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The diagnostic value of complete blood count parameters in patients with subarachnoid hemorrhage

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ABSTRACT

Objectives: Diagnosis of subarachnoid hemorrhage (SAH) in patients presenting with headache is challenging and there has been any biomarker studied for excluding of SAH in those patients. We aim to determine the sensitivity of leukocytosis or left shift to exclude the diagnosis of SAH in ED patients presenting with headache.

Method: Adult patients with headache who received a computed tomography (CT) with the diagnosis of SAH and had a complete blood count (CBC) represent the case group, headache patients with normal CT and had a CBC represent the control group. The white blood cell (WBC) count and percentage of polymorphonuclear cells (PMNs%) taken during admission and within the first 6 and 12 h of admission were recorded.

Results: A hundred ninety seven patients with SAH and 197 patients without SAH were enrolled in to study. Sensitivity, specificity, NPV and PPV of leukocytosis or increase in PMNs% (left shift) in the diagnosis of SAH was 89.8% (84.5–93.5, 95% CI), 46.7% (39.6–53.9, 95% CI), 82.1% (73.5–88.4, 95% CI) and 62.8% (56.8–68.4, 95% CI) respectively on initial emergency department (ED) admission.

Conclusion: CBC should be considered as a noninvasive test for the exclusion of SAH in ED patients with 6 h observation.

1. Introduction

Headache constitutes 2.2% of emergency department (ED) admissions.[1] One of the most important differential diagnoses in emergency department patients with headache is subarachnoid hemorrhage (SAH).[2] The most useful standard test in diagnosis of SAH is noncontrast computed tomography (CT), but it is not appropriate to routinely use CT in patients with a headache, because of high cost and radiation exposure.[3,4] There is no noninvasive diagnostic test to differentiate SAH in patients with headache. Our goal is to present the sensitivity of leukocytosis or increase in PMNs% in the diagnosis of SAH in patients who admit to the emergency department with a complaint of headache.

2. Materials and methods

This retrospective, case-control study was conducted in a tertiary ED that has approximately 190,000 visits annually. Approval of the local ethics committee was received before the study.

Adult patients that admitted to ED between the January 2008 and November, 2013 who received a head CT with the prediagnosis of SAH were detected by the hospital automation system. Patients aged 14 years or older, who were diagnosed with nontraumatic SAH with noncontrast head CT and who had a complete blood count (CBC) during the ED admission constituted the study group.

Patients who were admitted to the ED during the same dates with complaint of headache and that were discharged after being diagnosed with a nonspecific headache (ICD-10 code R51) with a

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normal noncontrast head CT, were identified. Among these patients, those who are at the same age and of same gender as the study group were selected by using vassarstats randomization program (http://vassarstats.net/rand01.html), and thus formed the control group. For each patient in the SAH group, first patient with the same age and gender in the control group was selected. If multiple patients were present with the same age and gender, patients in the control group were selected consecutively. Patients with a history of trauma, patients who did not have CBC during admission to the ED, and patients who had a history of hematooncologic diseases were excluded from the study.

Hospital electronic records of patients in the study group and control group were reviewed and age, gender, white blood cell (WBC) count and percentage of polymorphonuclear cells (PMNs%) values taken during admission and within the first 6 and 12 h of admission, and patient's outcomes were recorded on the data collection form. Noncontrast head CT images of patients with SAH were reviewed by a neurosurgeon through picture archiving and communication system (PACS). Also, noncontrast head CT scans of patients in the control group were reviewed by a neurosurgeon and the results were confirmed to be negative for SAH. Each patients' CT scan was administered with 5 mm slices for the fossa and 10 mm slices for other areas through Siemens Somatom Emotion 16 slices helical CT scanner.

The WBC, PMNs% counts were determined by a technical hematological cell counter (LH 780 Analyzer, Beckman Coulter Inc., Miami, FL, USA). All samples were analyzed within 2 h, using ethylenediaminetetraacetic acid (EDTA) containing tubes. The expected WBC and PMNs% values in our laboratory ranged between 4.2 and 10.6 K/μL and 37–80%, respectively. The criterion for leukocytosis required the WBC value to exceed 10.600 K/μL and a differential with PMNs% over 80% was considered to be increase in PMNs%.

2.1. Analysis

All statistical analyses were performed with SPSS version 17.0 for Windows (SPSS Inc., IL. USA). Normally distributed variables were expressed as mean and SD, whereas those that were asymmetrically distributed were expressed as median and interquartile range (IQR). To compare proportions and rates, $\chi 2$ tests and a Fisher's exact test were used for categorical variables, an independent sample *t*-test was used for parametric variables, and a Mann Whitney *U* test was used for nonparametric variables. Two-tailed p values less than 0.05 were considered to be statistically significant.

3. Results

Five hundred fifty four out of 1339 ED patients, who were received a noncontrast head CT, with the prediagnosis of SAH during the study, were confirmed by CT to have SAH. Among these patients, 318 of them had a traumatic SAH, four of them did not have a CBC and head CT images of 35 of them were not found in PACS and consequently were excluded from the study. The study group consisted of 197 patients. 5037 patients who were admitted to the ED during the study, and who were discharged with the diagnosis of a nonspecific headache, as their CT results were negative for SAH, were identified. A hundred ninety seven of these patients formed the control group after randomization (Fig. 1).

Fourty-six percent (n = 92) of patients in the control and study groups were males, with a median age of 58 years (IQR:47–67). Mean WBC count and PMNs% count of SAH patients admitted to the ED were found to be higher than those of the control group (Table 1). Sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) of leukocytosis or an increase in PMNs% in the diagnosis of SAH was 89.8% (84.5–93.5, 95% CI), 46.7% (39.6–53.9, 95% CI), 82.1% (73.5–88.4, 95% CI) and 62.8% (56.8–68.4, 95% CI), respectively. Control CBC count was repeated within 6 h (mean ± SD 154.4 ± 85.3 min) after ED admission in 52 (26.3%) of the study patients and within 12 h (mean ± SD 302.7 ± 200.1 min) in 89 (45.1%) of them. Leukocytosis or an increase in PMNs% were positive in all of the patients with SAH administered a control CBC count within the first 6 and 12 h

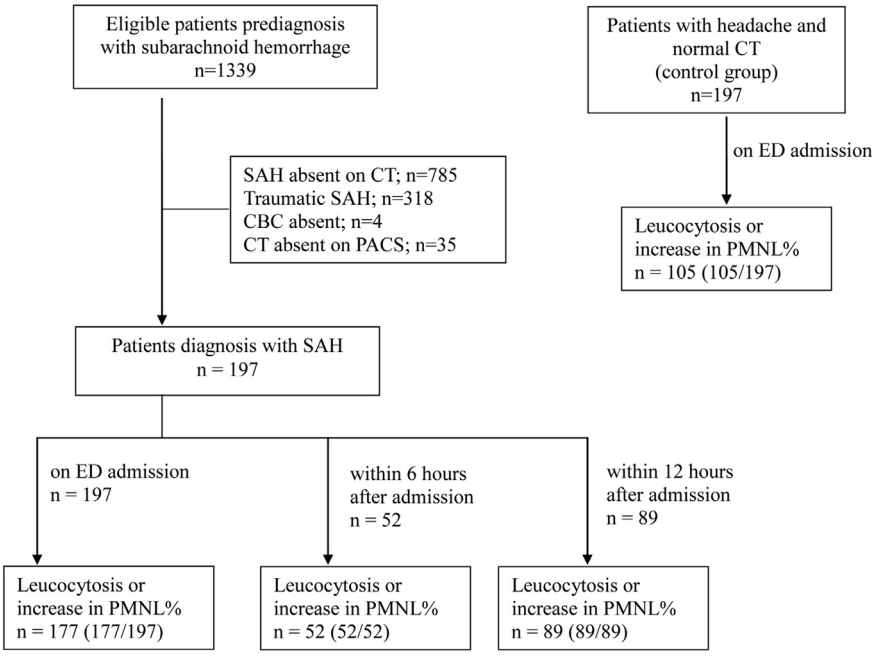

Fig. 1. Study flow chart. ED: emergency department, CT: computed tomography, SAH: subarachnoid hemorrhage, CBC: complete blood count, PMNL%: percentage of polymorphonuclear cells, PACS: picture archiving and communication system.

Table 1
Initial white blood cell count and the percentage of polymorphonuclear cells in patients with subarachnoid hemorrhage and control group.

	SAH group	Control group	p
WBC (K/μL) (mean ± SD); [95% CI]	13.3 ± 4.7; [12.7–14]	9.5 ± 3.5; [9–10]	<0.001
PMNs (%) (mean ± SD); [95% CI]	76.7% ± 15.8; [74.4–78.9]	65.2% ± 12.8; [63.4–67]	<0.001

SAH: subarachnoid hemorrhage.
WBC: white blood cell.
PMNs%: percentage of polymorphonuclear cells.

(Table 2). According to CBC values on admission, for leukocytosis or an increase in PMNs%; (+)LR value was 1.69 (1.47–1.93; 95% CI) and (−)LR value was 0.22 (0.14–0.33; 95% CI).

In patients, mortality was found to be 30.9% (n = 61). The mean WBC count of patients who died was found to be higher than SAH patients who survived (14.36 ± 5.07 K/μL, [13.1–15.7; 95% CI] vs 12.89 ± 4.47 K/μL [12.1–13.7; 95% CI], p = 0.049). There were no significant difference between the PMNs% counts of the surviving and deceased patients (76.70 ± 15.26 [74.1–79.3; 95% CI] vs 76.55 ± 16.91 [72.2–80.9; 95% CI], p = 0.548).

4. Discussion

SAH constitutes 1% of patients presenting to ED with the complaint of headache.[5,6] The most frequently used diagnostic tests for SAH are noncontrast head CT and lumbar puncture (LP).[2–4,7] CT, because of its high cost and exposure of the patient to ionizing radiation, and LP, due to its invasive nature, cannot always be used as screening tests in patients with headache.[8,9] There is no noninvasive laboratory test that can differentiate SAH in patients admitted to the ED with the complaint of headache. In our study, we demonstrate that both the WBC count or PMNs% were found to be elevated within 6th or 12th hours of admission in all nontraumatic SAH patients. CBC has an excellent sensitivity (100%) to exclusion of SAH in nontraumatic headache patients in ED.

An increase in the WBC count is associated with a poor prognosis and increased mortality in patients with pulmonary embolism, acute myocardial infarction (AMI), intracranial hemorrhage and ischemic stroke, as has been shown in the literature.[10–13] In patients with AMI, stroke and pulmonary embolism, it was stated that leukocytosis occurs due to cellular stress and the overall inflammatory process.[10,11,13] It is thought that increased leukocyte and PMNs% counts in patients with SAH is related to increased excitatory amino acid levels, ischemic changes, pro-inflammatory cytokine release, brain damage, and increased sympathetic and adrenocortical activity.[14,15]

McGirt et al. reported that in patients with SAH whose leukocyte count is 15 × 10 × 9/L during admission, are three times more likely to develop vasospasm, and suggested early aggressive treatment.[16] Parkinson D et al. stated that the mortality rate is over 50% in patients with SAH whose leukocyte count is 20.000 K/μL and above .[17] In our study, the median WBC count of patients who died was higher than that of control group. However, no study researching the sensitivity of an increase in leukocytosis and PMNs% in the diagnosis of SAH has been previously published.

In our study, we found that sensitivity of leukocytosis and an increased PMNs% on ED admission in the diagnosis of SAH was 89.8%. It may not be possible to safely rule out a disease such as SAH, which has a high mortality rate, depending on only one normal CBC. It can only be a rational approach to rule out the SAH in patients who have normal CBC results at 6 and 12 h after presentation. Administration of these methods would serve to be cost effective and protect patients from possible complications of LP and CT.

On the other hand, an increase in leukocytosis and PMNs% was detected in over half of the control group. In previous studies, it was stated that leukocytosis is seen in other headache etiologies such as migraine, temporal arteritis (giant cell arteritis), hypertension.[18–20] Therefore, the specificity of an increase in leukocytosis or PMNs% on admission was found to be only 46.7% in the diagnosis of SAH. Hence, CBC can only be used to rule out SAH in patients with headache who were found to be normal in control tests, not to confirm SAH.

4.1. Limitations

Diagnosis of SAH in the control group was ruled out with noncontrast head CT. Nevertheless, the diagnosis of SAH should not be merely ruled out with CT. Because this is a retrospective study there might be some patients both among the study and the control group that may have an infectious and/or inflammatory process or already using medications altering the WBC levels or have malignancy. The other limitation, control CBC after ED admission was not applied to the control group, therefore diagnostic specificity, NPV, PPV and LR of CBC within 6th and 12th hours were not measured. Our results should not be generalized for the pediatric age group

Table 2
The frequency of increase in white blood cell count and the percentage of polymorphonuclear cells in the SAH and control group patients on admission and within the first 6 and 12 h.

All patients	CBC on admission n = 197			Control CBC performed within 6 h n = 52			Control CBC performed within 12 h n = 89		
	PMNs% ≥ 80% n (%)	Leukocytosis n (%)	PMNs% ≥80% or Leukocytosis n (%)	PMNs% ≥ 80% n (%)	Leukocytosis n (%)	PMNs% ≥80% or Leukocytosis n (%)	PMNs% ≥ 80% n (%)	Leukocytosis n (%)	PMNs% ≥ 80% or Leukocytosis n (%)
SAH (+)	143/192[a] (74.5)	145/197 (73.6)	177/197 (89.8)	46/50[a] (92)	46/52 (88.5)	52/52 (100)	83/87[a] (95.4)	74/89 (83.1)	89/89 (100)
SAH (−)	74/197 (37.6)	74/197 (37.6)	105/197 (53.3)	–[b]	–[b]	–[b]	-[b]	-[b]	-[b]

SAH: subarachnoid hemorrhage.
CBC: complete blood count.
PMNs%: percentage of polymorphonuclear cells.
[a] The percentage of polymorphonuclear cells results of 5 patients on admission and that of 2 patients within 6 and 12 h could not be reached.
[b] Due to the fact that complete blood count of control group patients was not performed within 6 and 12 h, the specificity, negative predictive value and positive predictive value could not be calculated.

and traumatic SAH patients. A significant proportion of patients (35 patients) diagnosed as nontraumatic SAH and admitted to the hospital were excluded from the study because of not having CT in the PASC system. CBC results of patients excluded in this way were analyzed separately. CBC was not obtained in 1 of 35 patients during the first visit, and control CBC was not obtained in 18 patients within 12 h of ED admission. Among the 34 patients who CBC was studied on admission, 33patients were positive for increase in the WBC count or PMNs% (sensitivity 97.1%). All of the 12 patients whose control CBC was studied within 6 h and all of the 16 patients whose control CBC was studied within 12 h were positive for increase in the WBC count or PMNs% (sensitivity 100%).

5. Conclusion

Leukocytosis or increase in PMNs% on ED admission was positive in 89.8% of patients with nontraumatic SAH. In all patients with SAH, one of these two findings is positive in the control CBC performed within 6 h. Six hours after the ED admission, the control CBC might be used to rule out SAH in patients with nontraumatic headache.

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