The Volume of the Spleen and Its Correlates after Acute Stroke

Nina L. Chiu, BS,* Brian Kaiser, DO,* Y Vien Nguyen, DO,†
Susan Welbourne, BSN, RN,‡ Chandana Lall, MD,† and Steven C. Cramer, MD*§

Background: Animal studies describe changes in the spleen following a stroke, with an immediate reduction in volume associated with changes in the counts of specific blood white blood cell (WBCs). This brain–spleen cell cycling after stroke affects systemic inflammation and the brain inflammatory milieu and may be a target for emerging therapeutic studies. This study aimed to evaluate features of this brain–spleen model in human patients admitted for acute stroke. *Methods:* Medical and imaging records were retrospectively reviewed for 82 consecutive patients admitted for acute stroke in whom an abdominal computed tomography scan was performed. *Results:* Mean ± SD splenic volume was 224.5 ± 135.5 cc. Splenic volume varied according to gender ($P = .014$) but not stroke subtype (ischemic versus hemorrhagic, $P = .76$). The change in splenic volume over time was biphasic ($P = .04$), with splenic volumes initially decreasing over time, reaching a nadir 48 hours after stroke onset, then increasing thereafter. Splenic volume was related inversely to percent blood lymphocytes ($r = -.36$, $P = .001$) and positively to percent blood neutrophils ($r = .30$, $P = .006$). *Conclusions:* Current results support that several features of brain–spleen cell cycling after stroke described in preclinical studies extend to human subjects, including the immediate contraction of splenic volume associated with proportionate changes in blood WBC counts. Splenic volume may be useful as a biomarker of systemic inflammatory events in clinical trials of interventions targeting the immune system after stroke. **Key Words:** Stroke—spleen—inflammation—white blood cell—lymphyocyte.

Introduction

After an ischemic stroke, the spleen is activated, affecting systemic inflammation and the brain inflammatory milieu. Animal studies describe a biphasic pattern of brain–spleen cell cycling after stroke. During an initial proinflammatory state, the spleen contracts over 1-4 days,[1-4] paralleled by increased release of lymphocytes and monocytes into the blood.[4,5] This is followed by a relatively immunosuppressed state.

Such insights into the biology of systemic responses to stroke are stimulating therapeutic discovery[3,6,7] and fostering human investigations focused on poststroke splenic events. A study of 29 patients with confirmed/suspected ischemic stroke or transient ischemic attack followed for 8 days found that splenic volumes tended to decrease by 24 hours then increase, and that splenic volume was inversely related to blood neutrophil, but not lymphocyte or monocyte, counts.[8] This study was an important exploration into splenic events following brain ischemia in humans; however, some findings did not agree with preclinical data, and several questions were not addressed such as findings after intracerebral hemorrhage.

From the *Department of Neurology, University of California, Irvine, California; †Department of Radiological Sciences, University of California, Irvine, California; ‡Decision Support Services, University of California, Irvine, California; and §Anatomy & Neurobiology, Physical Medicine & Rehabilitation, The Sue & Bill Gross Stem Cell Research Center, University of California, Irvine, California.

Received April 15, 2016; revision received June 23, 2016; accepted August 7, 2016.

Sources of funding: National Institutes of Health UL1 TR001414 and K24 HD074722.

Address correspondence to Steven C. Cramer, MD, UC Irvine Medical Center, 200 S Manchester Ave, Suite 206, Orange, CA 92868-4280. E-mail: scramer@uci.edu.

1052-3057/$ - see front matter

http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2016.08.012

The current study retrospectively reviewed medical records, brain imaging, and abdominal computed tomography (CT) scans from 82 patients admitted with acute ischemic or hemorrhagic stroke. The aim of this study was to examine splenic volume and its clinical correlates in relation to experimental animal data.[1-5]

Methods

Overview

All studies were carried out in accordance with the Institutional Review Board of the University of California, Irvine.

Participants

This retrospective study examined 100 consecutive patients admitted to the University of California Irvine Medical Center (1) with a discharge diagnosis of ischemic stroke or intracerebral hemorrhage, and (2) who also received an abdominal CT scan, ordered for a wide range of medical reasons. These 100 patients were admitted over a 5-year period.

Splenic Volume

Splenic volume was calculated directly from the abdominal CT scans. First, a radiologist specializing in abdominal imaging determined the maximum radius of the spleen in each of the 3 cardinal planes (anterioposterior, craniocaudal, and transverse). Splenic volume was then calculated as $4/3\pi * r1 * r2 * r3$, where r1, r2, and r3 stand for the 3 radii, respectively.

Volume of the Cerebral Infarct

Infarct volumes were determined directly from first brain imaging using MRIcro (http://www.cabiatl.com/mricro/mricro/mricro.html). For ischemic strokes, stroke volume was calculated directly from the magnetic resonance imaging scan (using the diffusion-weighted imaging pulse sequence) or if not available, head CT scan. For intracerebral hemorrhage, head CT scan was used.

Clinical Data

The clinical data extracted from the electronic medical record were age, gender, diabetes mellitus status, hypertension status, hyperlipidemia status, whether the patient received intravenous tissue plasminogen activator, type of stroke (ischemic versus hemorrhagic), time from stroke onset to abdominal CT, and time from stroke onset to the first complete blood count with differential. Data extracted from that complete blood count were total white blood cell (WBC) count, blood lymphocyte count (total and as a percent), and blood neutrophil count (total and as a percent), and blood monocyte count (total and as a percent).

Statistics

Parametric statistical methods were used for measures where the normality assumption was valid, using raw or transformed values, otherwise nonparametric methods were used. All analyses were two-tailed with alpha = .05 and used JMP 9.0 software (SAS, Cary, NC).

Results

Of the 100 patient records, abdominal CT was unavailable for 10 patients, performed prior to stroke onset in 2, head CT/MRI was not available in 2, time of stroke onset could not be determined in 2, and 2 patients did not have a new stroke, leaving 82 patients who are the focus of the current report. Clinical and radiological features for the 82 subjects are summarized in Table 1. Mean (±SD) splenic volume was 224.5 ± 135.5 cc. Examples of a smaller spleen and a larger spleen from among the 82 are provided in Figure 1. Incidental findings on the abdominal CT were common, the three most frequent examples of which were renal cyst in 16 subjects, diverticulosis in 12, and cholelithiasis in 10.

Splenic volume varied according to gender (251 ± 138 cc for males versus 185 ± 123 cc for females, $P = .014$) but not age ($P = .18$), stroke subtype (ischemic versus hemorrhagic, $P = .76$), or cerebral infarct volume.

The change in splenic volume over time was examined in 2 ways. The first asked whether splenic volume changed over time in a simple linear manner. Results were not

Table 1. *Clinical and radiological assessments*

Age (years)	65.9 ± 14.5
Gender	60% Male/ 40% Female
Diabetes mellitus	29%
Hypertension	71%
Hyperlipidemia	24%
Received tPA	8.8%
Volume of cerebral infarct (cc)	23.8 [5.7-70.3]
Type of stroke	66% Ischemic/ 34% Intracerebral hemorrhage
Time from stroke onset to abdominal computed tomography (days)	4.2 [.9-14.1]
Volume of spleen (cc)	224.5 ± 135.5
Time from stroke onset to WBC count (hours)	9.1 [2.5-26.1]
Blood total WBC count ($\times 10^3/\mu L$)	10.5 ± 4.0
Blood lymphocyte count ($\times 10^3/\mu L$)	1.6 ± .9
Blood WBC percent lymphocytes	17.4 ± 12.1%
Blood neutrophil count ($\times 10^3/\mu L$)	8.1 ± 4.0
Blood WBC percent neutrophils	73.6 ± 15.2%

Abbreviations: tPA, tissue plasminogen activator; WBC, white blood cell.

Values are mean ± SD or median [IQR].