Case Report

Middle Meningeal Artery Embolization for Refractory Chronic Subdural Hematoma Associated with Acute Myeloid Leukemia: A Case Report

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Objective: We describe a patient with leukemia–related chronic subdural hematoma (CSDH) who was successfully treated using the combination of surgical evacuation and middle meningeal artery (MMA) embolization.
Case Presentation: A 73-year-old man without apparent head trauma history was admitted to our hospital because of acute myeloid leukemia (AML). Head CT on admission revealed mild CSDH on both sides. Medical treatment options, including chemotherapy, were started. Since a decrease in platelet count and disseminated intravascular coagulation were observed on day 4, recombinant thrombomodulin was administered. As the patient exhibited signs of altered consciousness due to the enlargement of the right CSDH on day 10, we performed surgical drainage. Despite subsequent platelet transfusion and administration of goreisan, the right CSDH recurred within a short period. On day 17, we performed the second surgery and MMA embolization in one stage. The postoperative clinical course was favorable without recurrence of the hematoma. The patient eventually died on day 123 from a deterioration of his general condition.
Conclusion: Although MMA embolization has recently been recognized as an effective treatment option for recurrent CSDH, there are no published reports addressing the efficacy of MMA embolization for refractory CSDH associated with hematological malignancies. Findings from the management of this case suggest that MMA embolization can be the effective treatment option for CSDH in patients with severe hemorrhagic diathesis due to AML.

Keywords ▶ acute myeloid leukemia, chronic subdural hematoma, middle meningeal artery embolization

Introduction

Chronic subdural hematoma (CSDH) is one of the most common neurosurgical diseases across the world.[1,2] Burr hole surgery has long been the gold standard treatment for CSDH.[1,2] However, approximately 10%–20% of patients with CSDH show recurrence after the removal of the hematoma.[1]

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Recent reviews have described the usefulness of middle meningeal artery (MMA) embolization in the treatment of refractory CSDH.[1–5] Among the risk factors of intractable CSDH, cancer is the most frequent comorbidity associated with CSDH requiring MMA embolization.[6] However, the efficacy of MMA embolization for the treatment of recurrent CSDH in patients with hematological malignancies has yet to be explored.

Here, we present a case with acute myeloid leukemia (AML) and subsequent disseminated intravascular coagulation (DIC) in association with refractory CSDH, which was successfully treated using the combination of surgical evacuation, MMA embolization, and medical management.

Case Presentation

A 73-year-old man with complaints of fever, headache, and right cervical lymph node swelling was referred to our hospital. Systemic CT demonstrated swelling of the submandibular, accessory, cervical, axillary, paraaortic, hilar,
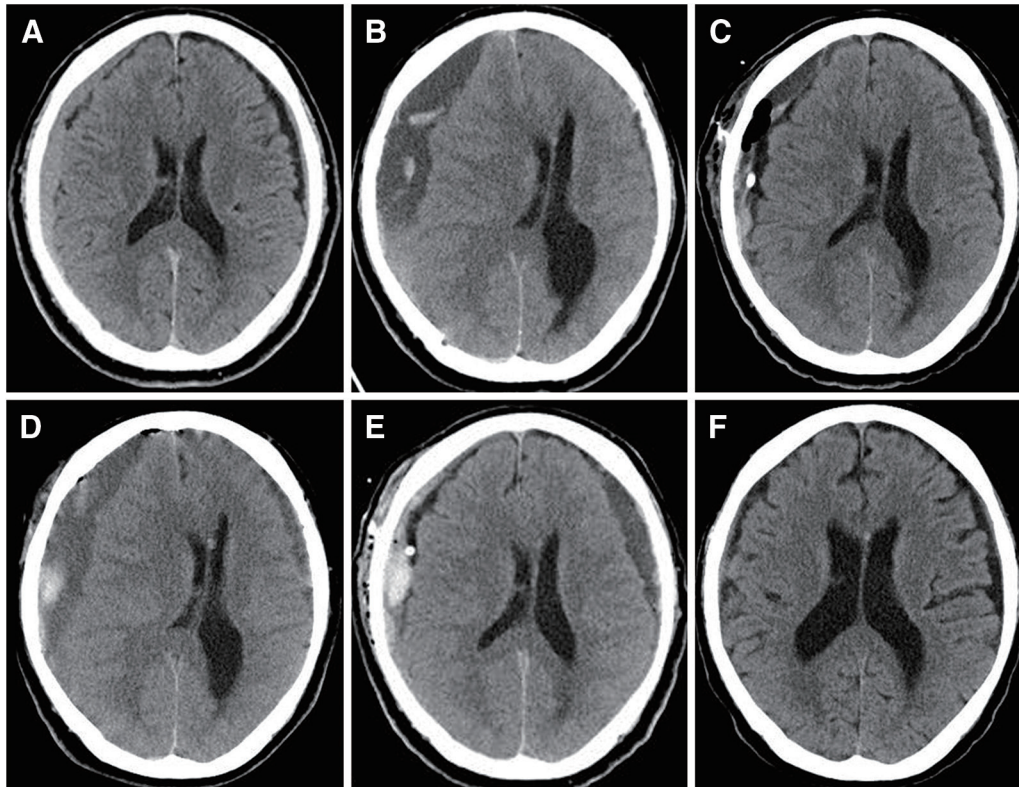
Fig. 1 **(A)** CT image on admission shows the presence of bilateral mild chronic subdural hematoma. **(B)** CT image on day 10 shows an increase in the size of the hematoma with midline shift to the left. **(C)** CT image on day 11 shows a decrease in the size of the right hematoma. **(D)** CT image on day 17 shows recurrence of the right hematoma. **(E)** CT image on day 18 shows a decrease in the size of the right hematoma. **(F)** CT image on day 100 shows resolution of the bilateral hematoma

iliac, and mesenteric lymph nodes. Head CT revealed small CSDHs on both sides (**Fig. 1A**), although an apparent head trauma history was not confirmed. As the patient did not show any neurological deficits, we concluded that surgery was not indicated for the treatment of CSDH at this time.

Blood work-up on admission showed a white blood cell count of 6830/μL (normal: 3300–8600/μL; neutrophils: 39.5%; eosinophils: 1.0%; basophils: 0.4%; lymphocytes: 22.8%; monocytes: 39.5%; and blasts: 11.0%), decrease in hemoglobin level to 10.8 g/dL (normal: 13.7–16.8 g/dL), and decrease in platelet count to 130000/μL (normal: 158000–348000/μL) (**Fig. 2**). Bone marrow aspirate smears showed a composition of 50.2% blasts. Genetic and molecular studies later demonstrated no mutations in the tyrosine kinase domain or the internal tandem duplications of the FMS-like tyrosine kinase 3 gene. A diagnosis of AML with maturation (FAB M4) was established.

Oral hydroxycarbamide therapy was started on day 1. However, as it proved ineffective, it was discontinued on day 2. Azacitidine was administered subcutaneously daily from day 3 to day 10. The patient was also administered oral venetoclax from day 7 to day 10.

The blood test on day 4 revealed a platelet count of 78000/μL; fibrin/fibrinogen degradation product (FDP) level of 127.6 μg/mL (normal: <5.0 μg/mL); plasma fibrinogen level of 447 mg/dL (normal: 181–378 mg/dL); prothrombin time-international normalized ratio (PT-INR) of 1.2 (normal: 0.91–1.08); D-Dimer level of 91.1 μg/mL (normal: <1.0 μg/mL); antithrombin III level of 86% (normal: 80%–130%); plasmin-α2 plasmin inhibitor complex (PIC) level of 8.3 μg/mL (normal: <0.8 μg/mL), and thrombin-antithrombin complex (TAT) level of 24.5 ng/mL (normal: <3 ng/mL) (**Fig. 2**). The International Society on Thrombosis and Haemostasis (ISTH) DIC score was 6, indicating a diagnosis of overt DIC with ongoing hyperfibrinolysis.

To treat DIC, recombinant thrombomodulin was administered intravenously from day 2 to day 5. Intravenous prednisolone was administered from day 2 to day 10 to treat the hemophagocytic syndrome.

On day 11, the patient became unconscious due to an increase in the size of the right CSDH (**Fig. 1B**).
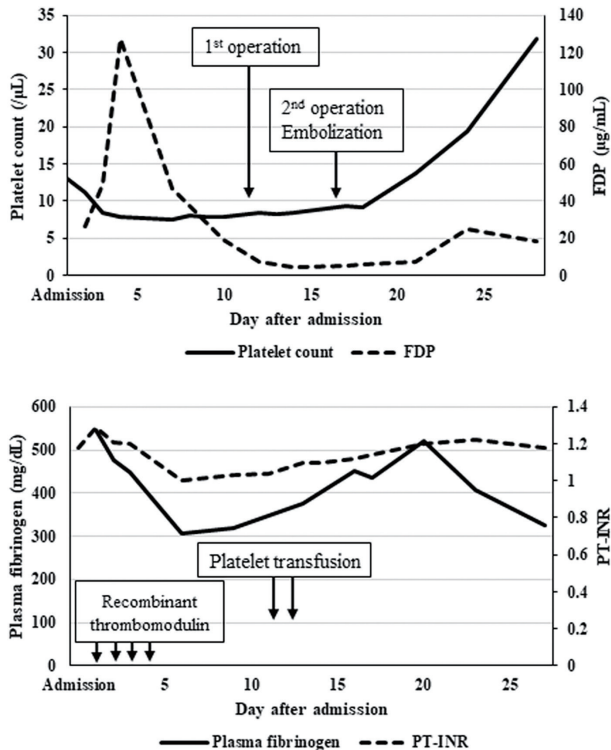
Fig. 2 Platelet count, FDP, plasma fibrinogen, PT-INR, and clinical course. The platelet count remained low on day 13 despite the platelet transfusions on day 11 and day 12. FDP: fibrin/fibrinogen degradation products; PT-INR: prothrombin time-international normalized ratio

Accordingly, we performed a burr hole drainage. CT on day 12 revealed a reduction in the size of the CSDH (**Fig. 1C**). Subsequently, the patient showed complete resolution of the neurological deficits. Since a blood test on day 10 revealed a low platelet count (79000/μL), the patient was given 10 units of platelets on each of days 11 and 12. However, the platelet count on day 13 was unexpectedly low at a level of 82000/μL (**Fig. 2**). Since the patient only marginally responded to sequential platelet transfusions, platelet transfusion refractoriness was suspected.

Additionally, we began the oral administration of a herbal medicine, goreisan, from day 14. However, the patient gradually lost consciousness and developed a left hemiparesis.

CT on day 17 showed a recurrence of the right CSDH and midline shift (**Fig. 1D**). Further blood work-up showed a platelet count of 94000/μL, FDP level of 5.0 μg/mL, plasma fibrinogen level of 452 mg/dL, PT-INR of 1.12, antithrombin III level of 113.5%, PIC level of 1.9 μg/mL and TAT level of 2.9 ng/mL (**Fig. 2**). The DIC score was 2.

Although the DIC score improved, we concluded that endovascular treatment was necessary to prevent further enlargement of the hematoma.

On day 17, we performed the second burr hole drainage surgery and subsequent MMA embolization under local anesthesia in one stage. The right radial artery was punctured, and a 5-Fr guiding sheath (ASAHI FUBUKI Dilator; ASAHI INTECC, Aichi, Japan) was advanced into the right external carotid artery. The angiography demonstrated no abnormal vascular networks nor cotton wool-like staining in the territory of the right MMA (**Fig. 3A**). Thereafter, we inserted a microcatheter (Excelsior SL-10; Stryker Neurovascular, Fremont, CA, USA) into the anterior convexity branch of the right MMA and embolized the peripheral segment of the branch using 20% N-butyl-2-cyanoacrylate (NBCA) (**Fig. 3B**). The final angiography revealed an occlusion of the right anterior convexity branch and preservation of the posterior convexity branch (**Fig. 3C**). No perioperative complications were observed. Oral goreisan was discontinued after the endovascular therapy.

Postoperative CT showed a decrease in the size of the right hematoma and improvement of the midline shift (**Fig. 1E**). On day 48, as peripheral blood blasts were confirmed to be absent, the patient was discharged with no neurological deficits.

The hematologists subsequently managed the patient for AML. From day 50, intravenous azacitidine and oral venetoclax were administered for 5 and 14 days, respectively. The percentages of peripheral blood blasts and bone marrow blasts on day 84 were 4.0% and 11.0%, respectively, suggesting the recurrence of AML. From day 85, intravenous aclarubicin hydrochloride and cytarabine were administered for 4 and 14 days, respectively. Whereas blood investigations on day 98 showed an extensively low platelet count of 21000/μL, CT on day 100 showed no recurrence of the CSDH on both sides (**Fig. 1F**). The patient eventually died on day 123 as a result of a deterioration in his general condition.

Discussion

The recent review elucidates the contemporary etiological concept of CSDH as follows. The first bleeding occurs in dural border cells following mild trauma, then inflammatory cells are drawn to the border cell layer. At this point, new membranes form from activated inflammation. Angiogenic factors promote the formation of new capillaries within the outer membrane, and the hematoma gradually enlarges.[2]

The risk factors of CSDH recurrence include a history of hypertension, oral administration of antithrombotic
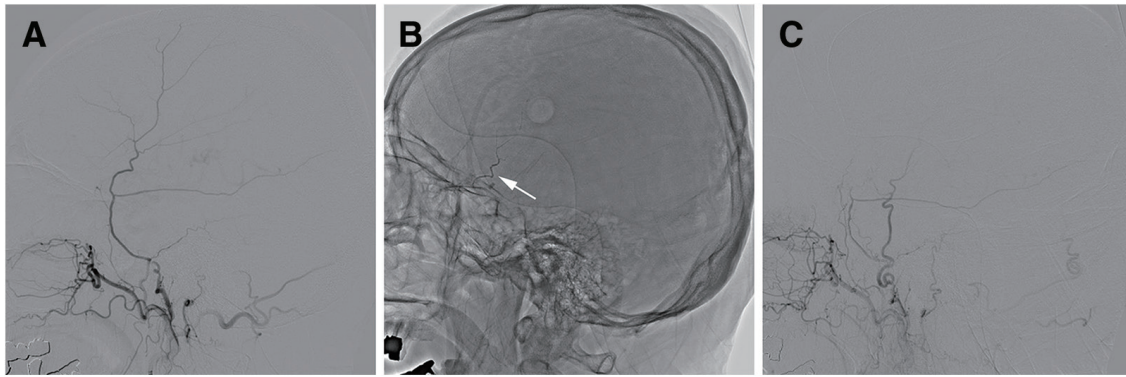
Fig. 3 Right external carotid angiograms (lateral view). (**A**) The pretreatment image shows the right MMA without abnormal vascular networks in the territory. (**B**) Craniogram after embolization shows the glue cast (white arrow) in the pterional segment of the MMA. (**C**) The postoperative image shows the occlusion of the right MMA distal to the orifice of the posterior convexity branch. MMA: middle meningeal artery

drugs, hepatic dysfunction, hemodialysis, terminal malignancy, cerebral atrophy, old age, presence of a cerebrospinal fluid shunt, separated- or trabecular-type hematoma, and coagulopathy.[4,6–9]

MMA embolization, which is performed to inhibit blood reflux into pathologic structures receiving blood through meningeal arteries, can control bleeding from the CSDH membrane and eventually enhance the spontaneous resolution of hematoma.[8] Several cytokines, including interleukin-6 and -8, tumor necrosis factor-α, thrombomodulin, vascular endothelial-derived growth factor, and basic fibroblast growth factor, induce the development of the outer membrane and growth of hematomas.[10] This process might be blocked by MMA embolization.[10]

Additionally, pharmacological approaches, including the use of corticosteroids, tranexamic acid, angiotensin-converting enzyme inhibitors, and goreisan, have been proposed to prevent surgery without clear evidence.[5,11] In our case, goreisan failed to prevent the recurrence of CSDH after the first surgery.

Many factors are associated with the development of subdural hematoma in patients with AML. Chemotherapy or bone marrow transplantation, leukocytosis, thrombocytopenia (platelet count <10000/μL), sepsis, DIC, and drugs (such as prednisone) increase the risk of bleeding.[12] Additionally, occlusion of the blood–brain barrier by tumor cells may promote the enlargement of the subdural hematoma.[12]

Only a few reports in the literature have described the clinical course of patients with AML and refractory CSDH.[9,13] In one case report, the hematoma was surgically evacuated, and then oral atorvastatin was administered, resulting in no recurrence of the CSDH.[13] One large study included two cases of refractory CSDH and associated AML that were treated using MMA embolization.[9] However, details of the clinical course after MMA embolization and surgical outcomes of the patients were not described in this case series.

In the present case, the patient with AML showed signs of DIC, thrombocytopenia, and platelet transfusion refractoriness. DIC might lead to platelet transfusion refractoriness mainly due to increased platelet consumption.[14] This clinical course strongly suggests a severe hemorrhagic tendency in this patient.

The previous case series and review show that most of the cases of recurrent CSDH treated with MMA embolization had abnormal vascular networks with a cotton wool appearance on the MMA angiography.[15–17] MMA angiography in the patient reported herein did not show the aforementioned angiographic characteristics. However, MMA embolization is most likely the only promising, reasonable treatment option at present for patients such as the one reported herein in whom pharmacological therapy after the first surgery failed to prevent the recurrence of CSDH. From hindsight, we should have embolized the right MMA immediately after the first surgery.

Patients in whom a transfemoral approach is adopted are significantly more likely to experience access-site complications and neurological complications as compared with patients in whom a transradial approach is adopted.[18] Considering the hemorrhagic tendency in the present case, we selected the transradial-access route to avoid complications related to the groin puncture.

In our case, the platelet count on day 24 returned to normal. Accordingly, the improvement of the hemorrhagic

tendency might contribute to the favorable outcome of MMA embolization. However, the right CSDH did not recur even after the relapse of AML and a significant decrease in the platelet count. This clinical course indicates that the efficacy of MMA embolization could be maintained over the long term.

According to previous literature, embolization of both the anterior and posterior convexity branches is recommended to achieve extensive devascularization of the MMA.[16,17] In this case, we embolized the anterior convexity branch because the posterior convexity branch could anastomose with the posterior meningeal artery and finally the vertebral artery.[19] However, the anterior convexity branch has potential dangerous anastomoses with anterior and posterior ethmoidal arteries and the contralateral MMA.[19] The angiographic anatomy of the MMA should be assessed thoroughly to prevent complications, especially when using a liquid embolic material.

Aside from hemorrhagic complications, patients with AML develop several comorbidities, such as disease- and treatment-related immunosuppression, which can cause life-threatening infections.[20] Accordingly, the prevention of perioperative infectious complication is also crucial. Collaboration of neurosurgery and internal medicine is necessary for the successful treatment of the refractory CSDH related to hematological malignancy.

Conclusion

In this case report, we described a case with CSDH associated with AML. Since the hematoma enlarged after the burr hole surgery, we performed MMA embolization to prevent recurrence. This case showed that MMA embolization could be an effective treatment option even for refractory CSDH related to hematological malignancies.

Disclosure Statement

All authors have no conflict of interest.

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