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Case Report

Therapeutic Suggestions for Chronic Subdural Hematoma Associated with Idiopathic Thrombocytopenic Purpura: A Case Report and Literature Review

Hajime Takase,[1,2] Junya Tatezuki,[2] Naoki Ikegaya,[1,2] Daisuke Yamamoto,[2] Mizuki Hashimoto,[2] Makoto Takagi,[2] Yasuhiko Mochimatsu,[2] and Nobutaka Kawahara[1]

A 66-year-old woman who was previously diagnosed with idiopathic thrombocytopenic purpura (ITP) presented with mild right-sided hemiparesis and drowsiness. Head computed tomography (CT) imaging demonstrated a massive left chronic subdural hematoma (CSDH) with a midline shift. Because initial laboratory data showed a significantly decreased blood platelet count ($0.3 \times 10^4/mm^3$), medical treatments such as platelet transfusion, intravenous immunoglobulin (IVIG), and high-dose corticosteroid therapy, were initiated. She clinically and radiologically responded well to these treatments without any surgical intervention. In addition to presenting our case, we searched the PubMed and Ichushi Web databases to comprehensively illustrate clinical characteristics and treatment outcomes of similar cases. Including the present case, we found 19 reports and 23 cases of CSDH associated with ITP in the literature, and assessed 17 reports and 21 cases that were written in English and Japanese. None or mild neurological symptom were seen in 13 cases, and severe, such as coma and hemiparesis, were described in the younger 8 cases with significant difference. All except one were first treated with medical therapies. Most cases of the former group responded well to conservative therapy. On the other hand, most in the latter eventually needed surgical treatment in addition except recent two cases including the present case. CSDH associated with ITP is rarely described, and its management remains controversial. However, this report highlights multiple continuous medical treatments under strict observation and general care might be a useful alternative to avoid surgery in cases presenting with severe neurological deficits and extremely low platelet counts.

Keywords: idiopathic thrombocytopenic purpura, chronic subdural hematoma, intravenous immunoglobulin therapy, high-dose corticosteroid therapy, conservative therapy

Introduction

Intracranial hemorrhage is a rare and often fatal complication of idiopathic thrombocytopenic purpura (ITP), constituting 0.1–2% cases,[1–4] usually as an acute onset form, such as intracerebral and subarachnoid hemorrhage (ICH and SAH) or acute subdural hematoma (ASDH).[5–10] Thus far, a total of 19 reports and 23 cases of ITP-associated chronic subdural hematomas (CSDHs) have been reported.[11–28] In this report, we describe a characteristic CSDH case associated with ITP, which includes a comprehensive review of the literature and highlights the treatment option of these disorders.

Case Report

I. Patient history and initial examination

A 66-year-old Japanese woman, who was diagnosed with chronic ITP 8 years previously at an outpatient department and was previously treated with continuous corticosteroid administration and a three-drug combination therapy for *Helicobacter pylori*, presented with worsening nausea, headache, mild right-sided hemiparesis, and drowsiness. The patient had a history of autoimmune hepatitis, diabetes mellitus (suspected to be steroid-induced), hypertension, and mild head trauma 10 days before presentation. In addition, the patient reported that nausea and headache developed 2 days before admission, and drowsiness was indicated upon admission.

On admission, her right-sided motor paralysis was dominant in the upper extremity, and the result of a motor muscle test was 4/5. An initial physical examination revealed neither fever nor neck stiffness, and an initial laboratory examination showed a significantly decreased platelet count of $0.3 \times 10^4/mm^3$ and a low hemoglobin level of 9.5 g/dl. Prothrombin time was 14.0 s (normal, 10.5–13.5 s), and activated partial thromboplastin time was 49.7 s (normal, 25.0–35.0 s). Brain computed tomography (CT) imaging revealed an iso-dense area on left frontoparietal convexity with a midline shift, indicating massive CSDH (Fig. 1).

II. Initial treatment and clinical course

Considering the patient's clinical CSDH manifestations, surgery was generally indicated. However, the combination of a low platelet count and surgery was considered to be a fatal risk for this patient. Therefore, the patient was reluctantly started on 15 U of random donor platelet transfusions and intravenous prednisolone at 1 mg/kg body weight with gradual tapering under strict blood sugar control along with other supportive therapy. She was also administered

[1]Department of Neurosurgery, Graduate School of Medicine, Yokohama City University, Yokohama, Kanagawa
[2]Department of Neurosurgery, Yokohama City Minato Red Cross Hospital, Yokohama, Kanagawa

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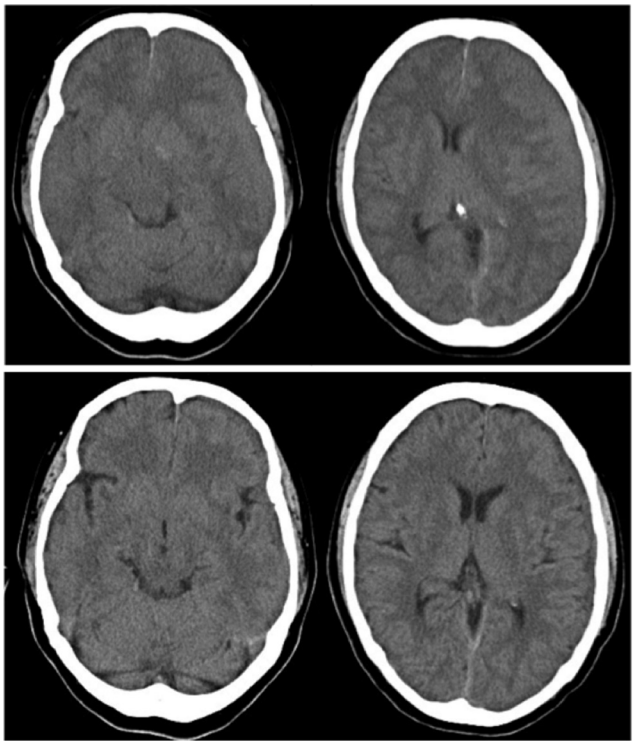

Fig. 1 Brain computed tomography showing subdural hematoma on the left side and compression of the left ventricle with a midline shift on admission (upper), and resolution of the subdural hematoma with normalization of the left ventricle after treatment (day 25) (lower).

high-dose intravenous immunoglobulin (IVIG) at 0.4 g/kg body weight. On day 3, all physiological findings including severe headache, nausea, drowsiness, and hemiparesis improved. The patient was clinically, hematologically, and neuroradiologically normalized 10 days after presentation without any surgical intervention (Fig. 1), and her platelet count increased to $21 \times 10^4/mm^3$.

Literature Review

In addition to a detailed presentation of the present case, we retrieved cases from the PubMed (www.ncbi.nlm.nih.gov/pubmed) and Ichushi Web (Japan Medical Abstracts Society; http://www.jamas.or.jp/about/english.html) databases using the terms "subdural hematoma," "ITP," and "thrombocytopenia" to comprehensively illustrate ITP-associated CSDH. We extracted data on patient age, gender, traumatic episode history, initial blood platelet count, clinical symptoms, and treatment and outcome. In addition, we defined the signs indicating neurological severity (i.e., any hemiparesis or severe disturbance of consciousness which presented 100 or more in Japan Coma Scale) as severe symptom, divided the cases into two groups, asymptomatic/mild and severe symptoms, and compared the patient age, gender, traumatic episode history, and platelet count to investigate the risk factor of severe symptoms. In this review, we considered all patients with iso- or low-density areas located in the subdural space on CT without an acute clinical course to have CSDH.

Wilcoxon signed-rank test was used to compare patient age and blood platelet count, whereas Fisher's exact probability test was used to compare gender, traumatic episode history, surgical procedure, and clinical outcome. JMP version 11 statistical software (SAS Institute Inc., Cary, North Carolina, USA) was used for statistical analyses, and $p < 0.05$ was considered statistically significant.

Including our case, we found 23 cases of ITP-associated CSDH reported in the literature and assessed a total of 21 cases that were written in English and Japanese as presented in Table 1. ITP-associated CSDH occurred in patients of all ages, although the mean patient age was 42.0 years (range, 9–88 years; median age, 41 years). Two cases were children, while the remaining were primarily middle-aged adults. Of note, five cases were males, while 16 were females (female to male ratio, 3:1). Three (14%) cases had a history of trauma, but such histories were not available in two cases. The initial mean blood platelet count was $2.1 \times 10^4/mm^3$, and seven (33%) were high-risk cases with a platelet count $< 1.0 \times 10^4/mm^3$. Three cases (14%) had no symptoms, whereas the remaining 18 (86%) exhibited some symptoms, primarily increased intracranial pressure, and 8 (38%) demonstrated severe signs, such as hemiparesis or coma. Twenty cases were initially treated with single or multiple medical therapies using platelet transfusion, IVIG, or corticosteroid therapy. Azathioprine, ascorbic acid, and traditional Chinese medicine were given in one case, which had a good outcome. Eight (38%) cases underwent surgery but none included splenectomy. In severe cases, the patients primarily received prior surgical intervention. Otherwise, two recent cases that received only medical treatment had successful outcomes. Two patients died because of poor general condition and progressive renal failure due to systemic lupus erythematous.

Discussion

ITP is defined as an isolated low platelet count due to antiplatelet autoantibody production, which may lead to bleeding of various organs, and is now generally considered a benign disease. Although ITP rarely causes intracranial hemorrhage (0.1–2% cases in the literature), it is considered a poor prognostic factor.[2,5,29] The onset of most instances of intracranial hemorrhage with ITP occurs acutely, such as that seen with ICH, SAH, or ASDH, or may even occur spontaneously. In cases of ITP-associated intracranial hemorrhage, the incidence of CSDH is rare and was present only in 23 cases retrieved from the literature, including the present case.

The onset of ITP-associated CSDH is not age-specific, but seems to occur more often in females, which is similar to the incidence of ITP in the general population.[30] A significant amount of severe cases occurred in younger patients and, in general, younger CSDH patients presented with symptoms resulting from increasing intracranial pressure, whereas older patients showed hemiparesis or consciousness disorders.[31,32] However, the reasons for these discrepancies remain unclear because of the limited number of cases. Analysis of the other parameters, including blood platelet count, showed no statistically significant differences (Table 2). Overall,

Table 1 Chronic subdural hematomas associated with idiopathic thrombocytopenic purpura

Series	Age (years)	Sex	Trauma	Platelet count (10^4/mm^3)	Neurological symptoms	Severity signs	Preoperative treatment	Surgery[a]	Outcome
González et al. (1984)[13]	10	F	–	1.0	CD	Coma, Hemiparesis	PLT, S	+	Survived
Chen et al. (1986)[12]	58	F	–	1.8	HA	–	IVIG	+	Survived
Kolluri et al. (1986)[18]	18	M	–	3.0	CD, Seizure	Coma, Hemiparesis	PLT, S, Fresh blood	+	Survived
Ishikura et al. (1988)[16]	20	M	+	N/D	HA, CD	Coma	IVIG	+	Survived
Ito et al. (1990)[17]	69	M	–	< 0.5	CD (nearly alert)	Hemiparesis	IVIG	+	Survived
Sebe et al. (1990)[23]	41	M	–	0.7	HA, V, PE	–	S, IVIG	+	Survived
Miyamoto et al. (1997)[19]	51	F	+	0.5	HA, CD (nearly alert)	–	PLT, S, IVIG	+	Survived
Gupta et al. (1997)[14]	65	F	–	7.5	–	–	S	–	Survived
Sreedharan et al. (2000)[26]	38	F	–	3.0	–	–	S	–	Survived
Izumiyama et al. (2000)[28]	9	F	–	0.3	HA	Hemiparesis	PLT	+	Survived
Hirano and Ueoka (2001)[15]	88	F	–	0.5	HA	–	S, Azathioprine, Ascorbic acid, TCM	–	Survived
Singh et al. (2004)[25]	27	M	N/D	4.0	HA, N, V, PE	–	PLT, S	–	Survived
Seçkin et al. (2006)[24]	57	F	–	0.1	–	–	–	–	Survived
Panicker et al. (2009)[20]	60	F	–	2.5	HA, PE	–	IVIG	–	Survived
	48	F	–	1.6	HA, V, PE	–	So	–	Survived
	38	F	–	3.0	HA, V, PE	–	So	–	Survived
	26	F	–	3.0	HA, CD, V	Coma	PLT, S	–	Expired
	42	F	–	3.0	HA, V, PE	–	So	–	Expired
Chatterjee et al. (2010)[27]	33	F	–	2.0	HA, V, Bil.VI palsy	–	PLT, S	–	Survived
Patnaik et al. (2012)[21]	19	F	N/D	3.0	HA, V	Hemiparesis	PLT, S	–	Survived
Current study	66	F	+	0.3	HA, V, CD (drowsiness)	Hemiparesis	PLT, S, IVIG	–	Survived
Ryzhko et al. (2010)[22]					in Russian				
Alimoradi et al. (2011)[11]					in Danish				

HA: headache, CD: conscious disturbance, V: vomiting, PE: papillary edema, N: nausea, PLT: platelet transfusion, S: steroids, IVIG: intravenous immunoglobulin G, TCM: traditional Chinese medicine, N/D: not described, So: something not described about the contents, F: female, M: male, [a] burr hole evacuation.

these results indicated that younger age, rather than initial platelet count, was a more significant risk factor for ITP-associated severe CSDH.

The management of ITP-associated CSDH remains controversial, and previous treatments primarily included surgery, such as burr hole evacuation. However, in 1997, Gupta et al.[14] first reported the efficacy of medical treatment for an asymptomatic case, thereafter, this medical intervention has resulted in good outcomes not only in asymptomatic cases but also in those with mild symptoms. Moreover, in recent years, this therapy has also been applied for severe cases and resulted in good outcomes. These results suggest that asymptomatic or mild cases can be conservatively treated, and although severe cases may eventually require surgical intervention, those with low platelet counts may benefit from continuous multiple medical treatments and avoid surgery.

The literature review revealed several successful medical treatments for CSDH with ITP. Steroid therapy is the first line and most popular treatment for ITP; it was actually used in 12 (71%) of 17 cases to inhibit immune-mediated platelet

Table 2 Statistical assessments of each groups divided by clinical symptoms

Clinical symptoms	Total	None or mild (n = 13)	Severe (n = 8)	*p*
Sex (%)				0.33[b]
Male	5	2 (15)	3 (38)	
Female	16	11 (85)	5 (62)	
Median age (range)	41	48 (27–88)	19.5 (9–69)	0.046[a]
Trauma[c] (%)				0.48[b]
+	3	1 (8)	2 (29)	
–	16	11 (92)	5 (71)	
Median PLT count (10^4/mm^3)[d] (range)	2.0	2.0 (0.1–7.5)	2.0 (0.3–3.0)	0.49[a]
Surgical intervention (%)	8	3 (23)	5 (62)	0.16[b]
Mortality (%)	2	1 (8)	1 (13)	1.00[b]

[a]Wilcoxon signed rank test, [b]Fisher's exact test, [c]one case in each group was not described and was excluded, [d]one case in positive group was not described in detail and was excluded. PLT: platelet transfusion.

destruction, antibody production, and the overall progression of the subdural hematoma itself.[24] Prednisone administration (1 mg/kg body weight) is recommended because of its reliable response rate,[33] and dexamethasone is also preferred because of its efficacy to reduce cerebral edema.[5] Although an important side effect of steroid therapy is drug-induced diabetes mellitus, the blood glucose levels of our patient, who already had diabetes mellitus, were closely monitored. IVIG was administered to seven ITP patients; all demonstrated benefits from the treatment once their platelet levels normalized.[34,35] The responses were reportedly rapid and lasted approximately for a few weeks. However, it is necessary to closely monitor IVIG administration because of potential side effects, such as hemolytic anemia.[36] Platelet transfusion, which was provided in nine cases, is an emergency procedure to transiently stabilize the platelet count before attempting other treatments, such as surgery, particularly in cases with low platelet counts. In contrast, some specialists suggest that medical intervention may trigger the destructive activation of platelets. Other therapies, such as immunosuppressive drugs, ascorbic acid, or traditional Chinese medicines (EK-49), however, have not been sufficiently investigated to substantiate the preferable results reported by Hirano and Ueoka.[15] Splenectomy, plasmapheresis, or intravenous anti-D immunoglobulin therapy were described as useful options to improve the platelet count, but there was no case report regarding its efficacy in a case of CSDH.[10]

Conclusion

CSDH is a rare complication of ITP. Younger age was a significant aggravating factor of ITP-associated CSDH in this study. Although management of these cases remains controversial, some medical therapies were empirically initiated, and surgical treatment was provided to address neurological deficits. However, recent clinical reports suggested continuous integrated medical treatment with steroids, platelet transfusions, and IVIG under strict observation may not only be effective preoperatively, but also be curative alternatives to surgical intervention. As a result, in the case where there may be severe neurological symptoms and thrombocytopenia, the preceding medical management presents important options and may be the safer.

Conflicts of Interest Disclosure

All authors have no conflicts of interests to declare.

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Corresponding author:
Nobutaka Kawahara, MD, PhD, Department of Neurosurgery, Graduate School of Medicine, Yokohama City University, 3-9 Fukuura, Kanazawa-ku, Yokohama, Kanagawa 236-0004, Japan.
✉ nkawa@yokohama-cu.ac.jp