiple small and large (>2 cm in diameter) disseminated lesions in a single vascular territory (MSLS), four (31%) patients had multiple small lesions in multiple vascular territories (MSM), and six (46%) patients had multiple small and large disseminated lesions in multiple vascular territories (MSLM). The vascular territories affected by first-ever stroke are shown in Table 2.

MRA revealed that eight patients had no significant stenosis or occlusion of the intracranial arterial vasculature, middle cerebral artery (MCA) occlusion was found in one patient, and distal arterial occlusions were detected in four. In all 13 patients, no significant stenosis or occlusion was observed on ultrasound of the carotid and vertebral arteries, however four patients had increased carotid intima-media thickness, and three had increased vertebral artery resistance index. Echocardiogram showed no sources of cardioembolism and did not find any aortic plaques in the ascending aorta or proximal arch.

Similar to first-ever stroke, four kinds of DWI lesion patterns, namely MSLM, MSM, MSLS, or MSS, were seen in recurrent strokes, and more MSLM/MSM were present than MSLS/MSS in both recurrent stroke and first-ever stroke. The frequencies of DWI lesion patterns and vascular territories affected by recurrent strokes are given in Table 2. As compared to first-ever stroke, MSLM was more frequent in recurrent strokes, but it did not differ significantly between them. The vascular territories affected by recurrent strokes were similar to those of first-ever strokes. For the individual patient, the recurrent stroke may affect a new