Medical Science

pISSN 2321–7359; eISSN 2321–7367

Myeloid sarcoma involving the central nervous system as initial presentation of acute myeloid leukemia patient: A case report

Waleed Murshid[1], **Badr Hafiz**[2*], **Raghad Aljohani**[3], **Daliyah Al Qulaiti**[3], **Omar Aljohani**[4]

To Cite:
Murshid W, Hafiz B, Aljohani R, Al-Qulaiti D, Aljohani O. Myeloid sarcoma involving the central nervous system as initial presentation of acute myeloid leukemia patient: A case report. Medical Science 2022; 26:ms394e2482.
doi: https://doi.org/10.54905/disssi/v26i128/ms394e2482

Authors' Affiliation:
[1]Professor and Consultant, Department of Neurosurgery, College of Medicine, Taibah University, Madinah, Saudi Arabia
[2]Medical Intern, College of Medicine, Taibah University, Madinah, Saudi Arabia
[3]Medical Intern, College of Medicine, Alrayan Colleges, Madinah, Saudi Arabia
[4]General Physician, College of Medicine, Taif University, Al Hawaiah, Saudi Arabia

***Corresponding author**
Medical Intern, College of Medicine, Taibah University, Madinah, Saudi Arabia
Email: badr_Hafiz@hotmail.com

Peer-Review History
Received: 14 September 2022
Reviewed & Revised: 15/September/2022 to 27/September/2022
Accepted: 27 September 2022
Published: 02 October 2022

Peer-review Method
External peer-review was done through double-blind method.

URL: https://www.discoveryjournals.org/medicalscience

ABSTRACT

Extra medullary leukemic infiltration of CNS is extremely rare, and its incidence is 3%. Myeloid sarcoma (MS) of the central nervous system (CNS) is associated with a poor prognosis and has an aggressive course. Most commonly associated with hematopoietic neoplasm and, rarely, occurs in an isolated fashion. Presentation of MS is highly variable, the patient might present with a newly neurological deficit due to mass effect that required neurosurgical consideration, and urgent debulking require as a life-saving measure as in our patients. Despite the controversial area in management of MS involving the CNS, we present a case of acute myeloid leukemia (AML) with MS involving the CNS. Our patient was treated surgically as it was life-saving since the patient presented with a focal neurological deficit. Our patient was admitted for the whole duration and followed conservatively by a multidisciplinary team (neurosurgery/hematology-oncology and intensivists). Clinical presentations, neuroimaging, immunohistochemical findings, and the prognostic indicators as well as the survival rates, are discussed.

Keywords: myeloid sarcoma, central nervous system, acute myeloid leukemia, extra-medullary disease pathology.

1. INTRODUCTION

Myeloid sarcoma (MS) is a rare extra-medullary leukemic infiltrative tumor with an incidence of 2-8% (Avni and Koren-Michowit, 2011). It is usually accompanied by acute myeloid leukemia (AML) and, rarely, occurs in an isolated fashion (Avni and Koren-Michowit, 2011). In 1823, Burns (Di Veroli et al., 2013); reported the first case of myeloid sarcoma and named it chloroma, while in 1903, Turk reported the first case of MS associated with AML (Di Veroli et al., 2013). MS is also known as Granulocytic Sarcoma, extra-medullary Leukemia, Myeloblastoma and chloroma (Avni and Koren-Michowit, 2011; Di Veroli et al., 2013). The term chloroma is derived from the greenish color and it is attributed to the existence of myeloperoxidase (MPO) enzyme (Avni and Koren-Michowit, 2011). MS occurs in various extra-medullary sites, most commonly the skin (28%), lymph nodes (16%), testis

(6%), biliary tract (3%) and the central nervous system (CNS) (3%) (Pileri et al., 2007; Struhal et al., 2008).

The CNS involvement include the subperiostium and dura matter, spinal cord and in rare occasions the brain parenchyma and thus appear as an intra-axial mass (Cervantes and Cayci, 2015). According to Cervantes and Cayci (2015) demonstrated four patterns of MS development in AML patients. The clinical presentation of MS is highly variable, and it mainly depends on the localization and size. Most commonly results in compressive symptoms in a form of severe pain or abnormal bleeding (Avni and Koren-Michowit, 2011). MS is not a common disease when it comes to the diagnosis. The detection of MS requires immunophenotyping, immunohistochemistry and radiological assessment which also play an important role in the risk stratification and management planning (Avni and Koren-Michowit, 2011).

The presence of immature myeloid cells in the extramedullary sites is characteristic for the immunohistochemistry findings of the tumour (Di Veroli et al., 2013). The most commonly used markers for diagnosing MS are CD68, CD117, MPO, CD43, lysozyme, CD56, CD99. The most sensitive are CD43, lysozyme and MPO as they are positive in more than 90% of cases (Avni and Koren-Michowit, 2011; Di Veroli et al., 2013; Pileri et al., 2007).

CNS involvement

The CNS involvement is rare, but should be suspected in any hematopoietic neoplasm case who present with a neurological sign and symptoms (Pileri et al., 2007). The mechanism of CNS involvement in MS is controversial and uncertain (Shallis et al., 2021). Azzarelli et al., (1977) explained the migration of the leukemic cells from the bone marrow through the Haversian canals to the periosteum and infiltrate the perivenous adventitial tissue connecting the dura matter and subarachnoid space. Others proposed that the extra medullary invasion and survival is attributed to the appearance of the specific glycoproteins such as CD56 that involved in the leukemic cells adhesion (Iizuka et al., 1992). CNS involvement is a poor prognostic indicator in MS (Mayadev et al., 2011). The sites of CNS involvement in MS are as the following order, most commonly in the spinal cord (54%) and the tumor located within the epidural layer causing cord compression and present with a myelopathy and radiculopathy (Olar et al., 2016). The brain involvement is (40%) and more common in the parenchyma than the dura (Olar et al., 2016). Mixed cerebral and spinal cord involvement was reported in (6%) (Olar et al., 2016).

2. CASE PRESENTATION

On March 7, 2022, a sixty-one-year-old Nigerian female patient presented to the emergency department with confusion and right-sided limb weakness, which progressed slowly over three days. On examination, the patient with BP of 230/109 mmHg she drowsy, and her Glasgow coma scale (GCS) was 13/15 M6E4V3, bilateral equal reactive pupils with right sided hemiplegia. Magnetic resonance imaging (MRI) with contrast of the brain showed a large multilobulated intra-axial mass involving the left parietal and temporal lobes (8.6 X 5 X 6 cm) with central cystic degeneration, necrosis and 1.45 cm shifting of the midline as a result from the surrounding vasogenic edema and compression on the left lateral ventricle and left cerebral peduncle effacing the left ambient cistern.An incidental finding of a right tentorial small meningioma, shown in (Fig.1).

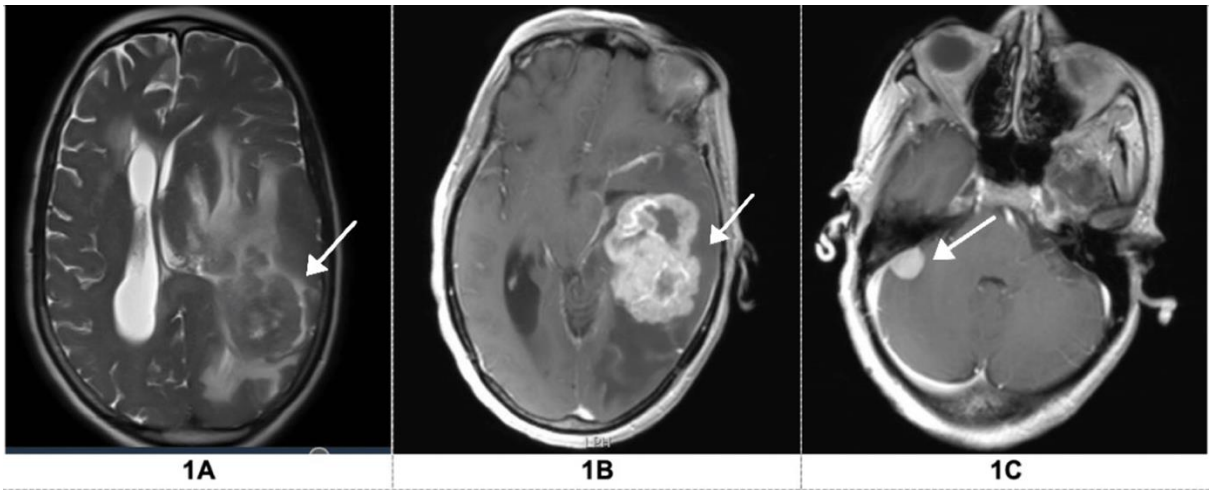

Figure 1 A Brain MRI with contrast preoperatively showed a large multilobulated intra-axial mass involving the left parietal and temporal lobes (8.6 X 5 X 6 cm) with central cystic degeneration, necrosis and surroundings with significant vasogenic oedema with a midline shift of 1.45 cm. **B**: mass effect on the left lateral ventricle and left cerebral peduncle effacing the left ambient cistern. **C**: An incidental finding of a right tentorial small meningioma

In emergency department settings, the patient received dexamethasone (8mg), amlodipine (5mg) for hypertension. The patient underwent an emergency decompressive craniotomy for the debulking of the brain tumor. Postoperative non-enhanced CT scan of the brain (Figure 2).

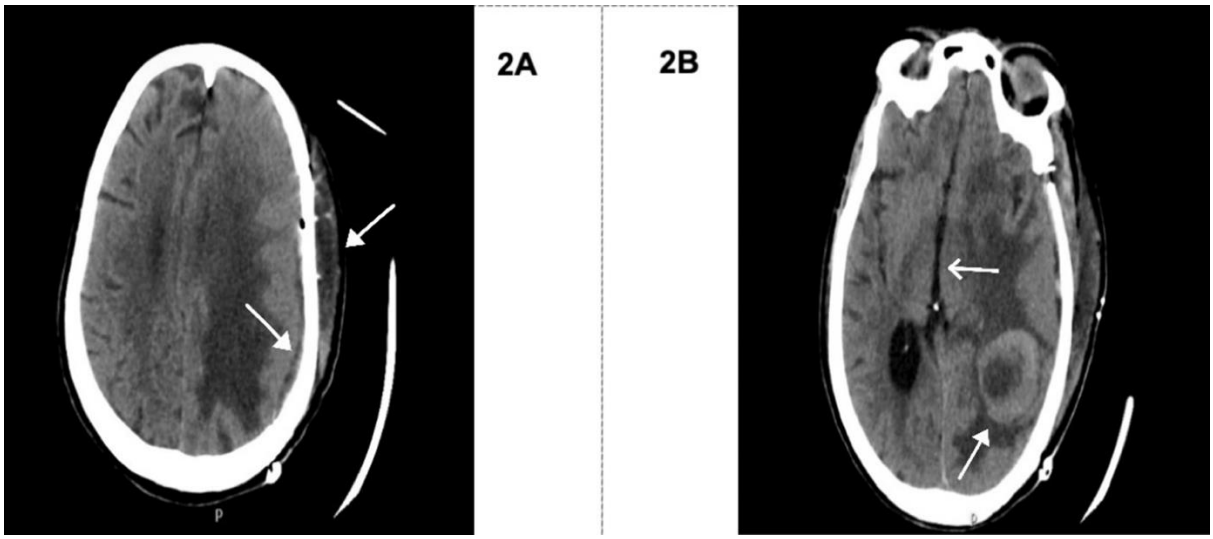

Figure 2 Non-enhanced CT scan of the brain. **A**: Post left parieto-temporal craniotomy changes; in form of left parieto-temporal subgaleal hematoma with subdural hematoma measuring 1.2 cm at maximum diameter. **B**: Multiple hyperdense foci at left temporal lobe at the resection site of the tumor, the largest measures are 1.3 X 1.5 X 1.5 cm in anteroposterior, transverse, and craniocaudal respectively, compatible with intraparenchymal hemorrhage, with rightward midline shift by 1 cm.

The immunohistochemistry studies revealed a sheet of immature mononuclear cells, positive for CD117 (c-kit), CD38 and strong patchy for CD45 and negative for MPO, CD68, CD43 and Tdt (Fig.3) suggesting a diagnosis of myeloid sarcoma. A bone marrow biopsy and peripheral blood smear examination were performed for potential marrow involvement. In bone marrow, hyper-cellular for age (cellularity 60-50%), dense focal infiltration with sheets of mononuclear cells is seen with increasing megakaryocytes in number. Immunohistochemistry study shows positive for MPO, CD68, CD03 scattered, negative for CD117, CD20 and CK-pan (Fig.4). The patient was diagnosed accordingly as AML with MS. The hematology team considered the patient not indicated for chemotherapy.

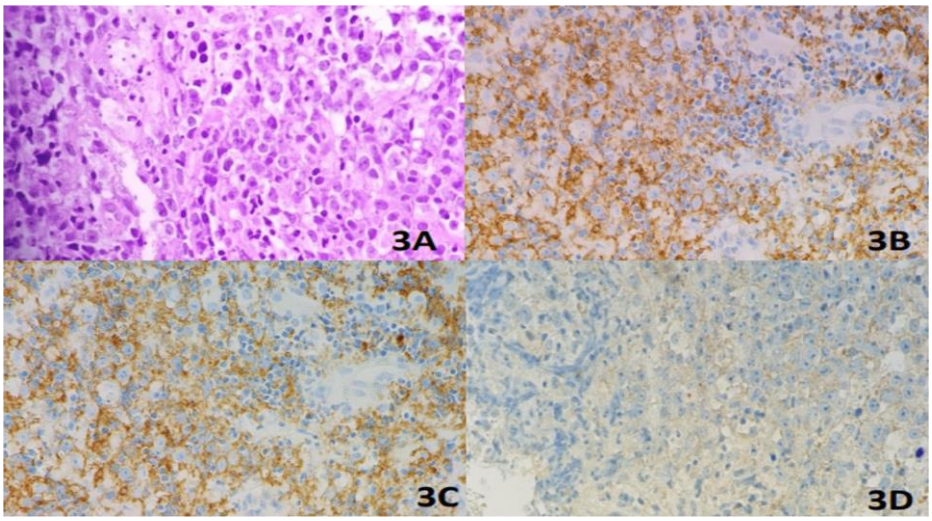

Figure 3 A: (H&E section) Diffuse area of large cells, having prominent nucleoli and extensive apoptosis. B-C: Tumor cells are positive for CD117 and CD38, D: Tumor cells are negative for Tdt. (*H&E: Hematoxylin and eosin, Tdt: Terminal deoxynucleotidyl transferase)

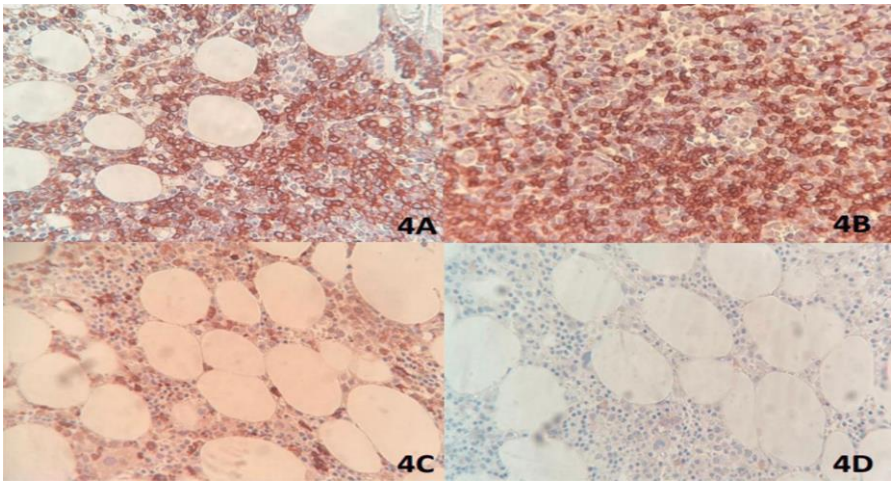

Figure 4 A-C: Tumour cells are positive for MPO, CD03 and CD68. D: Tumour cells are negative for CD117.
*MPO: Myeloperoxidase

Postoperatively she was doing well and GCS 14/15, the weakness subsided. She is doing well in general ward for twenty-fivedays managed conservatively and she sudden collapse with GSC 3/15, and brain CT scan showed increased vasogenic oedema with midline shifting by 1.6 cm. She underwent lifesaving decompressive craniotomy for the debulking of the brain tumor again. Unfortunately, despite all these measures and modalities, the patient deteriorated and only survived for approximately three months.

4. DISCUSSION

Poor prognostic indicators include age ≤15 years, black ethnicity, and MS in CML and/or MDS, CNS involvement and lymph node or soft tissue (Goyal et al., 2017; Jadhav et al., 2021). Additionally, patients (age ≥ 70 years) who had early systemic chemotherapy have been associated with the worst prognostic outcome compared to early surgery or radiation or no treatment (Goyal et al., 2017; Jadhav et al., 2021). Immunohistochemistry is essential in confirming the diagnosis and distinguishing its variants (Struhal et al., 2008). The most frequent markers expressed in MS are CD68KP1 followed by MPO, CD117, CD99, CD43, lysozyme, CD34, CD56 and terminal deoxynucleotidyl transferase (TdT) (Avni and Koren-Michowit, 2011; Marwah et al., 2019). However, the most sensitive markers are CD43 and lysozyme. Expression of CD117 showed to be associated with poorer outcomes (Marwah et al., 2019). In our particular case, the immunohistochemistry findings were positive for CD117 (c-kit), CD38 and strong patchy for CD45 in the brain biopsy. On the other hand, the biopsy from the bone marrow was positive for MPO, CD68, and CD03 scattered and diagnosed accordingly as AML with MS of CNS.

The usual outcome of MS is a poor 20% 5-year survival rate with appropriate therapeutic interventions. Most patients cannot survive and die in the first year from establishing the diagnosis; mostly due to relapse and infection (Jadhav et al., 2021). Complete remission rates after the first course of induction chemotherapy and the 3-year relapse-free survival (RFS) among patients with AML and MS were lower than with AML alone (Hu et al., 2021). The reports denoting the outcome of CNS involvement in MS patient are limited. Mayadev et al., (2011) showed that the outcomes in patients with extra medullary infiltration of AML including CNS involvement have a poor prognosis and outcomes, but their investigation did not focus specifically on CNS involvement. On the contrary, two studies by Bar et al., (2015) and Aoki et al., (2014) showed that there was no prominent differences in comparison between patients with AML without CNS involvement and those with CNS involvement, but the selected patient in those studies are limited to those who underwent a hematopoietic stem cell transplantation (HSCT) which can confound the study result.

In our case, the patient presented with compressive symptoms. However, she had marked initial improvement after surgical debulking alone with no chemotherapy or HSCT, but then she relapsed again and further debulking was done for her without improvement. The prognosis was very poor, and she only survived for three months.

5. CONCLUSION

Our case was challenged by MS of the CNS as the initial presentation of acute myeloid leukemia. Infiltrative brain tumors should be considered in the differentials of brain tumors. Furthermore, extra-medullary leukemic infiltrative tumor of CNS is extremely rare, which is also associated with poor prognosis and has an aggressive course. Early detection of leukemic infiltration in CNS required a neurosurgical consideration warrant in any patient who presents with a newly onset neurological complaint with or without known hematological malignancy. Regarding the confirmation of MS in CNS, the radiographic findings are nonspecific and can mimic other intracranial or spinal pathologies. Hence, tissue diagnosis is the gold standard for treating such cases. MS of CNS should be in the differential diagnosis, even in the absence of evidence of underlying disease. Due to the limited data regarding the therapeutic strategies for such a disease, we believe Early detection of CNS involvement in MS patients along with a proper management plan is the cornerstone in improving the patients outcomes, including the morbidity and survival rate.

Acknowledgement

I am sincerely thankful to Dr. Waleed Murshid for his immense help in finishing this work. I would also thank the writers who all contributed in this case report.

Author Contributions

Waleed Murshid: Helped in writing the case presentation and discussion as well as supervising the writing and reviewing the final manuscript before submission.

Badr Hafiz: Helped in collecting the data, writing the abstract, case presentation, discussion, conclusion and manuscript submission.

Raghad Aljohani: Helped in collecting the data, writing the abstract, case presentation, discussion, and conclusion.

Daliyah Al Qulaiti: Helped in collecting the data, writing the abstract, case presentation, discussion, and conclusion.

Omar Aljohani: Helped in writing the abstract, discussion and conclusion.

Informed consent

Written and oral informed consent was obtained from the patient included in the study.

Funding

This study has not received any external funding.

Conflicts of interest

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

REFERENCES AND NOTES

1. Aoki J, Ishiyama K, Taniguchi S, Fukuda T, Ohashi K, Ogawa H, Kanamori H, Eto T, Iwato K, Sakamaki H, Morishima Y, Nagamura T, Atsuta Y, Takami A. Outcome of allogeneic hematopoietic stem cell transplantation for acute myeloid leukemia patients with central nervous system involvement. Biol Blood Marrow Transplant 2014; 20(12):2029-33. doi: 10.1016/j.bbmt.2014.09.001
2. Avni B, Koren-Michowitz M. Myeloid sarcoma: current approach and therapeutic options. Ther Adv Hematol 2011; 2(5):309-16. doi: 10.1177/2040620711410774.
3. Azzarelli V, Roessmann U. Pathogenesis of central nervous system infiltration in acute leukemia. Arch Pathol Lab Med 1977; 101(4):203-5.
4. Bar M, Tong W, Othus M, Loeb KR, Estey EH. Central nervous system involvement in acute myeloid leukemia patients undergoing hematopoietic cell transplantation. Biol Blood Marrow Transplant 2015; 21(3):546-51. doi: 10.1016/j.bbmt.2014.11.683
5. Cervantes GM, Cayci Z. Intracranial CNS Manifestations of Myeloid Sarcoma in Patients with Acute Myeloid Leukemia: Review of the Literature and Three Case Reports from the Author's Institution. J Clin Med 2015;4(5):1102-12. doi: 10.3390/jcm4051102
6. Di Veroli A, Micarelli A, Cefalo M, Ceresoli E, Nasso D, Cicconi L, Mauramati S, Ottaviani F, Venditti A, Amadori S. Recurrence of a t(8;21)-Positive Acute Myeloid Leukemia in

the Form of a Granulocytic Sarcoma Involving Cranial Bones: A Diagnostic and Therapeutic Challenge. Case Rep Hematol 2013; 2013:245395. doi: 10.1155/2013/245395

7. Goyal G, Bartley AC, Patnaik MM, Litzow MR, Al-Kali A, Go RS. Clinical features and outcomes of extramedullary myeloid sarcoma in the United States: analysis using a national data set. Blood Cancer J 2017; 7(8):e592. doi: 10.1038/bcj.2017.79
8. Hu G, Lu A, Wu J, Jia Y, Zuo Y, Ding M, Zhang L. Characteristics and prognosis of pediatric myeloid sarcoma in the cytogenetic context of t(8;21). Pediatr Hematol Oncol 2021; 38(1):14-24. doi: 10.1080/08880018.2020.1803462
9. Iizuka Y, Aiso M, Oshimi K, Kanemaru M, Kawamura M, Takeuchi J, Horikoshi A, Ohshima T, Mizoguchi H, Horie T. Myeloblastoma formation in acute myeloid leukemia. Leuk Res 1992; 16(6-7):665-71. doi: 10.1016/0145-2126(92)90017-2
10. Jadhav T, Baveja P, Sen A. Myeloid sarcoma: an uncommon presentation of myeloid neoplasms; a case series of 4 rare cases reported in a tertiary care institute. Autops Case Rep 2021; 11:e2021339. doi: 10.4322/acr.2021.339
11. Marwah N, Bhutani N, Budhwar A, Sen R. Isolated myeloid sarcoma of the temporal bone: As the first clinical manifestation of acute myeloid leukemia in a patient of down's syndrome. Int J Surg Case Rep 2019; 58:77-80. doi:10.1016/j.ijscr.2019.03.027
12. Mayadev JS, Douglas JG, Storer BE, Appelbaum FR, Storb R. Impact of cranial irradiation added to intrathecal conditioning in hematopoietic cell transplantation in adult acute myeloid leukemia with central nervous system involvement. Int J Radiat Oncol Biol Phys 2011; 80(1):193-8. doi: 10.1016/j.ijrobp.2010.01.062
13. Olar A, Lapadat R, Davidson CJ, Stein TD, Dahiya S, Perry A, Gheorghe G. Central nervous system involvement by myeloid sarcoma: a report of 12 cases and review of the literature. Clin Neuropathol 2016; 35(5):314-25. doi: 10.5414/NP300949
14. Pileri SA, Ascani S, Cox MC, Campidelli C, Bacci F, Piccioli M, Piccaluga PP, Agostinelli C, Asioli S, Novero D, Bisceglia M, Ponzoni M, Gentile A, Rinaldi P, Franco V, Vincelli D, Pileri A Jr, Gasbarra R, Falini B, Zinzani PL, Baccarani M. Myeloid sarcoma: clinico-pathologic, phenotypic and cytogenetic analysis of 92 adult patients. Leukemia 2007; 21(2):340-50. doi: 10.1038/sj.leu.240449
15. Shallis RM, Gale RP, Lazarus HM, Roberts KB, Xu ML, Seropian SE, Gore SD, Podoltsev NA. Myeloid sarcoma, chloroma, or extramedullary acute myeloid leukemia tumor: A tale of misnomers, controversy and the unresolved. Blood Rev 2021; 47:100773. doi: 10.1016/j.blre.2020.100773.
16. Struhal W, Oberndorfer S, Lahrmann H, Lindeck-Pozza E, Hess B, Nussgruber V, Pöhnl R, Dobner T, Grisold W. Myeloid sarcoma in the central nervous system: case report and review of the literature. Acta Clin Croat 2008; 47(1):19-24.