

Association of progressive intracranial necrotic lesion with acute myelogenous leukemia: A case report

Akiko Marutani, Kiyokazu Asada, Noriyuki Nishi, Tomonori Yamada

From Department of Neurosurgery, National Hospital Organization, Osaka Minami Medical Center, Kawachinagano, Osaka, Japan

Correspondence to: Akiko Marutani, Department of Neurosurgery, National Hospital Organization, Osaka Minami Medical Center, 2-1 Kido-Higashimachi, Kawachinagano, Osaka 586-8521, Japan. Tel.: +81-0721-53-5761, Fax: +81-0721-53-7010. E-mail: akiko@narmed-u.ac.jp

Received - 09 October 2018

Initial Review - 08 November 2018

Published Online - 10 March 2018

ABSTRACT

For patients with acute myelogenous leukemia (AML) and invasive central nervous system lesions, there are many possible differential diagnoses, including collagen diseases, infectious diseases, drug reactions or side effects, and vascular diseases. Herein, we describe the clinical course, diagnostic examinations, and treatment outcomes for a patient with AML complicated by a progressively enlarging intracranial necrotic lesion. As no tumor cells were seen on microscopic examination, and since the clinical symptoms improved after leukemia therapy, myeloid sarcoma was highly suspected. Taken together, this case suggests that a combination of the clinical course, radiological findings, and treatment history should be considered to eliminate other possible diagnoses.

Key words: *Acute myelogenous leukemia, case study, central nervous system, granulocytic sarcoma, tumor cells*

Central nervous system (CNS) diseases associated with acute leukemia should be discerned from a multitude of disease categories, including invasive collagen disease, infectious diseases, drug- or radiotherapy-related leukoencephalopathy, and vascular lesions [1]. It is difficult to differentiate several potential etiologies based only on the clinical presentation, and the definitive diagnosis is usually made by histopathological examination. It is important to present negative outcomes resulting from a misdiagnosis or delayed diagnosis to improve our knowledge in choosing the most appropriate therapeutic strategy. Herein, we report the diagnostic considerations and successful therapeutic response in a case of acute myelogenous leukemia (AML) complicated by a progressive intracranial necrotic lesion.

CASE REPORT

In April 2016, a 52-year-old man experienced right unilateral weakness and sensory loss but did not seek medical attention. 1 month later, he presented at a nearby general hospital complaining of progressive weakness and numbness of the right upper extremities and face. Cranial magnetic resonance imaging (MRI) findings at the time were unremarkable. Orthopedic evaluation was performed, and the patient was diagnosed with cervical spondylosis and treated conservatively. However, no improvement in symptoms was seen; therefore, he was admitted for further investigations in May.

On admission, neurological examination revealed Japan Coma Scale 1 (Glasgow coma scale: 3-5-6), right hemiparesis (manual/

muscle testing: 4-/5), and right hemisensory deficit, including of the face. The laboratory results were within normal limits, except for a low white blood cell count (1280/ μ L). His prothrombin time was 91.6 s, prothrombin international normalized ratio was 1.04, and D-dimer level was 1.5 μ g/mL. The cerebrospinal fluid (CSF) results revealed a cell count of 3/ μ L (polymorphonuclear leukocytes - 0% and monocytes - 100%); protein, 37 mg/dL; and glucose, 66 mg/dL. Blood and CSF cultures showed no evidence of bacterial, fungal, or viral infection. Contrast MRI showed partial enhancement and perifocal edema in the left subcortical parietal lobe, and both T1- and T2-weighted images showed low intensity (Fig. 1). He was followed up continuously because his condition remained unchanged.

In July, the laboratory data again revealed a low white blood cell count (1400/ μ L); therefore, the patient was referred to our institute's Department of Hematology. Bone marrow biopsy was performed, which showed a high number of large immature and dysfunctional red blood cells (megaloblasts) (62.8%) and reductions in granulocytes and neutrophils, leading to the diagnosis of leukemia. Subsequently, he was hospitalized for further examination and treatment.

Follow-up MRI showed expansion of the left parietal subcortical lesion, with increased contrast enhancement and edema (Fig. 2). Digital subtraction angiography revealed a slight vascular blush in the lesion area. To make a definitive diagnosis, a brain biopsy was performed using a pen. The intraoperative findings included partial whitish discoloration in the parietal gray matter, with several ischemic cortical arteries. Because the

lesion was located directly over the motor area, three 1 cm×1 cm blocks of discolored whitish cortex in the posterior aspect of the superior parietal lobule were removed. The cut surface of the parietal resection of the arteries revealed vessel wall thickening; moreover, the white-colored tissue with total occlusion of the vessel lumen was considered related to tumor growth.

Pathology results using the immunoblot method showed liquefactive necrosis, along with inflammatory lymphocytes (Fig. 3). There was no pathological evidence of tumor cells or any infectious lesion. The precise diagnosis of the intracranial lesion was unclear; however, a presumptive etiology secondary to AML was considered. On post-operative day 6, standard AML chemotherapy treatment was initiated with high-dose cytarabine. Steroids were administered at 1 week postoperatively, but the patient did not respond to treatment. By hospital day 33, the patient showed almost complete resolution of the hemisensory deficits and was able to walk without assistance. Contrast MRI at that time demonstrated substantial shrinkage of both the lesion and perifocal edema. At 1 month postoperatively, the CSF blasts were 11.4%; further treatment was determined to be ineffective, and a diagnosis of incomplete remission was made.

Therefore, the patient underwent whole brain radiotherapy (2.5 Gy×2 days) in combination with systemic radiotherapy (3 Gy/4 Fr×3 days). Bone marrow transplantation could not be performed due to lack of an appropriate donor. Instead, an umbilical cord transplant was performed to stimulate the production of neutrophils. Consequently, complete remission was achieved. 3 months postoperatively, the patient had recovered, with almost no

right hemiparesis and sensory deficits. Follow-up MRI at this time revealed reduced edema and contrast enhancement (Fig. 4). Written informed consent for publication of this report was obtained from the patient before surgery. Ethics approval was not sought.

DISCUSSION

The differential diagnoses for CNS diseases associated with AML infiltrative collagen diseases, infections, drug treatment side effects, and vascular diseases. Consequently, considering the grave consequences of misdiagnosis, early and accurate diagnosis and treatment are essential [2].

Progressive multifocal leukoencephalopathy (PML) due to John Cunningham viral infection is one of the most common infectious diseases associated with AML. Characteristic radiological features include periventricular and subcortical demyelinating plaques on MRI, with unilateral or bilateral asymmetric weakly enhancing lesions [3]. In addition, reactivation of herpes simplex has been reported to occur in 25–61% of leukemia patients during the chemotherapy induction phase [4,5]. In our case, because the patient was immunosuppressed, the presence of negative cultures ruled out an infectious etiology, despite a high signal on diffusion-weighted MRI.

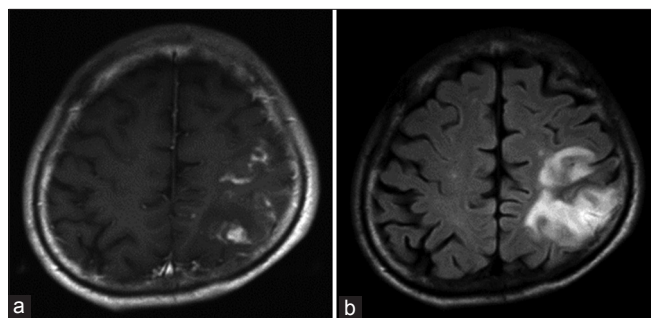


Figure 1: Magnetic resonance imaging revealed partial enhancement (a) and fluid-attenuated inversion recovery imaging revealed perifocal edema of the left subcortical parietal lobe (b)

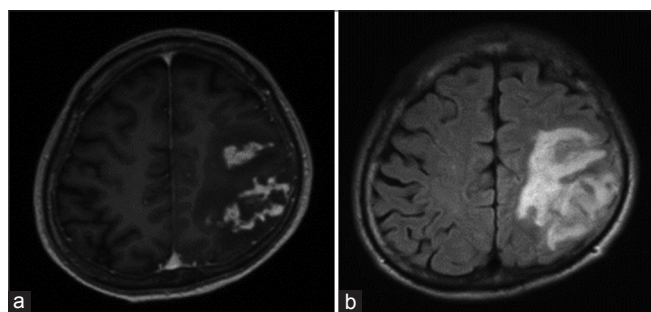


Figure 2: On the 14th day of admission, cranial magnetic resonance imaging showed expansion of the left parietal subcortical lesion, with increased contrast enhancement (a) and edema was noted on fluid-attenuated inversion recovery imaging (b)

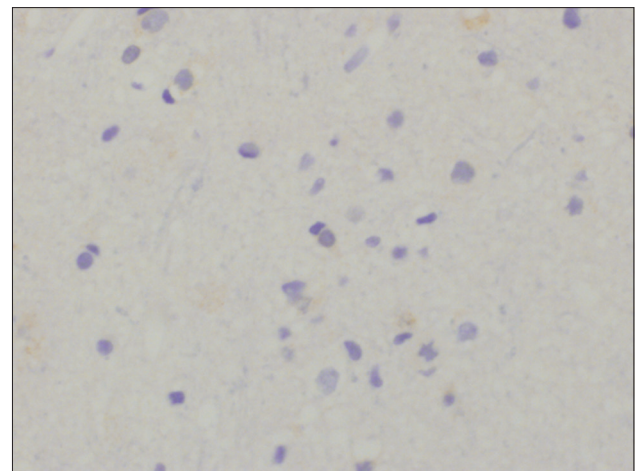


Figure 3: Permanent tissue pathology results showed liquefactive necrosis, along with a portion that included inflammatory lymphocytes

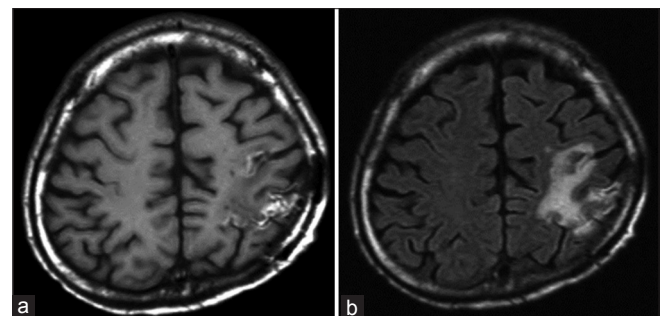


Figure 4: 3 months postoperatively, the patient had recovered, with almost no neurological deficits. At that time, follow-up magnetic resonance imaging revealed a reduction of the previously observed contrast enhancement (a) and edema on fluid-attenuated inversion recovery imaging (b)

Post-methotrexate leukoencephalopathy reportedly accounts for the majority of cases of leukemia-related encephalopathy, while intracranial radiation accounts for the remaining cases, with progression occurring within several months to years [6]. Typically, acute disseminating encephalomyelitis is characterized by a good response to treatment with steroids, with increased CSF cell counts, and mild bilateral cortical enhancement on MRI. However, in our case, there was a poor response to steroids, and based on the radiological findings and CSF results, this was, hence, an unlikely cause.

Regarding PML, although drug-induced etiologies are common, because there was only mild enhancement on MRI, the findings suggested an atypical form of PML. In addition, while there have been reports of cases related to drugs such as tacrolimus [7] because the radiological findings for reversible posterior leukoencephalopathy usually involve bilateral distribution in the occipital and parietal lobes, this was also an unlikely cause. Thus, because our case had an unremarkable history and no medication history, the likelihood of drug-related etiology was ruled out.

Stroke presenting as the first symptom of hematological disease has been reported to occur in 1.27–13.5% of all vascular diseases; among these, there have been few reports on leukemia. Most of the cases of stroke as a complication of leukemia have been observed during the treatment phase; these include reports of hemorrhagic infarction due to mycotic embolic dissemination and agranulocytosis, invasive leukemia cells and massive leukocytosis due to multiple intracerebral hemorrhages, and intracerebral hemorrhage due to disseminated intravascular coagulation and coagulopathies [8]. In our case, though the clinical and radiological findings on MRI and digital subtraction angiography were not typical for cerebral infarction, the possibility of infarction could not be completely ruled out.

Finally, the prognosis of granulocytic sarcoma is closely related to the prognosis of AML, with an effective response to intensive chemotherapy and local radiotherapy [9]. The incidence of granulocytic sarcoma is 2.9–6.8% in myelogenous leukemia autopsy cases [10]. Therapy is based on the treatment of myelogenous leukemia and comprises mainly chemotherapy; however, for cases of granulocytic sarcoma, the prognosis is poor, with a reported average survival of only 8 months [11].

Considering the occurrence of AML and the progressive enlargement of the lesion, we suspect that the primary pathology of our case involves a granulocytic sarcoma or metastatic tumor. However, because the pre-operative abdominal, thoracic computed tomography was unremarkable and the specific tumor markers were negative, the possibility of a metastatic tumor can essentially be ruled out. The lack of any evidence of tumor cells on the pathological examination may be explained by the need to perform a limited resection due to the location of the lesion and the presence of unclear borders. In addition, the location of the lesion may have shifted, which would have resulted in difficulty performing a resection.

Based on the above, we consider that myeloid sarcoma

was the most likely diagnosis, because the lesion regressed, and the clinical symptoms improved after leukemia treatment. However, complete remission was not achieved until whole brain radiotherapy in combination with systemic radiotherapy and umbilical cord transplant could be performed.

CONCLUSIONS

The differential diagnosis in patients with immunosuppression due to the treatment of hematogenous diseases and who have concomitant CNS lesions should consider the patient's clinical condition and course. It is necessary to use a combination of radiological and laboratory findings to make the diagnosis. Delays in the treatment of AML with associated CNS disease, which has a poor prognosis, can result in serious sequelae. When the location of the lesion is in a critical brain area controlling speech, motor functions, or senses, it becomes more difficult to treat brain tumors successfully. The present case illustrates the necessity of considering a combination of factors to rule out other possible diagnoses; this will permit starting appropriate therapy as early as possible.

REFERENCES

1. Imataki O, Tamai Y, Inoue N, Watanabe K, Abe Y, Kawakami K, *et al.* A case of relapsed acute myeloid leukemia with brain white matter lesions. *Gan To Kagaku Ryoho* 2007;34:643-6.
2. Arboix A, Besses C. Cerebrovascular disease as the initial clinical presentation of haematological disorders. *Eur Neurol* 1997;37:207-11.
3. Whiteman ML, Post MJ, Berger JR, Tate LG, Bell MD, Limonte LP, *et al.* Progressive multifocal leukoencephalopathy in 47 HIV-seropositive patients: Neuroimaging with clinical and pathologic correlation. *Radiology* 1993;187:233-40.
4. Lam MT, Pazin GJ, Armstrong JA, Ho M. Herpes simplex infection in acute myelogenous leukemia and other hematologic malignancies: A prospective study. *Cancer* 1981;48:2168-71.
5. Saral R, Burns WH, Prentice HG. Herpes virus infections: Clinical manifestations and therapeutic strategies in immunocompromised patients. *Clin Haematol* 1984;13:645-60.
6. Glass JP, Lee YY, Burner J, Fields WS. Treatment-related leukoencephalopathy. A study of three cases and literature view. *Medicine (Baltimore)* 1986;65:154-62.
7. Bartynski WS, Boardman JF. Distinct imaging patterns and lesion distribution in posterior reversible encephalopathy syndrome. *AJNR Am J Neuroradiol* 2007;28:1320-7.
8. Kawanami T, Kurita K, Yamakawa M, Omoto E, Kato T. Cerebrovascular disease in acute leukemia: A clinicopathological study of 14 patients. *Intern Med* 2002;41:1130-4.
9. Neiman RS, Barcos M, Berard C, Bonner H, Mann R, Rydell RE, *et al.* Granulocytic sarcoma: A clinicopathologic study of 61 biopsied cases. *Cancer* 1981;48:1426-37.
10. Liu PL, Ishimaru T, McGregor DH, Okada H, Steer A. Autopsy study of granulocytic sarcoma (chloroma) in patients with myelogenous leukemia, Hiroshima-Nagasaki 1949-1969. *Cancer* 1973;31:948-55.
11. Mansi JL, Selby PJ, Carter RL, Powles RL, McElwain TJ. Granulocytic sarcoma: A diagnosis to be considered in unusual lymphoma syndromes. *Postgrad Med J* 1987;63:447-9.

Funding: None; Conflict of Interest: None Stated.

How to cite this article: Marutani A, Asada K, Nishi N, Yamada T. Association of progressive intracranial necrotic lesion with acute myelogenous leukemia: A case report. *Indian J Case Reports*. 2018;4(1):4-6.