CASE REPORT

Myelodysplastic hematopoiesis mimicking the bone marrow in a mediastinal myelolipoma

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Introduction

There are wide varieties of diseases that cause mediastinal tumors. However, the differential diagnosis of the mediastinal tumors closely relates to the anatomic location. Neurogenic tumor is the most common cause of the posterior mediastinal tumor, but bronchogenic cyst, enteric cyst, diaphragmatic hernia, meningocele, and paravertebral abscess may occur [1]. One of the rare causes of posterior mediastinal tumor is extramedullary hematopoiesis (EMH), which is well recognized in congenital hemolytic anemia [2, 3]. EMH is classified as myelolipoma when fat tissue is predominant, lymphocytes, especially when aggregates are present, when erythroid hyperplasia is absent, or the tumor is solitary, but there is no clear distinction between the two diseases, and the pathogenesis of myelolipoma remains unclear [4]. Up to now, there are approximately twenty-five reports of mediastinal myelolipoma found in the literature [5, 6]. To the best of our knowledge, this is the first report of mediastinal myelolipoma associated with myelodysplastic syndrome (MDS) documenting the relation with the hematopoiesis of the bone marrow.

The images in Figure 1A and B show stump samples of a mediastinal tumor and bone marrow, respectively, obtained from the same patient. The tumor was determined to be a myelolipoma of the posterior mediastinum, and the patient was diagnosed with MDS. These images are very similar, making it difficult to determine the origin of the tissues. The similarity of the two tissues supports the hypothesis that bone marrow cell migration is involved in the histogenesis of myelolipoma.

This case also represents an unusual extramedullary involvement in a patient with MDS.

Case Report

A tumor was found incidentally in the posterior mediastinum of a 73-year-old man when he was treated for pneumonia. The blood test showed mild anemia with hematocrit 25.7% (normal range 38–52%), hemoglobin level 12.3 g/dL (normal range 13–18 g/dL), red cell count 3,840,000 per mm³ (normal range 4,000,000–5,500,000 per mm³), platelet count 88,000 per mm³ (normal range...
160,000–410,000 per mm³), and white cell count 7000 per mm³ (normal range 3800–8500 per mm³); the white cells consisted of 58.3% neutrophils (normal range 40–70%), 9.0% lymphocytes (normal range 15–40%), and 25% eosinophils (normal range 0–7%). A bone marrow smear (Fig. 1C and D) revealed dysplastic megakaryocytes and erythroblasts with megaloblastic changes and an increased number of eosinophils can be observed in both samples (May–Grunwald–Giemsa staining, 200 ×). (C, D) Bone marrow smear showing the dysplastic features of megakaryocytes (C) and erythroblasts (D) (May–Grunwald–Giemsa staining, 200 ×). (E) Computed tomography of the chest with the tumor (white arrow) in the right posterior mediastinum. (F, G) Hematoxylin- and eosin-stained sections demonstrating a robustly encapsulated tumor containing adipocytes and hematological tissue (F, 4 ×) and bone marrow elements with trilineage hematopoiesis and an increased number of eosinophils (G, 20 ×).

### Table 1. Differential count* of bone marrow smear and tumor stump sample.

| Cell type               | Bone Marrow (%) | Tumor (%) |
|-------------------------|-----------------|-----------|
| Neutrophilic series (total) | 48.2            | 38.4      |
| Myeloblast              | 2.0             | 1.6       |
| Promyelocyte            | 0.2             | 2.0       |
| Myelocyte               | 3.2             | 7.0       |
| Metamyelocyte           | 13.6            | 7.4       |
| Band                    | 12.2            | 10.4      |
| Segmented               | 17.0            | 10.0      |
| Eosinophilic series (total) | 5.2           | 8.8       |
| Basophilic series (total) | 0.2             | 6.6       |
| Erythrocyte series (total) | 35.6           | 32.8      |
| Lymphocytes             | 5.6             | 8.2       |
| Plasma cells            | 1.4             | 0.4       |
| Monocytes               | 3.0             | 4.6       |
| Megakaryocytes          | 0               | 0         |
| Reticulum cells         | 0.8             | 0.2       |
| Myeloid to erythroid ratio | 1.51           | 1.64      |

* Differential count was carried out by examining 500 nucleated cells in the May/Grunwald/Giemsa-stained samples.

The MDS diagnosis (refractory cytopenia with multilineage dysplasia). Computed tomography revealed that the tumor was oval shaped, 38 mm in diameter, and clearly encapsulated (Fig. 1E). By magnetic resonance imaging, the tumor lesion showed moderate signal intensity both on T1-weighted and on T2-weighted signal. As the radiographic findings were not typical for neurogenic tumors, the tumor was surgically removed. Pathologically, the tumor was composed of fat and hematopoietic tissues with trilineage cells in different developmental stages, and it was diagnosed as myelolipoma (Fig. 1F and G). A differential count of the tumor stump sample demonstrated that it was composed of 53.8% myeloid cells, 32.8% erythroid cells, and 8.2% lymphoid cells. This was similar to the bone marrow sample, which comprised 53.6% myeloid cells, 35.6% erythroid cells, and 5.6% lymphoid cells. A mild increase in the number of eosinophilic cells was also observed in both tissues (Table 1). Surface antigen screening of the tumor cells was performed using flow cytometry method and confirmed the existence of myeloid lineage (CD13- and CD33-positive) cells, erythroid lineage (glycophorin A-positive) cells, megakaryocyte lineage (CD41-positive) cells, B lymphocytes (CD19-positive), and T lymphocytes (CD3-positive), without the expansion of immature CD34-positive cells. Chromosome analysis by the G-banding method showed complex abnormalities (46, XY, –2, –7, der (11)add(11)(p11.2) add(11)(q23), add(12)(q13), del(20)(q11.2q13.3), +mar1, +mar2) in 19 of 20 cells examined, which was observed after analyzing the bone marrow cell as well. The tumor
was solitary and it was completely removed; there was no
evidence of recurrence 3 years after surgery.

Discussion
Here, we presented an atypical case of extramedullary
disease in a patient with MDS. Compared with leukemia,
the manifestation of extramedullary disease is infrequent
in MDS, and tumors develop only occasionally. Generally,
these tumors consist of immature cells of the myeloid lin-
eage and are often described as myeloid sarcoma. It may
be the first sign of leukemia and often shows poor prog-
nosis, whether by lack of effective therapy or by transfor-
tion to leukemia in many cases. The most commonly
involved sites are skin, bone, and lymph nodes [7]. From
the previous reports, we were able to find only one case
of mediastinum myeloid sarcoma associated with MDS
[8]. In the case presented here, the tumor was solitary
and contained differentiated myeloid cells in various
developmental stages, as well as significant amounts of
adipocytes and lymphocytes, and was therefore diagnosed
as myelolipoma.

Myelolipoma is a rare benign tumor typically found in
the adrenal gland, with rare extra-adrenal cases. In these
rare cases, lesions tend to be presacral, but they can occur
in many locations [4, 9–15]. Only a few studies reported
mediastinal myelolipoma cases and the majority of them
were found in the posterior mediastinum [5, 16]. Because
of the rarity of myelolipomas, a definitive diagnosis using
only radiographic studies is difficult, and some myelolipo-
mas may become extremely large [16]. However, most
mediastinal myelolipomas are removed surgically without
recurrence [5], which is in contrast to the prognosis of
extramedullary disease of MDS.

There are several hypotheses regarding the origin and
pathogenesis of this tumor, such as that it arises from the
metaplasia of stromal cells [17] or the remnants of primi-
tive fetal mesenchymal cells [4]. These cells may serve as
niche cells for the migration of bone marrow cells [18].
As concomitant endocrine disorders and hemolytic ane-
mia are often observed, prolonged hormone- [17] and
erthropoietin-induced [10] hyperstimulation of these
cells may contribute to tumor growth. Nonrandom X
chromosome inactivation [19] and cytogenetic abnormali-
ties [18] may explain the neoplastic characteristics of this
tumor. In this case, the clonal chromosomal abnormali-
ties detected in myelolipoma were identical to those
detected in the bone marrow cells, indicating the bone
marrow origin and neoplastic expansion of this tumor.

Conflict of Interest
None declared.

Authorship
HT: She is the hematologist for the diagnosis of MDS
and also responsible for this manuscript. KT: He was
responsible for the surgical resection of the mediastinal
tumor. KT: He was the pathologist for the diagnosis of
myelolipoma and MDS.

References
1. Duwe, B. V., D. H. Sterman, and A. I. Musani. 2005.
Tumors of the mediastinum. Chest 128:2893–2909.
2. Angelucci, E., and D. Baronciani. 1994. Extramedullary bone
marrow tumor in thalassemia. Haematologica 79:393–394.
3. Xiros, N., T. Economopoulos, E. Papageorgiou, G.
Mantzios, and S. Raptis. 2001. Massive hemothorax due to
intrathoracic extramedullary hematopoiesis in a patient
with hereditary spherocytosis. Ann. Hematol. 80:38–40.
4. Fowler, M. R., R. B. Williams, J. M. Alba, and C. R. Byrd.
1982. Extra-adrenal myelolipomas compared with
extramedullary hematopoietic tumors: a case of presacral
myelolipoma. Am. J. Surg. Pathol. 6:363–374.
5. Xiong, Y., Y. Wang, and Y. Lin. 2014. Primary
myelolipoma in posterior mediastinum. J. Thorac. Dis. 6:
E181–E187.
6. Lin, F., Q. Pu, L. Ma, C. Liu, J. Mei, H. Liao, et al. 2015.
Surgical treatment of primary mediastinal myelolipoma.
Interact. Cardiovasc. Thorac. Surg. 21:206–210.
7. Byrd, J. C., W. J. Edenfield, N. S. Dow, C. Aylesworth, and
N. Dawson. 1996. Extramedullary myeloid cell tumors in
myelodysplastic-syndromes: not a true indication of
impending acute myeloid leukemia. Leuk. Lymphoma
21:153–159.
8. Ravandi-Kashani, F., J. Cortes, and F. J. Giles. 2000.
Myelodysplasia presenting as granulocytic sarcoma of
mediastinum causing superior vena cava syndrome. Leuk.
Lymphoma 36:631–637.
9. Amin, M. B., S. K. Tickoo, and D. Schultz. 1999.
Myelolipoma of the renal sinus. An unusual site for a rare
extra-adrenal lesion. Arch. Pathol. Lab. Med. 123:631–634.
10. Au, W. Y., P. C. Tam, S. K. Ma, and K. Y. Lam. 2000.
Giant myelolipoma in a patient with thalassemia
intermedia. Am. J. Hematol. 65:265–266.
11. Massey, G. S., J. B. Green, and W. L. Marsh. 1987.
Presacral myelolipoma. Cancer 60:403–406.
12. Omdal, D. G., D. E. Baird, B. S. Burton, W. W. Goodhue,
and E. M. Giddens. 1997. Myelolipoma of the thoracic
spine. AJNR Am. J. Neuroradiol. 18:977–979.
13. Nishizaki, T., T. Kanematsu, T. Matsumata, C. Yasunaga,
S. Kakizoe, and K. Sugimachi. 1989. Myelolipoma of the
liver. A case report. Cancer 63:930–934.
14. Gheith, S., R. Boulay, and D. Cornfield. 2009. Small
lymphocytic lymphoma/chronic lymphocytic leukemia in a
pelvic myelolipoma. Int. J. Clin. Exp. Pathol. 2:95–98.
15. George, S. A., M. T. Manipadam, and R. Thomas. 2012. Primary myelolipoma presenting as a nasal cavity polyp: a case report and review of the literature. J. Med. Case Rep. 6:127.
16. Vaziri, M., A. Sadeghipour, A. Pazooki, and L. Z. Shoolami. 2008. Primary mediastinal myelolipoma. Ann. Thorac. Surg. 85:1805–1806.
17. Selye, H., and H. Stone. 1950. Hormonally induced transformation of adrenal into myeloid tissue. Am. J. Pathol. 26:211–233.
18. Chang, K. C., P. I. Chen, Z. H. Huang, Y. M. Lin, and P. L. Kuo. 2002. Adrenal myelolipoma with translocation (3;21)(q25;p11). Cancer Genet. Cytogenet. 134:77–80.
19. Bishop, E., J. N. Eble, L. Cheng, M. Wang, D.R. Chase, A. Orazi, et al. 2006. Adrenal myelolipomas show nonrandom X-chromosome inactivation in hematopoietic elements and fat: support for a clonal origin of myelolipomas. Am. J. Surg. Pathol. 30:838–843.