Conflict of Interest: The author of this paper has no conflicts of interest, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

References

1. Vannier E, Krause PJ. Human babesiosis. N Engl J Med 2012;366:2397-2407.
2. Haass KA, Sapiano MRP, Savinkina A, Kuehnert MJ, Basavaraju SV. Transfusion-transmitted infections reported to the National Healthcare Safety Network Hemovigilance Module. Transfus Med Rev 2019;33:84-91.
3. Lubin AS, Snydman DR, Miller KB. Persistent babesiosis in a stem cell transplant recipient. Leuk Res 2011;35:77-78.
4. Browne S, Ryan Y, Goodyer M, Gilligan O. Fatal babesiosis in an asplenic patient. Br J Haematol 2010;148:494.
5. Zhao Y, Love KR, Hall SW, Beardell FV. A fatal case of transfusion-transmitted babesiosis in the state of Delaware. Transfusion 2009;49:2583-2587.

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Isolated Mediastinal Myeloid Sarcoma after *NPM1*-Positive Pediatric Acute Myeloid Leukemia

NPM1-Pozitif Pediatrik Akut Myeloid Lösemi Sonrası İzole Mediastinal Myeloid Sarkom

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To the Editor,

Myeloid sarcoma (MS) is a rare extramedullary mass that consists of immature myeloid cells. The most common locations are the soft tissue, bone, periosteum, orbit, and lymph nodes [1,2]. Mediastinal involvement is very rare and most commonly reported with concurrent bone marrow involvement [3]. Herein we present a previously treated nucleophosmin (*NPM1*)-positive acute myeloid leukemia (AML) patient who later presented with isolated mediastinal MS.

A 9-year-old female patient presented with fatigue and weakness. Physical examination revealed no pathological findings. Blood tests demonstrated hemoglobin of 12.2 g/dL, hyperleukocytosis (100,500/µL), and thrombocytopenia (43,000/µL) with 88% blasts in the peripheral blood smear. Bone marrow aspirate revealed 90% blasts with M1 subtype. Treatment was started according to the AML-BFM 2012 protocol. Conventional cytogenetic analysis failed due to lack of spontaneous mitosis and fluorescent in situ (FISH) analysis for t(8;21), inv(16), t(15;17), and t(9,22) from bone marrow samples revealed negative results. Molecular genetic analysis in the peripheral blood showed *NPM1* positivity and *FLT3-ITD* negativity. Morphologic and molecular remission was obtained at the end of the first induction block. She presented with back pain and fever seven months after cessation of maintenance treatment. Computed tomography (CT) of the thorax showed a solid mass of 84x75x41 mm in the anterior mediastinum (Figure 1). Bone marrow examination was normal; however, peripheral blood showed *NPM1* positivity. Conventional cytogenetic analysis from the bone marrow was within normal limits, while *NPM1* could not be studied from bone marrow. Her previous CT scans that were performed for investigation of invasive pulmonary aspergillosis were all normal. Fine-needle aspiration biopsy of the mass was performed; histopathological examination revealed myeloblasts that were positive for myeloperoxidase, CD15, and CD33. Microscopic examination of the imprint of the biopsy also revealed myeloblasts of M1 subtype (Wright stain). Major reduction in tumor mass (7 mm residual tumor) and *NPM1* negativity were achieved after one block of FLAG (fludarabine, cytarabine, filgrastim) and two blocks of FLAG-mitoxantrone. The patient underwent successful bone marrow transplantation from a matched unrelated donor and has been in remission for one year.

MS of the mediastinum is very rare; most of the cases have been reported as initial presentation with concurrent bone marrow involvement [3,4,5]. MS as a relapse has been more frequently reported in post-transplant patients compared to those treated without allogeneic hematopoietic stem cell transplantation [6,7]. Our patient is unique as she presented with isolated mediastinal MS after chemotherapy treatment. Another important point about our patient is that the *NPM1* positivity was detected at

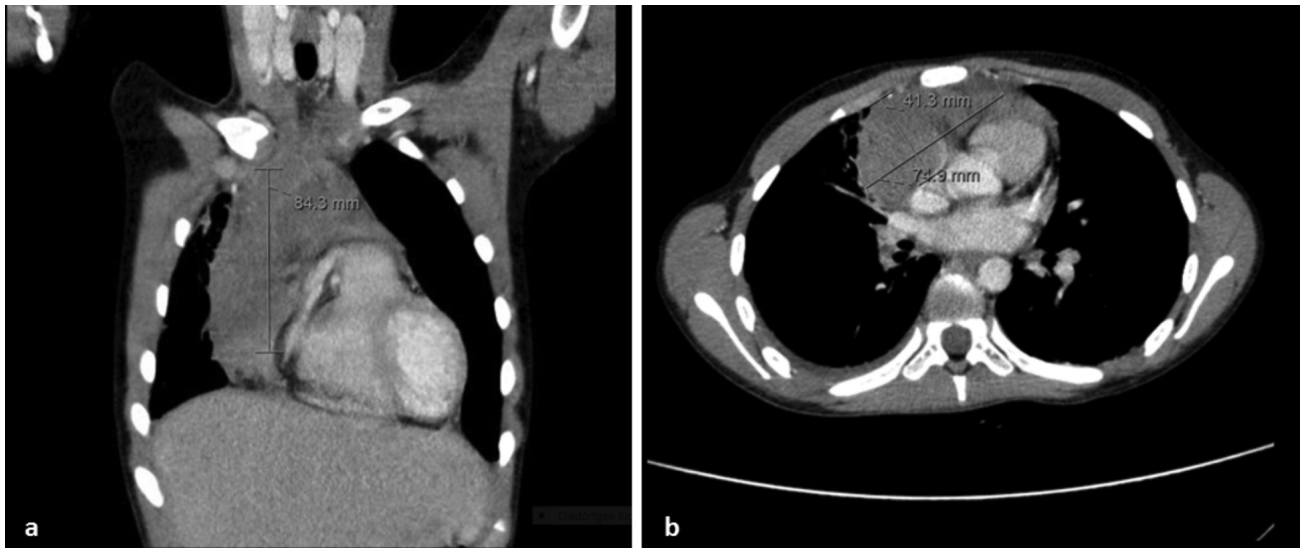

Figure 1. Computed tomography of the thorax showing anterior mediastinal mass in coronal (a) and axial (b) sections.

the same time as MS. The incidence of MS has been known to be higher in certain cytogenetic abnormalities, in particular t(8,21) [1,6]. Falini et al. [8], in their study with 181 MS samples, identified *NPM1* mutations as the most frequent molecular lesion in MS, defining the molecular status in 15% of cases. Our patient was negative for t(8:21) but had *NPM1* positivity.

In conclusion, even though *NPM1* is not a poor prognostic factor for AML, it should be kept in mind that patients with *NPM1* positivity may later present with MS, as in the case of our patient, who presented with isolated MS of the mediastinum months after cessation of chemotherapy.

Keywords: Acute myeloid leukemia, Myeloid sarcoma, Mediastinal mass, *NPM1*

Anahtar Sözcükler: Akut myeloid lösemi, Myeloid sarkom, Mediastinal kitle, *NPM1*

Informed Consent: Written informed consent for publication was obtained from the patient and her parents.

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References

1. Bakst RL, Tallman MS, Douer D, Yahalom J. How I treat extramedullary acute myeloid leukemia. Blood 2011;118:3785-3793.
2. Klco JM, Welch JS, Nguyen TT, Hurley MY, Kreisel FH, Hassan A, Lind AC, Frater JL. State of the art in myeloid sarcoma. Int J Lab Hematol 2011;33:555-565.
3. Ramasamy K, Lim Z, Pagliuca A, Devereux S, Ho AY, Mufti GJ. Acute myeloid leukaemia presenting with mediastinal myeloid sarcoma: report of three cases and review of literature. Leuk Lymphoma 2007;48:290-294.
4. Nounou R, Al-Zahrani HH, Ajarim DS, Martin J, Iqbal A, Naufal R, Stuart R, Roberts G, Gyger M. Extramedullary myeloid cell tumours localised to the mediastinum: a rare clinicopathological entity with unique karyotypic features. J Clin Pathol 2002;55:221-225.
5. Au WY, Ma SK, Chan AC, Liang R, Lam CC, Kwong YL. Near tetraploidy in three cases of acute myeloid leukemia associated with mediastinal granulocytic sarcoma. Cancer Genet Cytogenet 1998;102:50-53.
6. Samborska M, Derwich K, Skalska-Sadowska J, Kurzawa P, Wachowiak J. Myeloid sarcoma in children-diagnostic and therapeutic difficulties. Contemp Oncol (Pozn) 2016;20:444-448.
7. Yoo SW, Chung EJ, Kim SY, Ko JH, Baek HS, Lee HJ, Oh SH, Jeon SC, Lee WS, Park CK, Lee CH. Multiple extramedullary relapses without bone marrow involvement after second allogeneic hematopoietic stem cell transplantation for acute myeloid leukemia. Pediatr Transplant 2012;16:125-129.
8. Falini B, Lenze D, Hasserjian R, Coupland S, Jaehne D, Soupir C, Liso A, Martelli MP, Bolli N, Bacci F, Pettirossi V, Santucci A, Martelli MF, Pileri S, Stein H. Cytoplasmic mutated nucleophosmin (NPM) defines the molecular status of a significant fraction of myeloid sarcomas. Leukemia 2007;21:1566-1570.

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