ISSN No:-2456-2165

Isolated CNS Relapse in Favourable Acute Myeloid Leukemia Presenting as Cerebello-Pontine Angle Tumor

[1.] Dr Vishnu Sharma
Department of General Medicine
SMS Medical College
Jaipur, India

[2.] Vansh Bagrodia
Final MBBS Student
SMS Medical College
Jaipur, India

Abstract:- We report a case of a woman in her late 40s with favourable acute myeloid leukemia [45X,-X, t(8;21)] who achieved complete remission after her initial diagnosis, presented with isolated central nervous system (CNS) relapse as left cerebello-pontine angle tumor which was further diagnosed as a extramedullary CNS myeloid sarcoma which is a rare presentation.

I. INTRODUCTION

Acute myeloid leukemia (AML) is a clonal neoplasm of the bone marrow and blood where hematopoietic stem cell precursors of the myeloid lineage acquire various genetic mutations and undergo unregulated proliferation. AML can be classified as favourable risk (e.g., RUNX1-RUNX1T1, CBFB-MYH11,mutatedNPM1 without FLT3-ITD, orbZIP in-frame mutated CEBPA), intermediate risk (e.g., mutated NPM1 and FLT3-ITD, wild-type NPM1 without FLT3-ITD, or MLLT3-KMT2Ac), or adverse risk (e.g., DEK-NUP214, KMT2A rearranged, BCR-ABL1, del(5q), abnormal(17p), monosomal and complex karyotype) based on cytogenetic profiles. Previously, the standard chemotherapy regimen of daunorubicin and cytarabine led to a five-year survival rate of 40–45% in patients 50–55 years of age, and less than 10–15% in patients 60 years of age and older.

Older patients tend to have higher risk cytogenetics, with one study demonstrating more involvement of chromosomes 5, 7, and 17p. In addition, when stratified by risk category, patients younger than age 56 have increased overall survival compared with older patients. Occasionally, patients have extramedullary manifestations, such as leukemia cutis and myeloid sarcoma. Appropriate therapy depends on the characteristics of each specific acute leukemia, patient characteristics, and goals of care.[1] AML is typically treated with intensive initial therapy (induction) followed by repetitive cycles of intensive post-remission therapy (consolidation). Induction chemotherapy most commonly consists of anthracycline plus cytarabine. Several acceptable post-remission approaches are used; often these are repetitive high-dose cytarabine based regimens.

II. CASE

We report a case of a space occupying lesion in Cerebello-pontine angle found to be a central nervous system myeloid sarcoma due to extramedullary relapse in a female patient in her late 40s who was a known case of AML successfully treated with chemotherapy.

Patient initially came with complaints of progressively increasing weakness, fatigue fever and bone pain. A peripheral smear done revealed 85% blasts and bone marrow aspiration and biopsy suggested diagnosis of acute leukemia. Immunophenotyping by flow cytometry reported CD45 dim~82% blasts population which express dim CD13, dim CD15, moderate CD33, heterogenous CD34, bright HLADR, heterogenous CD117, dim CD123, dim CD19 (32%) and positive for cytoplasmic MPO, cytogenetics showed 45X,-X, t(8;21)(q22;q22)and NGS panel for myeloid mutation did not reveal any mutation. This established the diagnosis of favourable risk category Acute Myeloid Leukemia according to 2017 European Leukemia Net Risk Stratification for AML in patient.

Patient was treated with induction with Cytarabine and Daunorubicin (7+3 regimen) and she achieved complete remission on bone marrow with MRD negativity. Following which patient was given 3 cycles of consolidation chemotherapy with Cytarabine 3gm/m^2 twice a day on day 1, 3 & 5. Her treatment course was complicated by episodes of febrile neutropenia which was treated with antibiotics.

Patient remained asymptomatic for a few months after completion of chemotherapy but then presented with complaints of tinnitus, dizziness, vertigo, headaches, and gait unsteadiness for which CNS relapse of AML was suspected.

Contrast enhanced MRI of Brain was done which revealed a well-defined extra-axial mass lesion in left Cerebello-pontine angle cistern measuring 30 x 35 mm. It appeared heterogenously hypointense signal on T1W images and hyperintense signal on T2W images, causing mass effect over adjacent brainstem, left cerebellar hemisphere and 4th

ventricle. It showed homogenous enhancement on post contrast images.

Given the background history of AML, CNS myeloid sarcoma was suspected for which CSF was done which showed blasts. Flow cytometry on the CSF revealed blasts with expression of CD13, CD33, CD34, HLA-DRand cMPO, thus establishing the diagnosis of CNS relapse with myeloid sarcoma (MS). Her complete blood count, peripheral smear and bone marrow did not show evidence of systemic AML recurrence.

Patient was then initiated ontwice weekly intrathecal chemotherapy with complete symptomatic improvement and clearance of blasts from CSF in two weeks. Subsequently she was given FLAG (Fludarabine, AraC with G-CSF) followed by cranial irradiation and was also counselled for allogenic hematopoietic stem cell transplant. But the patient decided not to go for allogenic hematopoietic stem cell transplant and succumbed to infections 2 months after initiation of salvage chemotherapy.

III. DISCUSSION

Myeloid Sarcoma (MS) most frequently develops in patients with AML but can occur in association with accelerated-phase chronic myeloid leukemia, MDS, and, rarely, in the absence of marrow involvement. The frequency with which certain MS sites are accompanied by marrow involvement has not been adequately studied. The clinical manifestations of MS are diverse given the various sites of occurrence, with signs and symptoms determined by its specific location and size. The most common locations include the soft tissue, bone, periosteum, and lymph nodes; however, numerous sites have been described. Central nervous system (CNS) involvement is rare.[2]Overall, the incidence of MS in CNS is only 0.4% of total population. Leukaemia cells invade the CNS viacranial BM, vertebra, or orbital bones and migrate to underneath brain parenchyma due to disruption of BB.[3]

CNS leukemic infiltration may present in one or more of the following intracranial forms: (1) meningeal disease, as “carcinomatous meningitis”; (2) intravascular tumor aggregates throughout the brain, as “carcinomatous encephalitis”; or (3) focal tumor masses, as “myeloid sarcomas”. When AML manifests as a solid tumor outside the bone marrow, i.e., myeloid sarcoma, the imaging features can be mistaken for some conditions other than the myeloid sarcoma. The main reason is that their appearance on MRI has a broad differential diagnosis, and proper diagnosis of MS can only be made if the imaging findings are correlated with the clinical history and laboratory findings.[4]

In our case, a contrast enhanced MRI of Brain revealed a well-defined extra-axial mass lesion in left Cerebello-pontine angle cistern measuring 30 x 35 mm. It appeared heterogenously hypointense signal on T1W images and hyperintense signal on T2W images, causing mass effect over adjacent brainstem, left cerebellar hemisphere and 4th ventricle. It showed homogenous enhancement on post contrast images.

MS is classified into granulocytic, monoblastic, or myelomonocytic based on the predominant cell type. Microscopically, the characteristic pattern is Indian file pattern, and the MIB index is usually high. IHC and immunophenotyping (IPT) are essential for a correct diagnosis. MS has IPT features identical to leukemic cells, the most common positive markers are CD68, MPO, CD117, CD99, CD34, Tdt, CD56, CD61, CD30, glycophorin, and CD4. MS in those with t(8:21) translocation of AML have a predilection for MS of the CNS.[5] Our case was positive for CD13, CD33, CD34, CD45, HLADR, and MPO.

The currently recommended treatment for MS is combination chemotherapy similar to AML. There is no prognostic clinical or pathologic features, however, in patients who undergo allogeneic bone marrow transplantation, the survival is better.[5]

Our patient was given salvage chemotherapy with FLAG followed by cranial irradiation and was then counselled for allogenic hematopoietic stem cell transplant.

IV. CONCLUSION

The differential diagnosis in a patient with well-defined extra-axial mass lesion in left Cerebello-pontine angle cistern mainly includes meningioma, schwannoma, etc. But our case concludes that though it is rare, but an isolated CP angle tumor in a previous case of AML, successfully treated with chemotherapy, should include the diagnosis of CNS myeloid sarcoma due to extramedullary relapse of AML.

Conflicts of Interest -

No conflicts of interest declared.

REFERENCES

[1]. Dadrass F, Esmail F, Regmi A, et al. Isolated leukemia cutis as extramedullary relapse of acute myeloid leukemia. Clin Case Rep. 2022;10:e06009. doi: 10.1002/ccr3.6009
[2]. Richard L. Bakst, Martin S. Tallman, Dan Douer, Joachim Yahalom; How I treat extramedullary acute myeloid leukemia. *Blood* 2011; 118 (14): 3785–3793. doi: https://doi.org/10.1182/blood-2011-04-347229
[3]. Hardianti MS, Lasut RA (2021) Myeloid Sarcoma Presented as a Relapse in Acute Myeloid Leukemia: Case Reports and Review of the Literature. J Leuk. 9:276.

[4]. 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 May 21;4(5):1102-12. doi: 10.3390/jcm4051102. PMID: 26239467; PMCID: PMC4470219.
[5]. Narayanan G, Soman LV, Haridas L, Sugathan H. Isolated Intracranial Myeloid Sarcoma Occurring as Relapse in Acute Myeloid Leukemia. J Neurosci Rural Pract. 2017 Jul-Sep;8(3):466-468. doi: 10.4103/jnrp.jnrp_376_16. PMID: 28694637; PMCID: PMC5488578