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Original article

The relationship between anemia and recurrence of ischemic stroke in patients with Trousseau's syndrome: A retrospective cross-sectional study

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ABSTRACT

Objectives: The relationship between cancer and thrombosis was first recognized by the French internist Armand Trousseau in 1865. Trousseau's syndrome is a spectrum of symptoms that result from recurrent thromboembolism associated with cancer or malignancy-related hypercoagulability. In this study, we investigated whether demographics, clinical features, or laboratory findings were able to predict recurrent stroke episodes in patients with Trousseau's syndrome.
Methods: In total, 178 adult patients were enrolled in this retrospective cross-sectional study. All patients had been admitted to the emergency room of our hospital between January 2011 and September 2014 and were diagnosed with acute ischemic stroke. Patients were divided into two groups: patients with malignancy (Trousseau's syndrome), and patients without malignancy.
Results: There were several significant differences between the laboratory results of the two patient groups. For patients with Trousseau's, the hemoglobin levels for those with one stroke was 12.29 ± 1.81, while those in patients who had experienced more than one stroke was 10.94 ± 2.14 ($p = 0.004$).
Conclusions: Trousseau's syndrome is a cancer-associated coagulopathy associated with high morbidity and mortality rates. In this study, anemia was associated with increased stroke recurrence in patients with malignancy (Trousseau's syndrome).

1. Introduction

Among the neurological diseases, cerebrovascular diseases are the most common in developed countries. Stroke is the most common cause of death in these countries, and neoplastic diseases (cancer and hematologic tumors) are the second most common cause. However, stroke is a rare complication of cancer therapy, and does not occur as often as metastasis or neurotoxicity.[1,2]

A retrospective autopsy study of a large cohort of cancer patients performed by Graus et al showed that 15% of cancer patients have evidence of cerebrovascular disease, and about half of these patients have clinical symptoms of stroke.[3]

In this study, we retrospectively analyzed the *demographic*, clinical, and *laboratory* data of cancer and cancer-free patients that presented with acute ischemic stroke in the emergency department.

2. Materials and methods

2.1. Study population

A retrospective cross-sectional study including 178 adult patients was carried out after taking approval from institutional ethics committee. We retrospectively investigated patients who were

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admitted to our emergency department (ED) with ischemic stroke between January 1st, 2011 and July 15th, 2014. Medical history and physical examination data were obtained from all patients who were diagnosed with acute ischemic stroke**.** Acute ischemic stroke diagnoses were confirmed by further imaging tests of the *brain,* including computed tomography (*CT*) and diffusion-weighted magnetic resonance imaging (DW-*MRI*).

The ischemic stroke patients were divided into two groups: group 1; patients with active cancer (Trousseau's) and group 2; those without. Active cancer was defined as a confirmed malignancy, which was either treated or untreated in the six months before stroke.[4] Demographic characteristics and clinical data were collected and evaluated. These two groups were then divided into subgroups: those who had had one stroke (groups 1A and 2A) and those who had more than one (groups 1B and 2B). Patients who were diagnosed with transient ischemia or who had no evidence of either acute or chronic infarction after neuroimaging were excluded from the study. Patients with primary brain cancer and patients who had intracranial metastases were also excluded since these patients were thought to have different underlying stroke mechanisms.

2.2. Statistical analysis

All data was analyzed using SPSS software (version 15.0; SPSS Inc., Chicago, IL). The chi-square test was used to compare stroke risk factors and subtypes between cancer patients who had experienced one ischemic stroke and those who had experienced more than one. A student's t-test was used to compare biomarkers between the two groups. P value of <0.05 was considered statistically significant.

3. Results

Among the 200 adult patients referred to the ED with stroke, we identified 178 patients who were diagnosed as acute ischemic stroke. Nine patients with transient ischemia, eight patients with primary brain cancer and five patients who had intracranial metastases were excluded from the study. The active cancer group (group 1) included 91 patients (60 male, 31 female), and the stroke without cancer group (group 2) included 87 (56 male, 31 female). The mean age was 65.18 ± 11.98 among those with cancer and 62.80 ± 12.23 among those without; this difference was not significant (p = 0.193). Among the patients with active cancer, 24 had previously experienced a stroke whereas in the group without cancer, 15 had previously experienced a stroke. The demographic and clinical characteristics are shown in Table 1.

Laboratory tests, including blood urine nitrogen, creatinine, aspartate transaminase, alanine transaminase, hematocrit, D-dimer, C-reactive protein, hemoglobin, and platelet counts, were obtained for all patients, and significant differences were found between groups for all parameters (p < 0.05). The patients' laboratory values are shown in Table 2.

Patients with active cancer were divided into two subgroups based on the number of strokes experienced after malignancy diagnosis: only one stroke (n = 67; group 1A) or more than one (n = 24; group 1B) were. Hemoglobin and hematocrit levels were significantly greater among patients who had only one stroke: hemoglobin, 12.29 ± 1.81 vs. 10.94 ± 2.00 (p = 0.004, Fig. 1) and hematocrit, 37.15 ± 5.34 vs. 33.70 ± 6.51 (p = 0.012). Laboratory values for the two subgroups are shown in Table 3.

Among patients without cancer, laboratory values did not differ between those who had experienced only one stroke (n = 72; group 2A) and those who had multiple strokes (n = 15; group 2B) (Table 4).

Table 1
Demographic and clinical characteristics of ischemic stroke patients with malignancy (group 1) versus those with no malignancy (group 2).

	Group 1 (n = 91)	Group 2 (n = 87)	p^a
Age (years)	65.18 ± 11.98	62.80 ± 1 2.23	0.193
Gender (Female/Male)	31/60	31/56	0.828
Smoking	64	52	
Drinking	44	21	
Previous stroke history	24	15	
Hypertension	50	59	
Diabetes mellitus	27	36	
CAD	40	32	
Hyperlipidemia	18	4	
COPD	11	7	
CHF	9	1	
Liver Cirrhosis	5	–	
CRF	3	1	

Group 1, the ischemic stroke patients with malignancy (trousseau group); Group 2, the ischemic stroke patients with no malignancy; CAD, coronary arterial disease; COPD, chronical obstructive pulmonary disease; CHF, chronical heart failure; CRF, chronical renal failure.
[a] Student's t-test.

Table 2
Laboratory values of ischemic stroke patients with malignancy (group 1) and those patients with no malignancy (group 2) at the time of presentation.

Parameters	Group 1 (n = 91)	Group 2 (n = 87)	p^a
BUN (mg/dl)	25.19 ± 14.29	18.05 ± 7.01	<0.001
Cre (mg/dl)	1.02 ± 0.47	0.90 ± 0.30	0.034
AST (U/L)	(13–584)	(9–88)	0.004
ALT (U/L)	(6–236)	(6–71)	0.001
Hematocrit (%)	36.24 ± 5.84	41.20 ± 5.20	<0.001
D.dimer (ug FEU/ml)	(0.10–11.55)	(0.10–8.70)	<0.001
CRP (mg/dl)	(0.10–27.60)	(0.10–14.40)	<0.001
Hemoglobin (g/dl)	11.93 ± 1.98	13.61 ± 1.92	<0.001
Platelets ($\times 10^3 \mu L$)	262.58 ± 107.45	233.25 ± 66.35	<0.001

Group 1, the ischemic stroke patients with malignancy (trousseau group); Group 2, the ischemic stroke patients with no malignancy. BUN, blood urine nitrogene; Cre, creatinine; AST, aspartate transaminase; ALT, alanine transaminase; CRP, c-reactive protein.
[a] Student's t-test.

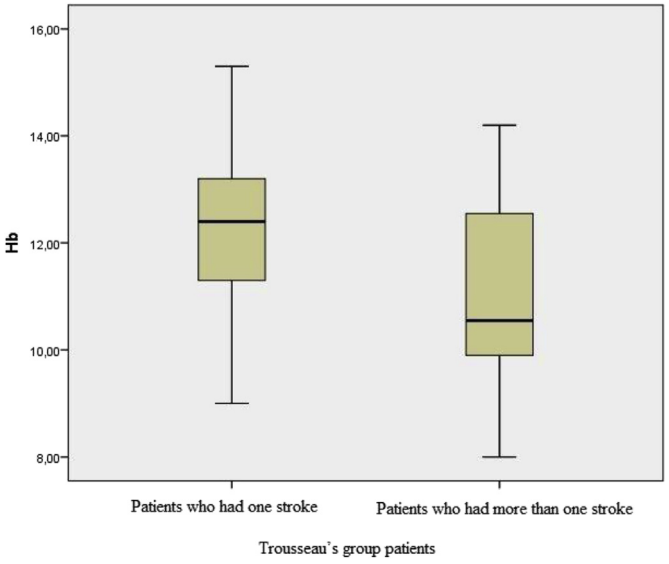

Fig. 1. Comparison of hemoglobin levels (median (interquartile range)) between Trousseau's group patients who had one stroke (group 1A) and those patients who had more than one stroke (group 1B) at the time of presentation.