Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.9580-22
Intern Med 62: 453-457, 2023
http://internmed.jp

【 CASE REPORT 】

Epidural Spinal Cord Compression as the Presenting Manifestation of Acute Myeloid Leukemia: A Case Report and Literature Review

Tomoko Fujikawa[1], Kenji Kishimoto[1], Shotaro Inoue[1], Akihiro Nishimura[1], Ryunosuke Tojo[1], Suguru Uemura[1], Sayaka Nakamura[1], Atsuro Saito[1], Aiko Kozaki[1], Toshiaki Ishida[1], Takeshi Mori[1], Masashi Higashino[2], Junji Koyama[2], Atsufumi Kawamura[2], Daiichiro Hasegawa[1] and Yoshiyuki Kosaka[1]

Abstract:

We herein report a rare case of spinal cord compression due to epidural involvement of acute myeloid leukemia (AML). A 14-year-old boy presented with a 7-day history of back pain, paraplegia and hypoesthesia. Contrast-enhanced computed tomography revealed an epidural mass. Emergency laminectomy and resection of the mass were performed. Histopathologically, the resected mass was comparable to an extramedullary mass of AML. Chemotherapy was initiated, and complete remission was achieved. Neurological sequelae remained after the treatment. Based on the present and previous reports, spinal cord compression from epidural AML involvement may progress rapidly.

Key words: spinal cord compression, extramedullary infiltration, acute myeloid leukemia

(Intern Med 62: 453-457, 2023)
(DOI: 10.2169/internalmedicine.9580-22)

Introduction

Extramedullary infiltration (EMI) is occasionally observed in patients with acute myeloid leukemia (AML). EMI is also referred to as granulocytic sarcoma, myeloid sarcoma, or chloroma. The incidence rate of EMI is estimated to be 9% among patients with AML (1), while that of EMI in childhood is 18-25% (2, 3), suggesting that it may be more common in children than in adults. Common EMI sites are the skin, orbit, and lymph nodes. Furthermore, spinal epidural involvement is rare in patients with AML, with a population-based cohort study reporting that it was detected in 2.3% of pediatric patients with EMI (2).

Spinal cord compression is an oncological emergency that can lead to permanent paralysis, sensory loss, and bladder and bowel dysfunction. In adulthood, the most common primary tumors that result in spinal cord compression are derived from the breast, lung, and prostate gland (4), whereas sarcomas, neuroblastomas, and metastatic Wilms tumors are frequent causes of spinal cord compression in childhood (5, 6). Previous reports have suggested that spinal cord compression caused by spinal epidural EMI in patients with AML is extremely rare, and its clinical features and neurological outcomes are not well known.

We herein report a patient with AML who initially presented with spinal cord compression.

Case Report

A 14-year-old boy presented with dull pain in the upper back that had started 7 days before admission to our hospital and gradually exacerbated until admission. Five days before admission, he had developed muscle weakness in his lower extremities. One day before admission, he was admitted to the referral hospital because of severe back pain and difficulty walking. He was transferred to our hospital because of bladder and bowel dysfunction.

[1]Department of Hematology and Oncology, Kobe Children's Hospital, Japan and [2]Department of Neurosurgery, Kobe Children's Hospital, Japan
Received: February 12, 2022; Accepted: May 22, 2022; Advance Publication by J-STAGE: July 5, 2022
Correspondence to Dr. Kenji Kishimoto, ken@yacht.ocn.ne.jp

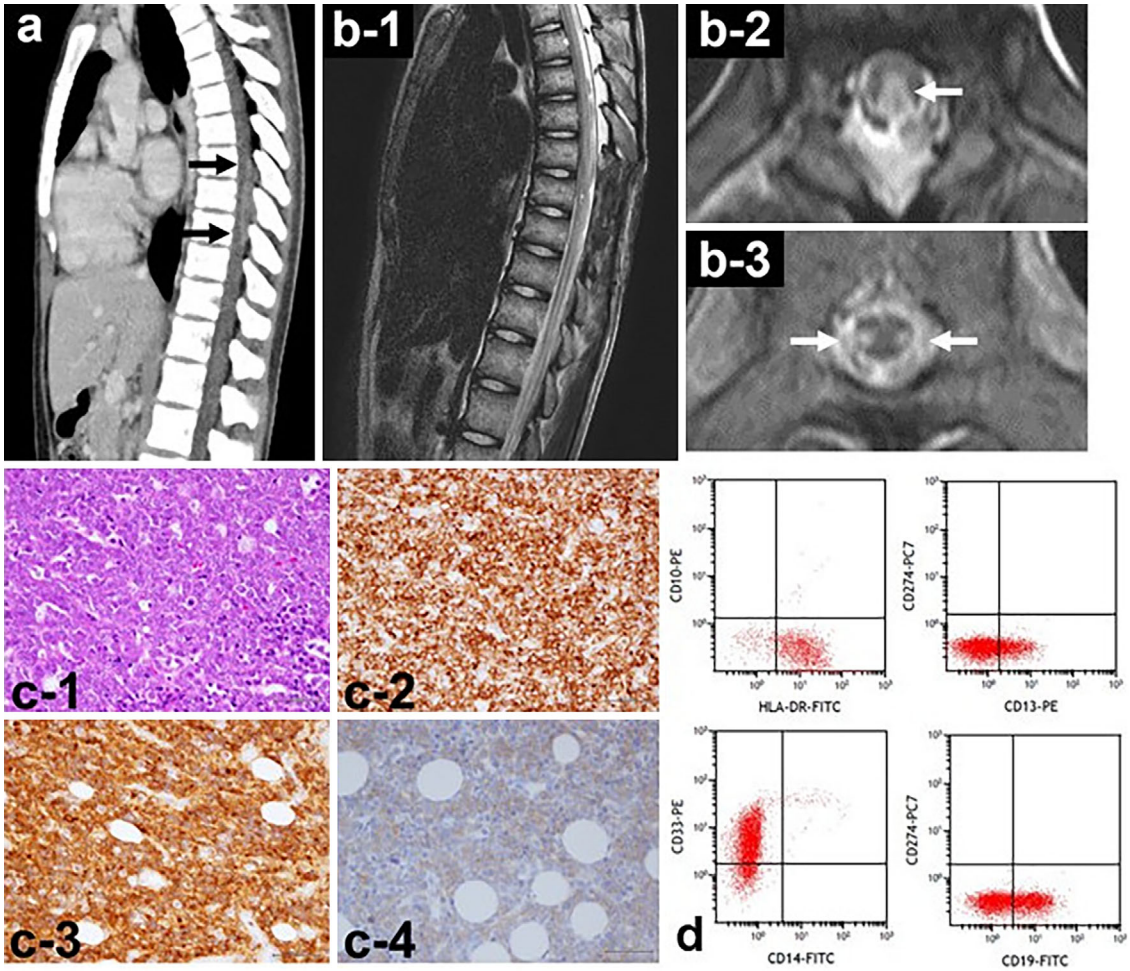

Figure 1. **a: Contrast-enhanced computed tomography at admission. The sagittal image showed a posterior epidural mass (arrows) at the seventh-ninth thoracic vertebra (T7-9) level. b: Spine magnetic resonance image three months after surgery (b-1). T2-weighted imaging revealed the hyperintensity of the posterior funiculus in the spinal cord higher than T6 (b-2) (arrow) and the lateral funiculus in the spinal cord lower than T10 (b-3) (arrows). c: Histopathological images of the resected mass stained with Hematoxylin and Eosin staining (c-1), CD34 (c-2), myeloperoxidase (c-3), and c-kit (c-4). d: A flow cytometry analysis of the bone marrow aspirate.**

On admission, he had incomplete paraplegia and hypoesthesia below the level of the ninth thoracic vertebra (T9). He had no history of a fever, fatigue, or bleeding. Laboratory examinations revealed a white blood cell count of 16,500/μL with 76.0% blasts, hemoglobin level of 9.9 g/dL, and platelet count of 8.6×10^4/μL. Contrast-enhanced computed tomography revealed a posterior epidural mass at the T7-9 level (Fig. 1a). Emergency laminectomy was performed on the day of admission, and the epidural mass was completely removed. The resected mass was 2.5×3.2×0.6 cm^3-sized, soft, extradurally located, and bled easily. A histological examination revealed neoplastic cells with small, round, and hyperchromatic nuclei that proliferated in diffuse cellular infiltrates. Immunohistochemical staining revealed that the tumor cells were positive for myeloperoxidase and CD34. Staining for CD3, CD13, CD33, and c-kit yielded negative results (Fig. 1c). A bone marrow examination showed 82.5% myeloid blasts, which was consistent with the morphological diagnosis of French-American-British (FAB) subtype M2. A flow cytometry analysis of bone marrow aspirate showed the expression of HLA-DR, CD13, CD19, and CD33 (Fig. 1d). Subsequent chromosomal analysis revealed 46, XY, t(8;21)(q22;q22) in 7/20 cells and 47, idem, and +4 in 13/20 cells. He was therefore diagnosed with AML with *RUNX1-RUNX1T1* (FAB AML-M2). Lumbar puncture showed a normal cerebrospinal fluid (CSF) cellular count and an absence of blasts. No extramedullary infiltration other than the epidural mass was detected.

Induction therapy consisting of high-dose cytarabine, mitoxantrone, and etoposide (7, 8) was initiated five days after surgery. After two cycles of induction therapy, he achieved complete remission (CR) and subsequently received a total of three cycles of consolidation chemotherapy. No radiation therapy for EMI was administered. Three months after laminectomy, the sensation of disturbance had almost disappeared. However, incomplete paraplegia and bladder and bowel dysfunction persisted. He could not stand alone and felt no desire to urinate or defecate. He remained in CR for

Table. Characteristics, Treatments and Outcomes of Patients with AML or Myeloid Sarcoma Presented as Spinal Cord Compression.

	Patients with epidural EMI
Patient number	23
Median age (IQR)	29 years (20-48 years)
Gender, n (%)	
Male	16 (70)
Concurrent AML	
Yes, n (%)	10 (43)
AML FAB, n	M2 : 4, M3 : 1
Symptom at onset, n	17
Back pain, n (%)	17 (100)
Paresthesia, n (%)	7 (30)
Neurological finding at diagnosis, n	20
Hypoesthesia, n (%)	13 (65)
Paralysis, n (%)	15 (75)
Bladder and bowel dysfunction, n (%)	5 (25)
CSF finding, n	10
Pleocytosis, n (%)	2 (20)
Leukemic cell, n (%)	3 (30)
Initial intervention	
Operation, n (%)	15 (65)
Radiation, n (%)	3 (13)
Chemotherapy, n (%)	5 (22)
Treatment	
Operation, n (%)	2 (9)
Operation+chemotherapy, n (%)	9 (39)
Operation+radiation, n (%)	2 (9)
Operation+chemotherapy+radiation, n (%)	5 (22)
Chemotherapy, n (%)	3 (13)
Chemotherapy+radiation, n (%)	2 (9)
Outcome	
Median obsrvation period (range)	10 months (6 days-3.5 years)
Remission, n	15, 17
Neurological improvement, n	9, 11

AML: acute myeloid leukemia, CSF: cerebrospinal fluid, EMI: extramedullary infiltration, IQR: interquartile range

eight months after the diagnosis.

T2-weighted magnetic resonance imaging (MRI) one day after surgery revealed hyperintense spinal cord lesions at T6-10 (Fig. 1b-1), which suggested spinal cord injury. Three months later, T2-weighted spinal MRI revealed hyperintensity of the posterior funiculus at a higher level than that of the injured lesion (Fig. 1b-2) and the lateral funiculus in the lower spinal cord (Fig. 1b-3), which suggested Wallerian degeneration.

Discussion

There is limited information on the clinical characteristics of patients with spinal epidural EMI of AML, although a number of case reports and case series studies have been published. We performed a literature search of all case reports published as original articles in English from January 2000 to June 2021 to describe the features of spinal cord compression due to AML or myeloid sarcoma. We searched the electronic database PubMed using the following keywords: 'acute myeloid leukemia' OR 'myeloid sarcoma' OR 'granulocytic' OR 'chloroma' combined with 'spinal' OR 'epidural' OR 'extradural.' We excluded the studies of patients with EMI associated with hematological malignancies other than newly diagnosed acute myeloid leukemia. We identified 23 patients with spinal epidural EMI, with or without AML (Table) (9-30). The median patient age was 29 (IQR: 20-48, range: 10-76) years old. Epidural EMIs associated with AML were detected in 10 patients (43%). Among the 23 patients, information on FAB classification was obtained from 5 (22%): 4 patients were classified as FAB M2, and 1 was classified as FAB M3. The most common site of epidural EMI was the thoracic spine (71%; Fig. 2). The most frequent symptom was back pain (n = 17, 77%). Motor dysfunction, ranging from muscle weakness to paraplegia, was present in 15 patients (68%). Hypoesthesia was present in 13 patients (59%), and bladder and bowel dysfunction were present in 5 patients (22%). Laminectomy

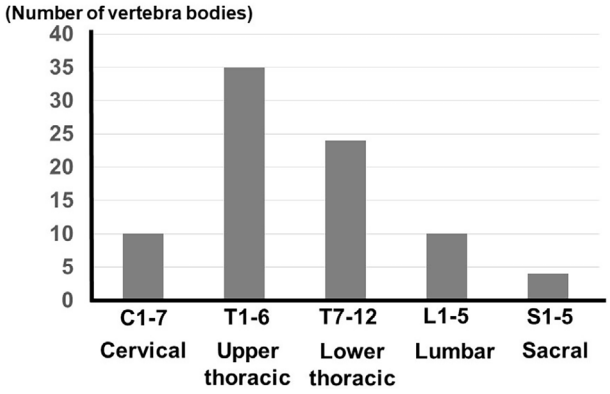

Figure 2. Distribution of the epidural extramedullary infiltration in the spine.

was performed as the first intervention in 15 (65%) patients. In addition, 18 patients (81.8%) received chemotherapy, and 11 patients (61.6%) received radiotherapy. Neurological outcomes were described in 11 patients (48%), and neurological symptoms improved in 9 of those 11 patients (82%).

Although spinal cord compression is a common oncologic emergency, the time course of spinal cord compression progression in patients with cancer has not been clarified. To date, several studies have described the clinical features of patients with cancer who have spinal cord compression. In a review of adult patients with spinal cord compression caused by cancer, 83-95% had pain at the time of the diagnosis that had persisted for a median of 8 weeks (4). In addition, Gunes et al. (5) reported that the median interval between the onset of symptoms and diagnosis was seven weeks in pediatric patients with malignancy. Another study on spinal cord compression in children with cancer reported that the median length of the interval was 11 days (6). Our patient showed a relatively rapid progression of neurological deficits, with a one-week interval between the symptom onset and the development of incomplete paraplegia, hypoesthesia, and bladder and bowel dysfunction. Furthermore, in our review, 5 patients (22%) had neurological symptoms that progressed in less than a week, suggesting that the symptoms progressed rapidly in patients with AML. These observations suggest that spinal cord compression in patients with AML may progress rapidly.

Neurological outcomes in patients with spinal cord compression depend on the rate of progression, timing of intervention, and pretreatment neurological status (4). Rades et al. (31) reported that neurological improvement was observed in only 12% of patients who developed symptoms of metastatic spinal cord compression less than 14 days before intervention. In contrast, among patients with an interval of more than 14 days between the symptom onset and intervention, symptom improvement was found in 86% of patients (31). Furthermore, Martino et al. (6) reported that, in children with spinal cord compression caused by cancer who had mild muscle weakness without walking disability for the legs at the diagnosis, motor deficits disappeared in 42.8%, whereas in patients with moderate muscle weakness with inability to walk, motor deficits disappeared in only 7.1% of cases. Incomplete paraplegia and bladder and bowel dysfunction persisted in our patient despite early intervention for spinal cord compression, implying the effect of the rapid and severe progression of symptoms. These findings support the importance of early detection and intervention in children with cancer-induced spinal cord compression. Given that spinal cord compression with AML may progress rapidly, a prompt diagnosis and intervention seem to be crucial for patients with suspected AML and symptoms including back pain or motor dysfunction to prevent neurological sequelae.

The authors state that they have no Conflict of Interest (COI).

References

1. Ohanian M, Faderl S, Ravandi F, et al. Is acute myeloid leukemia a liquid tumor? Int J Cancer **133**: 534-543, 2014.
2. Stove HK, Sandahl JD, Abrahamsson J, et al. Extrameddullary leukemia in children with acute myeloid leukemia: a population-based cohort study from the Nordic Society of Pediatric Hematology and Oncology (NOPHO). Pediatr Blood Cancer **64**: e26520, 2017.
3. Johnson DL, Alonzo TA, Gerbing RB, Lange BJ, Woods WG. Superior outcome of pediatric acute myeloid leukemia patients with orbital and CNS myeloid sarcoma: a report from the Children's Oncolgy Group. Pediatr Blood Cancer **58**: 519-524, 2012.
4. Prased D, Schiff D. Malignant spinal-cord compression. Lancet Oncol **6**: 15-24, 2005.
5. Gunes D, Uysal KM, Cetinlkaya H, et al. Paravertebral malignant tumors of childhood: analysis of 28 pediatric patients. Childs Nerv Syst **25**: 63-69, 2009.
6. De Martino L, Spennato P, Vetrella S, et al. Symptomatic malignant spinal cord compression in children: a single-center experience. Ital J Pediatr **45**: 80, 2019.
7. Rubnitz JE, Inaba H, Dahl G, et al. Minimal residual disease-directed therapy for childhood acute myeloid leukaemia: results of the AML02 multicentre trial. Lancet Oncol **11**: 543-552, 2010.
8. Tomizawa D, Tanaka S, Hasegawa D, et al. Evaluation of high-dose cytarabine in induction therapy for children with de novo acute myeloid leukemia: a study protocol of the Japan Children's Cancer Group Multi-Center Seamless Phase II-III Randomized Trial (JPLSG AML-12). Jpn J Clin Oncol **48**: 587-593, 2018.
9. Nimbalkar SM, Gupta RK, Dabadghao S, Aggarwal A. Craniospinal granulocytic sarcomas in childhood acute myeloid leukemia. Indian Pediatr **37**: 790-793, 2000.
10. Buckland ME, Scolyer RA, Donnellan MB, Brew S, Mcgee-Collett M, Harper CG. Spinal chloroma presenting with triplegia in an aleukaemic patient. Pathology **33**: 386-389, 2001.
11. Ugras S, Cirak B, Karakok M, Guven B. Spinal epidural granulocytic sarcoma (chloroma) in a non-leukemic child. Pediatr Int **43**: 505-507, 2001.
12. Fiegl M, Rieger C, Braess J, et al. Isolated epidural chloroma with translocation t(15;17) successfully treated with chemotherapy and all-trans-retinoic acid. Br J Haematol **122**: 688-689, 2003.
13. Landis DM, Aboulafia DM. Granulocytic sarcoma: an unusual complication of aleukemic myeloid leukemia causing spinal cord compression. A case report and literature review. Leuk Lymphoma **44**: 1753-1760, 2003.
14. Savranlar A, Ustundag Y, Ozer T, et al. A thoracic-epidural granulocytic sarcoma case that was diagnosed preceding the onset of

and that recurred co-incidental to acute promyelocytic leukemia, which developed after surgical treatment. Acta Med Okayama **58**: 251-254, 2004.

15. Nakashima S, Suzuki K, Watanabe K, et al. Detection of AML1/MTG8 fusion gene of spinal granulocytic sarcoma in a nonleukemic patient using the real-time polymerase chain reaction. J Orthop Sci **10**: 414-417, 2005.

16. Kalayci M, Sumer M, Yenidunya S, Ozdolap S, Acikgoz B. Spinal granulocytic sarcoma (chloroma) presenting as acute cord compression in a nonleukemic patient. Neurol India **53**: 221-223, 2005.

17. Howell DL, Abramowsky CR. Granulocytic sarcoma presenting as a large mediastinal mass with acute spinal cord compression in a non-leukemic child. Pediatr Blood Cancer **44**: 527, 2005.

18. Meltzer JA, Jubinsky PT. Acute myeloid leukemia presenting as spinal cord compression. Pediatr Emerg Care **21**: 670-672, 2005.

19. Balleari E, Panarello S, Capello E, et al. Granulocytic sarcoma: an unusual cause of spinal cord compression. Int J Clin Oncol **12**: 234-237, 2007.

20. Inoue T, Takahashi T, Shimizu H, et al. Spinal granulocytic sarcoma manifesting as radiculopathy in a nonleukemic patient. Neurol Med Chir **48**: 131-136, 2008.

21. Antic D, Verstovsek S, Elezovic I, et al. Spinal epidural granulocytic sarcoma in non-leukemic patient. Int J Hematol **89**: 95-97, 2009.

22. Takeda M, Yamaguchi S, Eguchi K, et al. Spinal epidural granulocytic sarcoma in a child precedent to clinical manifestation of acute myeloid lymphoma: case report. Neurol Med Chir **49**: 221-224, 2009.

23. Serefhanoglu S, Goker H, Aksu S, et al. Spinal myeloid sarcoma in two non-leukemic patients. Intern Med **49**: 2493-2497, 2010.

24. Kyaw TZ, Maniam JA, Bee PC, et al. Myeloid sarcoma: an unusual presentation of acute promyelocytic leukemia causing spinal cord compression. Turk J Haematol **29**: 278-282, 2012.

25. Xiao RZ, Long ZJ, Xiong MJ, Wang WW, Lin DJ. Diagnosis and treatment of a patient with isolated spinal granulocytic sarcoma: a case report. Oncol Lett **5**: 1229-1232, 2013.

26. Isshiki Y, Ohwada C, Togasaki E, et al. Acute myeloid leukemia concurrent with spinal epidural extramedullary myeloid sarcoma accompanied by a high CD25 expression and the FLT3-ITD mutation. Intern Med **53**: 1159-1164, 2014.

27. Yang C, Fang J, Xu Y. Isolated spinal myeloid sarcoma with rapid progression. Spine J **16**: e517-e518, 2016.

28. Pandey S, Gokden M, Kazemi NJ, Post GR. Hematolymphoid malignancies presenting with spinal epidural mass and spinal cord compression: a case series with rare entities. Ann Clin Lab Sci **49**: 818-828, 2019.

29. Kumar M, Sonia F, Hamadani SM, Abbas SA. A rare case of acute cord compression from spinal myeloid sarcoma: a complication of acute myeloid leukemia. Cureus **12**: e9502, 2020.

30. Gupta V, Ajam F, Conte G, et al. Liquid presenting as solid: a rare presentation of acute myeloid leukaemia as a solid epidural mass. Eur J Case Rep Intern Med **7**: 001802, 2020.

31. Rades D, Heidenreich F, Karstens JH. Final results of a prospective study of the prognostic value of the time to develop motor deficits before irradiation in metastatic spinal cord compression. Int J Radiat Oncol Biol Phys **53**: 975-979, 2002.