

Bilateral Chronic Subdural Hematoma is Associated with Rapid Progression and Poor Clinical Outcome

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Abstract

Chronic subdural hematoma (CSDH) has been recognized as a benign disease, but its clinical outcome is not well documented. This study aims to expand the knowledge base regarding the outcome of CSDH. We retrospectively reviewed clinical characteristics of CSDH operated in the Kobe City Medical Center General Hospital between June 2005 and June 2012. Variants included age at onset, sex, laterality, presence of headache, consciousness level, and risk factors for hemorrhage such as malignancy or intake of anticoagulants. A total of 368 cases were analyzed. Six patients (1.4%) had a poor outcome, defined as any morbidity or mortality at 7 days postoperatively. Bilateral hematoma was significantly associated with a poor outcome ($p = 0.041$). Warfarin use and malignancy, albeit statistically not significant, were more frequently observed in patients with a poor outcome. Bilateral CSDH was observed in 53 patients (14.4%). Age at onset, sex, history of malignancy, anticoagulant use, and antiplatelet use did not differ between bilateral and unilateral CSDH. Recurrence rate was not different between bilateral and unilateral CSDH (14.2% vs. 11.3%), but poor outcome as a result of brain herniation was significantly higher in bilateral than in unilateral hematomas (5.7% vs. 0.3%, $p = 0.01$). Bilateral CSDH was associated with rapid progression and showed worse outcome as a result of brain herniation in comparison with unilateral CSDH. Urgent trephination surgery for decompression of hematoma pressure may be recommended for bilateral CSDH.

Key words: chronic subdural hematoma, bilateral, acute deterioration, mortality, brain herniation

Introduction

Chronic subdural hematoma (CSDH) is one of the most common neurosurgical diseases, and is recognized as a benign hematoma that can be treated by trephination therapy using local anesthesia.^{1–6} The number of affected patients is increasing because of our aging population, and recent reports indicate that 2–4% of cases have a poor outcome even after successful surgical treatment.⁷ Previous reports analyzed mainly risk factors for recurrence and technical complications after trephination therapy, but few have focused on poor clinical outcome as a result of the progression of the disease.⁸ In this study, we analyzed the risk factors for CSDH, and our results reveal that bilateral involvement was

associated with a poor outcome attributable to brain herniation.

Materials and Methods

We retrospectively reviewed CSDH cases that were operated in the Kobe City Medical Center General Hospital between June 2005 and June 2012. Neurological symptoms associated with compression of the brain by hematoma were an indication for surgical treatment. Hematoma was evacuated by burr-hole surgery. When a patient had coagulation disturbance including therapeutic anticoagulation use or malignancy, preoperative treatment with vitamin K, fresh frozen plasma or prothrombin complex concentrate was administered. Patients who were treated conservatively were not analyzed in the study. Clinical record was obtained including age

at onset, sex, medical history including malignancy, medication including anticoagulants or antiplatelet drugs, laterality of hematoma, and clinical presentation such as headache, decline of consciousness, or motor weakness. We analyzed the relationship among these variants and the risk of recurrence, morbidity, and mortality. Poor clinical outcome was defined as modified Rankin scale of 5–6 at 7 days after surgery. The Student’s *t* test was used for continuous variables, and chi-square statistics or the Fisher’s exact test was used for categorical variables. Univariate and multivariate logistic regression analyses were also performed to identify independent risk factors. Age, sex, and variables with *p* < 0.1 in univariate analysis were selected for multivariate analysis. All these statistical analyses were performed using R statistical software. The study was approved by the institutional review board of our institution.

Results

A total of 368 patients were reviewed. Clinical characteristics of the population under study are shown

in Table 1. Average age at onset was 74.2 ± 12.8 years, and 246 (66.8%) patients were male. Motor weakness was the most common clinical presentation, observed in 274 of the 368 patients. Headache was observed in 72 patients. Forty-one patients (11.1%) used warfarin, 67 (18.2%) patients had a history of malignancy, 46 (12.5%) had dementia, and 16 (4.3%) had depression.

Six (1.6%) of the 368 cases had a poor clinical outcome. Bilateral hematoma, pupil abnormality (anisocoria and dilated pupils), and acute decline of consciousness were significantly associated with a poor outcome (*p* = 0.04, *p* < 0.001, and *p* < 0.01, respectively). Warfarin use and malignancy were more frequently observed in patients with a poor outcome, but these factors did not reach statistical significance. Bilateral hematoma was seen in 53 cases (14.4%), similar to the percentage in previous reports (16–45%). Average Glasgow Coma Scale (GCS) on admission was 14.0 ± 2.2. When we compared clinical characteristics between patients with bilateral and unilateral hematomas, there was no difference in age, sex, warfarin use, antiplatelet

Table 1 Comparisons of characteristics and clinical presentation between good outcome patients and poor outcome patients with chronic subdural hematoma

	Good outcome n (%)	Poor outcome n (%)	<i>p</i>
Number	362	6	
Age (mean ± SD)	72.5 ± 13.4 y	75.8 ± 7.5 y	0.332
Male	243 (67.1)	3 (50.0)	0.412
Warfarin use	39 (10.8)	2 (33.3)	0.136
Antiplatelet use	56 (15.5)	1 (16.7)	1
Hypertension	172 (47.4)	3 (50.0)	1
Hyperlipidemia	72 (19.8)	2 (33.3)	0.346
Diabetes mellitus	77 (21.3)	0 (0)	0.351
Liver disease	28 (7.7)	1 (16.7)	0.390
Dementia	46 (12.7)	0 (0)	1
Depression	15 (4.1)	1 (16.7)	0.236
Malignancy	64 (17.7)	3 (50.0)	0.076
Bilateral involvement	50 (13.8)	3 (50.0)	0.041*
GCS on admission	13.7 ± 3.3	8.8 ± 5.0	0.065
Consciousness disturbance	174 (48.1)	5 (83.3)	0.113
Anisocoria or dilated pupils	11 (3.0)	3 (50.0)	< 0.001*
Acute decline of deterioration	7 (1.9)	3 (50.0)	< 0.001*
Headache	69 (19.2)	3 (50.0)	0.094
Motor weakness	271 (77.7)	3 (50.0)	0.314

GCS: Glasgow Coma Scale, n: number of cases, SD: standard deviation, **p* < 0.05.

Table 2 Comparisons of characteristics and clinical presentation between unilateral and bilateral chronic subdural hematoma

	Unilateral, n (%)	Bilateral, n (%)	<i>p</i>
Number	315	53	
Age (mean ± SD)	72.2 ± 13.4 y	74.2 ± 12.8 y	0.303
Male	214 (67.9)	32 (60.4)	0.379
Warfarin use	32 (10.2)	9 (17.0)	0.157
Antiplatelet use	52 (16.5)	5 (9.4)	0.222
Hypertension	152 (48.1)	23 (43.4)	0.555
Hyperlipidemia	69 (21.8)	5 (9.4)	0.041*
Diabetes mellitus	73 (23.2)	4 (7.5)	0.001*
Liver disease	26 (8.2)	3 (5.9)	0.782
Dementia	41 (13.0)	5 (9.4)	0.653
Depression	9 (2.9)	7 (13.2)	0.004*
Malignancy	9 (3.4)	8 (15.1)	0.700
Consciousness disturbance	158 (50.2)	21 (39.6)	0.182
Anisocoria or dilated pupils	8 (2.5)	6 (11.3)	0.008*
Acute decline of consciousness	0 (0)	10 (18.9)	< 0.001*
Headache	56 (17.9)	16 (30.2)	0.060
Motor weakness	239 (79.4)	35 (66.0)	0.048*
Recurrence	45 (14.2)	6 (11.3)	0.672
Morbidity	0 (0)	1 (1.9)	0.144
Mortality	3 (0.9)	2 (3.8)	0.152
Morbimortality	3 (0.9)	3 (5.7)	0.041*
CSDH-related morbimortality	1 (0.3)	3 (5.7)	0.010*

CSDH: chronic subdural hematoma, n: number of cases, SD: standard deviation, * $p < 0.05$.

use, or malignancy (Table 2). Dyslipidemia and diabetes mellitus were more frequently observed in unilateral CSDH, and bipolar disorder was more frequently observed in bilateral CSDH (Table 2). Headache, pupil abnormality, and acute decline of consciousness were more often seen in patients with bilateral CSDH, and hemiparesis was more frequent in patients with unilateral CSDH. The recurrence rate of hematoma was 14.2% for unilateral and 11.3% for bilateral cases, which was not statistically different ($p = 0.67$). A poor clinical outcome was observed in three (5.7%) patients with bilateral hematoma and three (0.9%) with unilateral hematoma. Among these, poor outcome resulting from brain herniation due to hematoma expansion was observed in three cases (5.7%) of bilateral CSDH and one case (0.3%) of unilateral CSDH, significantly higher in bilateral cases ($p = 0.01$; Table 3). Multivariate logistic regression analysis adjusted for age and sex showed that bilateral hematoma was significantly associated with

poor clinical outcome ($p = 0.037$; Table 4). Significant association was retained after further adjustment for medical history of malignancy ($p = 0.027$; Table 4).

Among 53 patients with bilateral involvement, consciousness disturbance was observed in 21 (39.6%), and 10 patients showed rapid deterioration of consciousness, with 6 declining to a GCS score of less than 8 at admission. All these patients showed anisocoria or bilateral dilated pupils; one patient died and others had severe disability (morbimortality rate, 3.8%). Among six cases of rapid progression, three patients had a history of malignancy and the other three a history of warfarin medication.

Representative Case

A 67-year-old man who had surgical resection of tongue carcinoma experienced headache for 1 month. He visited a local clinic after he felt motor weakness in both extremities with worsening of the

Table 3 Characteristics of six cases with poor clinical outcome

	Age	Sex	Past history	Outcome	Cause of outcome
Unilateral	74	F	Myelodysplastic syndrome	Death	Brain herniation
	68	F	Leukemia	Death	MOF
	85	M	DVT (Warfarin), COPD	Death	ARDS
Bilateral	83	M	Atrial fibrillation (Warfarin)	Vegetative state	Brain herniation
	67	M	Malignancy (post surgery)	Death	Brain herniation
	78	F	Malignancy (terminal stage)	Death	Brain herniation

ARDS: acute respiratory distress syndrome, COPD: chronic obstructive pulmonary disease, DVT: deep vein thrombosis, F: female, M: male, MOF: multiple organ failure.

Table 4 Multivariate logistic regression analysis showing risk factors for poor clinical outcome of patients with chronic subdural hematoma

	Univariate <i>p</i>	Age- and sex-adjusted <i>p</i>	Multivariate <i>p</i>
Bilateral	0.041	0.036	0.027
Malignancy	0.076	0.029	0.021

Multivariate *p* represents *p* value after adjustment for age, sex, bilateral, and malignancy.

headache. He was diagnosed with CSDH by computed tomography (CT) and was transferred to our hospital by ambulance. The patient sustained a decline of consciousness in the ambulance, and the GCS at admission was E1V1M1 (i.e., 3). CT images showed bilateral subdural hematoma with horizontal fluid level (niveau) on the right side (Fig. 1A, B). Low-density signal around the ambient cistern was not visualized and the third ventricle was detected posterior to the clivus, indicating the presence of uncus and downward herniation. Emergent simultaneous bilateral hematoma evacuation was performed with respiratory and cardiac controls. Intracranial pressure was high without apparent signs of intracranial hypotension. Postoperative CT showed disappearance of the CSDH and resolution of the uncus and downward herniation (Fig. 1C, D). Although surgical procedures were uneventful, the patient eventually died of diffuse brain ischemia (Fig. 1E, F).

Discussion

Our data show that the outcome of CSDH was not always benign, with 1.6% of cases having a poor clinical outcome, consistent with previous reports.⁷⁾ Bilateral involvement was raised as a predictor of rapid deterioration and poor outcome in CSDH, with a morbimortality rate of 3.8% (poor clinical outcome at 7-postoperative day was as high as 5.4%). Although there was no difference in the frequency

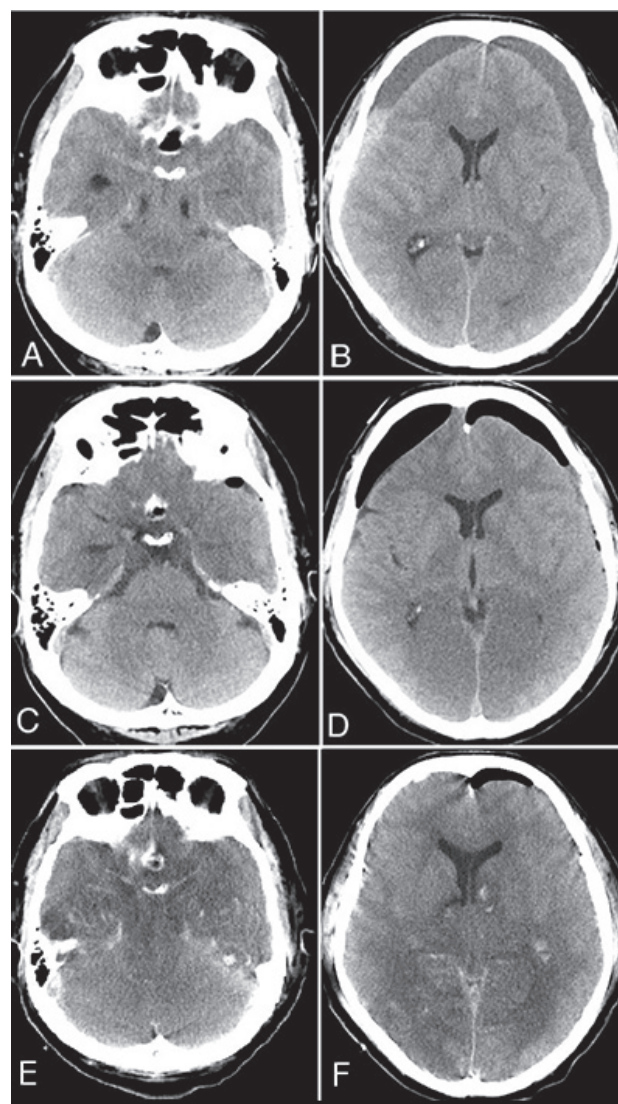


Fig. 1 A, B: A computed tomography (CT) scan showing a bilateral chronic subdural hematoma with uncus and downward herniation. C, D: Postoperative CT scan showing disappearance of the chronic subdural hematoma, and resolution of uncus and downward herniation. E, F: A CT scan 1 day after surgery showing diffuse brain ischemia by brain herniation.

of warfarin intake or medical history of malignancy between unilateral and bilateral CSDH, either of these two factors was observed in all cases with rapid worsening of clinical symptoms, suggesting that patients with bilateral CSDH with coagulation disturbance might be at the highest risk of acute deterioration and poor clinical outcome.

The risks of poor clinical outcome have been reported to be technical complications and poor clinical condition as a result of infection, liver dysfunction, and renal dysfunction.⁷⁾ Brain herniation resulting from CSDH has not frequently been reported, but in the present study four patients (1.1%; 3.8% of bilateral CSDH) had brain herniation. Among three cases of bilateral CSDH with brain herniation, all showed downward herniation, which leads to severe disability or death. If those who take warfarin or have a history of malignancy experience headache or neurological deficits, special attention should be paid regarding the presence of bilateral CSDH.

Bilateral involvement of CSDH was reported to be associated with the use of warfarin or antiplatelets.⁷⁾ However, in our patients there was no difference between unilateral and bilateral CSDH with respect to warfarin or antiplatelet use. Tsai et al. reported that patients with bilateral CSDH were more likely to show symptoms associated with increased intracranial pressure such as headache, but less likely to show symptoms associated with brain shift such as hemiparesis.⁷⁾ In fact, hemiparesis was more frequently seen in unilateral CSDH, with headache or acute deterioration of consciousness being more frequent in bilateral CSDH. Huang et al. cautioned that a diagnosis of bilateral CSDH could be delayed by a lack of specific symptoms.⁹⁾

Bilateral involvement was associated with rapid progression of CSDH in our series. Rapid decline of consciousness (mostly within a day after the first symptom) was also associated with a poor clinical outcome, with 3 of 10 such cases (30%) having a poor clinical outcome. It is not clear whether a specific medical history is associated with rapid progression. Our data indicate that warfarin use and a history of malignancy may be associated with rapid progression, but another report suggested that there is a risk of rapid progression regardless of medical history.¹⁰⁾ Clinical indicators of rapid progression were reported to be fluid level (low density in the upper portion of hematoma and high density in the lower portion of hematoma) on CT images, hypointensity hematoma on T₁-weighted magnetic resonance images, and hyper- or hypointensity hematoma on T₂-weighted images, all of which indicate fresh bleeding.¹⁰⁾ Taken together, bilateral CSDH or CSDH with radiological findings

of fresh bleeding should be treated immediately after diagnosis regardless of the medical condition at diagnosis.

Recent reports suggest that spontaneous intracranial hypotension may be associated with bilateral progression of CSDH.^{11–14)} If there are clinical signs indicating intracranial hypotension, such as orthostatic headache or low hematoma pressure at trephination, CT myelography and epidural blood patch at the site of the cerebrospinal fluid leak should be considered, otherwise patients who have received trephination therapy may develop tension pneumocephalus, epidural hematoma, or acute subdural hematoma.^{11,15)} In our series, none of 53 patients with bilateral involvement was diagnosed as spontaneous intracranial hypotension, although there was a possibility of missed diagnosis.

There are several limitations to the present study. First, we only included surgical cases, owing to the limited access to clinical information on non-surgical cases. However, because subclinical subdural hematomas are rarely detected and most patients have neurological symptoms that need surgical intervention as reported previously,⁴⁾ inclusion of non-surgical cases is unlikely to affect the results and conclusion of the present study. Second, details of CT findings are also lacking. As is shown in the previous report, CT findings such as fluid levels in hematomas may be associated with the clinical outcome.¹⁰⁾ However, bilateral involvement still remains an important indicator of poor clinical outcome.

Conclusion

CSDH is not necessarily benign. Bilateral hematoma has a higher risk of acute deterioration of clinical symptoms because of downward herniation, resulting in a poor clinical outcome. Thus, an urgent operation should be considered for CSDH with bilateral involvement, especially for those with coagulation disturbance.

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Conflicts of Interest Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this article. All authors have registered Self-reported COI Disclosure Statement Forms online through the website for the Japan Neurosurgical Society members.

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