



Usefulness of Middle Meningeal Embolization to Prevent Recurrent Spontaneous Chronic Subdural Hemorrhage

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Spontaneous chronic subdural hematoma (SDH) is a rare condition that could develop in association with hematologic disease. A 66-year-old male developed a chronic SDH as an initial manifestation of chronic myelomonocytic leukemia (CMML). He experienced recurrent chronic subdural hemorrhage and newly developed intracerebral hemorrhage. Considering the scheduled long-term chemotherapy, bilateral middle meningeal artery (MMA) embolization was performed to prevent recurrence of subdural hemorrhage. Although pancytopenia occurred during the 7 months' follow-up period, residual chronic subdural hemorrhage was absorbed without recurrence. To our best knowledge, this is the first report of CMML with spontaneous chronic SDH. MMA embolization is potentially a useful and safe treatment option in the challenging clinical situations with underlying pathologies.

J Cerebrovasc Endovasc Neurosurg.
2018 March;20(1):40-46

Received : 23 June 2017

Revised : 5 January 2018

Accepted : 5 March 2018

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Keywords Leukemia, Myelomonocytic, Subdural hematoma, Embolization

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INTRODUCTION

Chronic subdural hematoma (SDH) is commonly caused by trivial trauma followed by tearing of the cortical bridge veins or fragile vessels in the neomembrane, and repeated microhemorrhage.¹²⁾ Spontaneous chronic SDH is a very rare condition which can be developed in association with rupture of a cortical vessel, tumor, metastasis, or blood dyscrasias.¹⁴⁾²⁰⁾ We report a 66-year-old man who developed spontaneous chronic SDH that presented as the initial manifestation of chronic myelomonocytic leukemia (CMML). In addition, we reviewed the literature on chronic SDH associated with leukemic neoplasm and middle meningeal artery (MMA) emboliza-

tion to prevent recurrence of chronic SDH in high-risk patients.

CASE REPORT

Admission for chronic subdural hemorrhage

A 66-year-old right-handed male with a past medical history of hypertension and diabetes mellitus was admitted to our hospital for nausea, vomiting, and orbital pain for one day prior. He was on amlodipine and linagliptin. On the day of admission, the patient experienced a sudden severe right-sided weakness, without history of head injury or trauma. Head computed tomography (CT) scan conducted in the emergency room showed left-sided chronic SDH with sig-

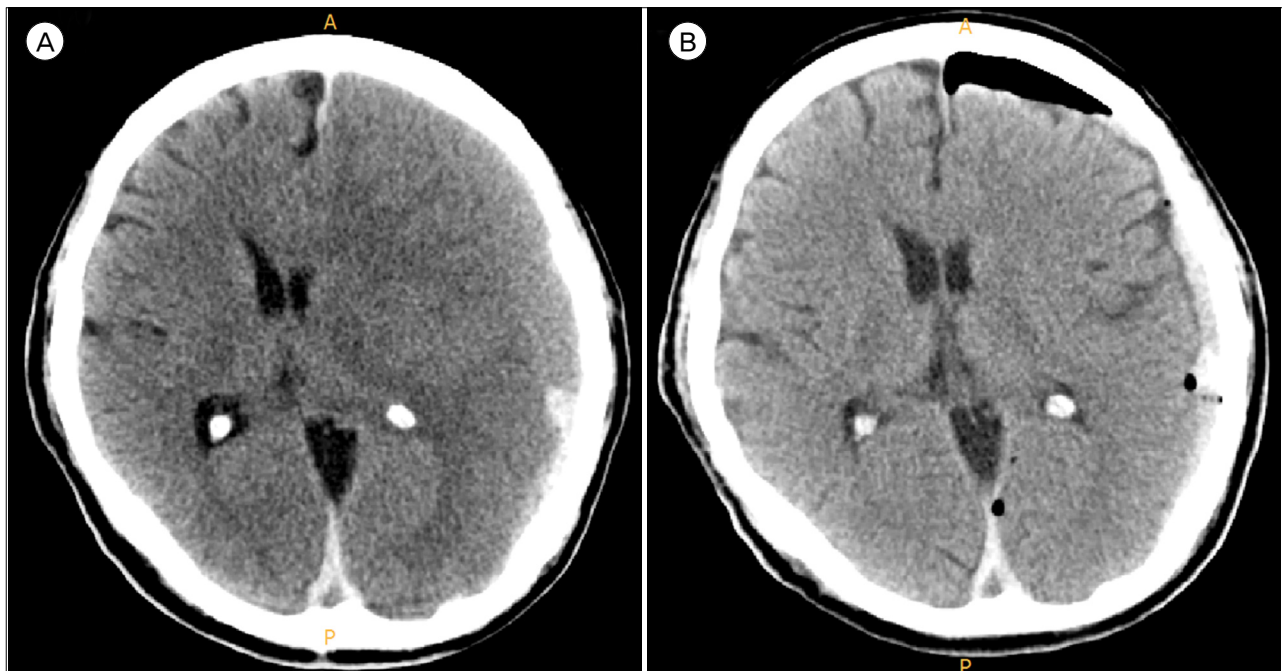


Fig. 1. (A) Unenhanced computed tomography (CT) scan at the time of admission showed left-sided isodensity chronic subdural hematoma. (B) CT scan performed after burr-hole drainage revealed decreased amount of subdural hematoma.

nificant mass effect (Fig. 1A). The patient was admitted to the neurosurgery department and underwent burr-hole drainage. Postoperative CT scan revealed decreased amount of SDH, and the symptoms of the patient were disappeared (Fig. 1B).

Detection of chronic myelomonocytic leukemia

At the time of evaluation, his mental status was alert and neurological examinations showed no focal deficits with full strength and intact sensation in bilateral extremities. Apart from an elevated blood pressure of 144/85 mmHg, his vital signs were stable. The patient was admitted to the neurosurgery department for further work-up including burr-hole drainage. Primary laboratory work-up showed elevated white blood cell (WBC) count of 59,300 cell/ μ L, with a significant left shift. Platelets count was 207,000/ μ L, with a hemoglobin level of 10.5 g/dL and a hematocrit of 43.8%. International normal ratio was 1.42, with prothrombin time and partial thromboplastin time values of 14.8 and 33.8 seconds, respectively. A repeat WBC count revealed an elevated level of 45,800 cell/ μ L.

Peripheral blood morphology revealed marked neutrophilia and monocytosis, and leucoerythroblastic feature (1/100 WBCs).

Based on these results, we suspected a hematological malignancy and referred the patient to the Hematology/Oncology department. Subsequently, the patient underwent a bone marrow biopsy with cytogenetics analysis including fluorescence in situ hybridization. The results revealed hypercellular marrow (almost 100% cellularity) and diffuse interstitial infiltration of immature cells suggesting leukemic involvement. BCR/ABL rearrangement was within normal range, and the Philadelphia chromosome was not detected. Findings of the peripheral blood cell counts and bone marrow studies were suggestive of CMML.

The patient was scheduled for treatment with 5 cycles of decitabin per every 4 weeks. In the first cycle, decitabin was administered at 20 mg/ m^2 over 1 hour daily for 5 days. A day later, the WBC count was dramatically decreased to 12,200 cell/ μ L. However, the patient complained of general weakness, and follow-

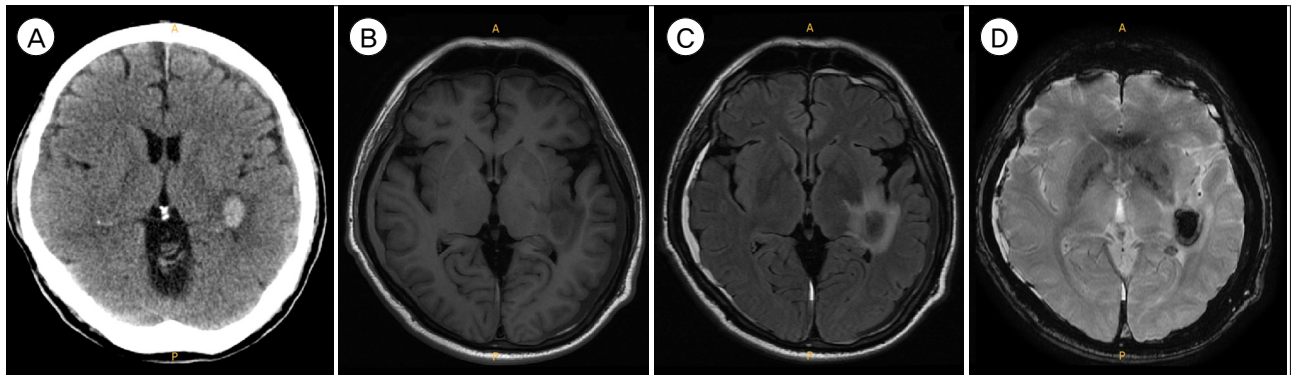


Fig. 2. (A) Unenhanced computed tomography scan and (B-D) magnetic resonance imaging performed 2 weeks later. Besides newly developed intracerebral hemorrhage in left insular-temporal lobe subcortical white matter with surrounding edema, scanty amount of subdural hematoma was noted in both fronto-temporo-parietal lobes. The signal intensity of left-sided hematoma was consistent with early late acute stage, and that of right-sided hematoma was consistent with subacute stage.

ing brain CT showed newly developed intracerebral hemorrhage in left insular-temporal lobe. Magnetic

resonance imaging to evaluate suspicious bilateral SDH, and revealed newly developed intracerebral

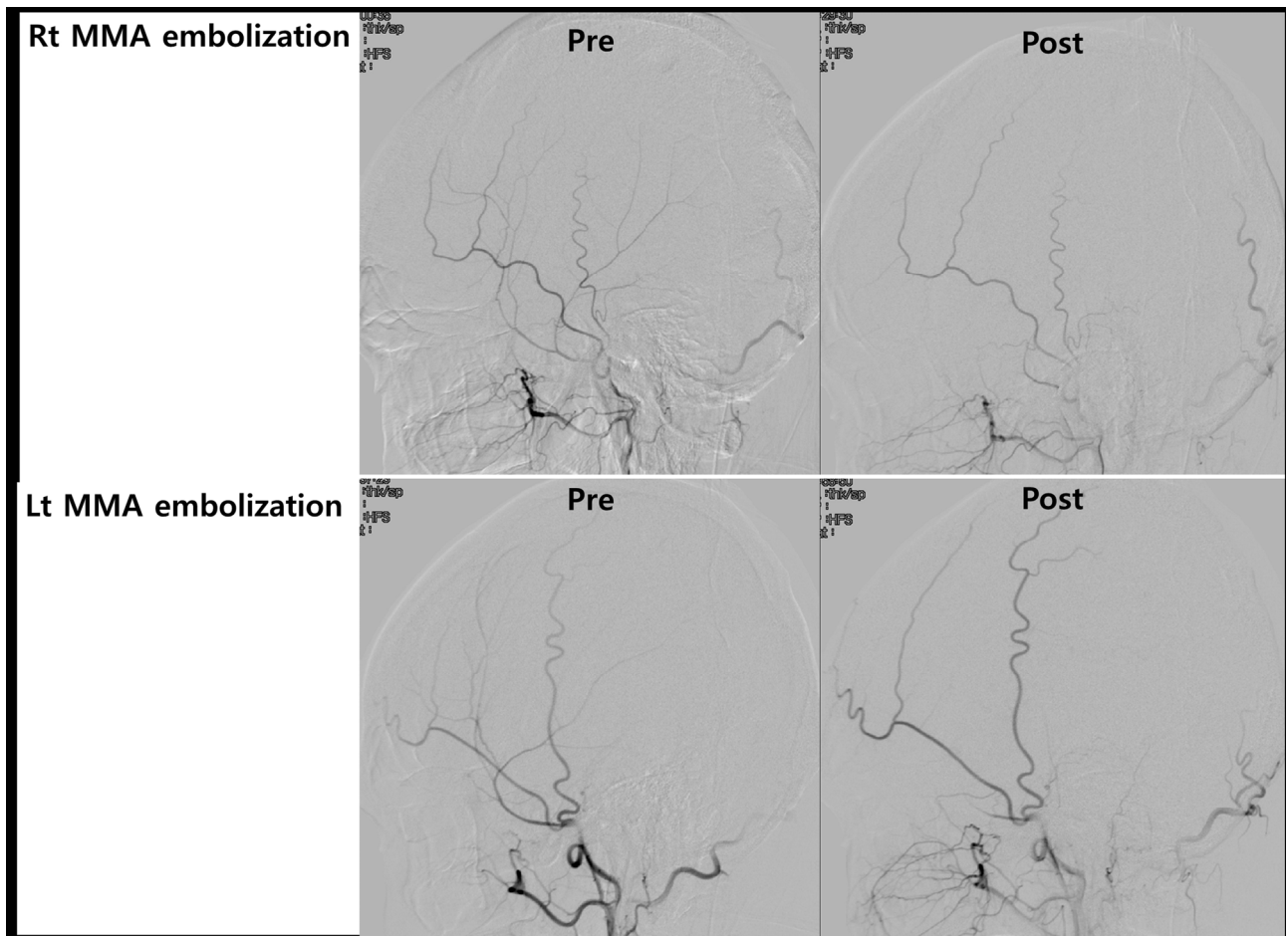


Fig. 3. Angiography imaging at pre- and post-embolization of bilateral middle meningeal artery. Rt = right; MMA = middle meningeal artery; Pre = pre-embolization; Post = post-embolization; Lt = left.

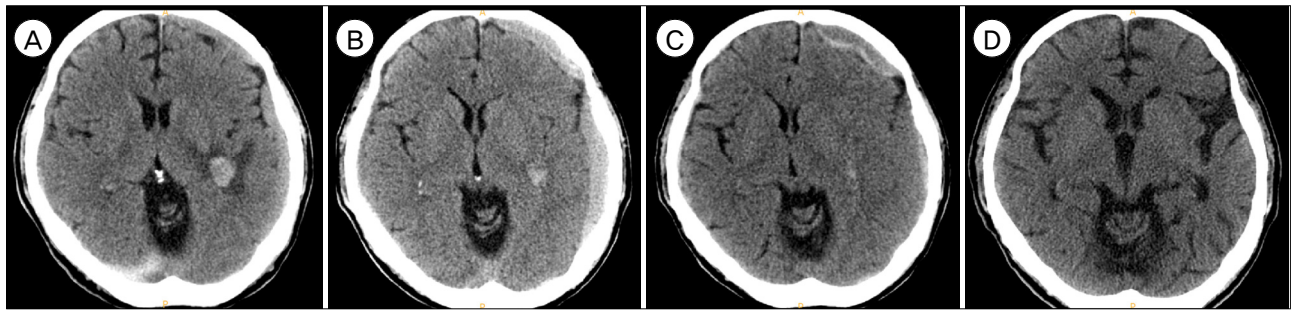


Fig. 4. Brain computed tomography (CT) performed at (A) 2 weeks, (B) 1 month, (C) 2 months, and (D) 5 months after bilateral middle meningeal artery embolization. Slightly increased subdural hematoma in left side was observed in the 2 months' follow-up CT, but the patient had no headache or neurological complaints correlated with imaging. Pancytopenia with neutropenic fever after the 2nd cycle of decitabin was the only complication. Brain CT performed 5 months later revealed complete resolution of subdural hemorrhage.

Table 1. Complete blood counts during the follow-up period

Events & managements		CBC counts		
		WBC	Hb	Platelet
At admission	Detection of left chronic subdural hematoma	59,300	10.5	207,000
After 1 week	Decitabine #1 cycle	36,700	7.9	165,000
After 5 weeks	Decitabine #2 cycle	2,100	11.5	265,000
After 2 months	Neutropenic fever	600	7.9	7,000
After 3 months	Decitabine #3 cycle	5,800	10.8	81,000
After 4 months	No clinical symptom	2,700	9.8	32,000
After 5 months	Decitabine #4 cycle	4,700	11	71,000
After 6 months	No clinical symptom	6,400	11	18,000
After 7 months	Decitabine #5 cycle	7,100	11.7	73,000

CBC = complete blood count; WBC = white blood cell; Hb = hemoglobin.

hemorrhage in left insular-temporal lobe subcortical white matter with surrounding edema. Also, scanty amount of SDH was noted in both fronto-temporo-parietal lobes (Fig. 2). The signal intensity of left-sided hematoma was consistent with early late acute stage, and that of right-sided hematoma was consistent with subacute stage.

Middle meningeal artery (MMA) embolization

Due to expected long-term chemotherapy and possibility of repeated intracranial hemorrhage, further management was required. For prevention of recurrent SDH, bilateral MMA embolization was conducted under local anesthesia (Fig. 3). Digital subtraction angiography showed no vascular abnormality in internal carotid artery and external carotid artery angiogram. Excelsior SL 10 microcatheter (Boston

Scientific, Fremont, CA, USA) was placed in the proximal portion of the MMA. After confirming absence of collateral flow between ophthalmic artery and MMA, MMA embolization was performed with polyvinyl alcohol particles (150-250 μm) mixed with contrast agent. Postoperatively, the patient complained of no headache or neurologic complications.

Clinical course

Over the 20 days following chemotherapy, WBC count was normalized to 5,930 cells/ μL , and platelet count was maintained at $> 80,000/\mu\text{L}$ after transient thrombocytopenia. As shown in Fig. 4, Brain CT at 2 months after bilateral MMA embolization showed slightly increased SDH in left side, but the patient had no headache or neurological complaints that were correlated with imaging. Under neurosurgical ob-

servation, he received 5 cycles of decitabin. He was admitted for neutropenic fever with pancytopenia after 2nd cycle of decitabin, but there was no further complication related with chemotherapy (Table 1). Brain CT performed 5 months later revealed complete resolution of subdural hemorrhage (Fig. 4).

DISCUSSION

CMML is a rare myeloid neoplasm defined as a clonal hematopoietic stem cell disorder which is characterized by absolute monocytosis ($> 1 \times 10^9/L$) in the peripheral blood, and the presence of myelodysplastic syndrome and myeloproliferative neoplasm features in the bone marrow by 2008 World Health Organization.²⁵⁾ It has an inherent risk for transformation to acute myeloid leukemia. The annual incidence of CMML is estimated at 4 per 100,000.¹⁹⁾²⁶⁾ The median age at diagnosis of disease ranges from 71 to 74 years, with a male predominance (1.5-3:1).²²⁾ Chemotherapy such as etoposide, cytarabine, all-trans retinoic acid, topotecan, 9-nitro-camptothecin (topoisomerase inhibitor), and lonafarnib (farnesyltransferase inhibitor) has been the mainstay of treatment for chronic myeloid leukemia (CML) since the 1990s.⁵⁾⁷⁾ However, the outcome has been disappointing due to the low response rates and high rates of toxicities. The overall response rates of these hypomethylating agents are estimated at 30-40%, with complete remission rates of 15%.²⁾³⁾

This case is the second case report of non-traumatic SDH associated with CMML, to our best knowledge. In 1912, Ichimura et al.⁸⁾ reported a 74-year-old man who was previously diagnosed as CMML and treated for non-traumatic SDH compromised platelet function due to ineffective erythropoiesis was the probable cause of SDH. There have also been a few reports on non-traumatic subdural hematomas in association with other leukemic malignancies during the disease progression or chemotherapy of such malignancies.⁶⁾²¹⁾ Imatinib mesylate (IM; Gleevec™, Novartis, Basel,

Switzerland), a potent and selective tyrosine kinase inhibitor that acts on Bcr/Abl product of the Philadelphia chromosome, has been used as the standard initial treatment for Philadelphia chromosome-positive CML.¹⁶⁾ Song et al.²¹⁾ reported occurrence of non-traumatic subdural hematomas in 6% (7/121 patients) of patients treated with IM for advanced CML. Subdural hematoma due to loss of complete molecular response associated with IM treatment of CML has also been reported.⁹⁾¹⁰⁾

Spontaneous acute SDH as the primary initial presenting manifestation of a CML is previously reported.¹⁾ A single case report described recurrent subdural hematoma as the sole manifestation of chronic lymphocytic leukemia. Other authors described a patient presenting with recurrent subdural hematomas as the primary manifestation of chronic lymphocytic leukemia.⁴⁾ Besides SDH, intracerebral hematoma was also presented as initial manifestation of CML.¹⁷⁾ This is the first case of SDH as initial manifestation of CMML. The presence of SDH in the absence of head trauma should be evaluated by basic blood work up, as well as careful medical history taking. Prompt diagnosis can be followed by prompt treatment for the causative disease. The limitation of this case report is the absence of cytological examination of the subdural fluid or dura mater. The surgical treatment was performed before hematologic evaluation. The presence of myeloid cells in the subdural fluid collection should be evaluated to rule out the malignant subdural effusion.¹⁸⁾

Our case had the risk of re-accumulation from the leukemia as well as the treatment. Apart from the disease progression, treatments with hypomethylating chemotherapy agents also induce the coagulopathy, which results in the rise of recurrence rates of SDH. In these situations, repeated burr-hole surgery or removal of the outer membrane with craniotomy has risks of bleeding or infection.¹¹⁾¹⁵⁾

Since first introduced in 2000 for patient with liver cirrhosis, transarterial MMA embolization has

emerged as the treatment option for frequently recurring chronic SDH.¹³⁾²³⁾ The therapeutic rationale follows from pathologic identification. Tanaka et al.²⁴⁾ identified that arteries originating from branches of the MMA that entered the outer membrane through histological study of dura mater and outer membrane. MMA contributes to the development of chronic SDH, by providing feeding vessels to the outer membrane that is connected with the dura matter. Angiographic findings of chronic SDH including diffuse MMA dilation and the abnormal vascular networks on outer membrane support this hypothesis.²³⁾²⁴⁾ In our case, embolization of the MMA was highly effective in the patient at high risk of recurrent chronic SDH. The patient required continuous chemotherapy, and transient thrombocytopenia occurred after each chemotherapy session. Nevertheless, remnant hematoma showed spontaneous resolution with no further recurrence.

CONCLUSION

This case is the first report of CMML diagnosed from spontaneous chronic SDH, with successful MMA embolization and no recurrence. MMA embolization is potentially a useful and safe treatment option in challenging clinical situations with underlying pathologies.

Disclosure

The authors have no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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