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Case Series

Myeloid sarcoma: experience from a hematology care centre of Eastern India

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ABSTRACT

Objectives: To describe the case series of patients with myeloid sarcoma with their clinicopathological characteristics, cytogenetics, molecular markers, prognosis, and outcome.

Material and Methods: Retrospective retrieval of data of myeloid sarcoma cases in acute myeloid leukemia was done from the electronic health records of our hospital and this case series includes the data of three years starting from January 2018 and the follow-up information was assimilated until December 2020.

Results: We present twelve patients in this case series with myeloid sarcoma and all these patients had bone marrow involvement at presentation. Most of the cases were less than 20 years of age and orbit (66.7%) was the commonest site of presentation in this series. Aberrant CD 19 expression on immunophenotyping was a common associate (66.9%) and t(8;21) was the commonest cytogenetic abnormality reported in our case series. Despite of high dose intensive therapy with daunorubicin and cytarabine followed by high-dose cytarabine (HiDAC) consolidation, patients had a median relapse-free survival and median overall survival of 160 days and 299.5 days respectively. Local radiotherapy for consolidation in two of our patients had no additional benefit.

Conclusion: Myeloid sarcoma is extramedullary collection of myeloid blasts with or without bone marrow involvement. They were commonly seen in young patients and t(8;21) being a common cytogenetic abnormality associated with it. The treatment outcome of patients with myeloid sarcoma seems dismal and systemic therapy remains the modality of choice.

Keywords: AML, Myeloid sarcoma, Clinic-opathological characteristics, Treatment outcome

INTRODUCTION

Myeloid sarcoma (MS) is an extramedullary manifestation (EM) of acute leukemia and they are defined as localized collection of myeloid blasts. They are also interchangeably named as chloroma or granulocytic sarcoma. Acute myeloid leukemia (AML) in 2%–10% of cases may be accompanied by MS which can present concomitantly or herald its leukemic presentation. MS have been reported with myelodysplastic syndrome (MDS), myeloproliferative neoplasm (MPN) or MPN/MDS.[1,2] Isolated masses or disseminated forms involving multiple organs have been reported in literature. With MS involvement of bone marrow is not always a rule.[1,2] It may invariably involve any body site, but has a predilection for skin, soft tissue, lymph node, periosteum, bone, and other visceral organs. This affinity could be attributed to expression of various antigens on the blasts; various chemokine receptors and adhesion molecules are

also contributory to this tropism.[1,2,3] Isolated myeloid sarcomas are treated with intensive systemic therapy as in case of AML. Local therapy in the form of surgery and radiotherapy have been tried for managing isolated MS but such cases usually progress to frank AML within 3–12 months.[2,4] This case series aims to highlight the clinical presentation, diagnosis and therapeutic modalities, and outcomes of our patients with MS.

MATERIAL AND METHODS

Retrospective retrieval of data was done from the electronic health record of Department of Hematology, NRS Medical College and Hospital. Documents of all patients of AML were reviewed and those presenting with de novo myeloid sarcoma were considered for inclusion in the study. This case series includes data of three years starting from January 2018 and the follow-up information was assimilated until December 2020. All the clinico-pathological and therapeutic details of 12 patients were charted and subsequently analyzed. All parameters like clinicopathological variables, therapy details, and outcomes were expressed in percentage. The median overall survival and median relapse free survival were calculated and have been expressed in days.

RESULTS

We report a case series of 12 patients with MS and all the details related to the clinical presentation, pathological findings, and therapy have been summarized and tabulated in Table 1. The diagnosis of MS was based on the biopsy or FNAC, imaging and bone marrow studies. The median age in our case series was 10.5 (range 2–62) years, and 6(50%) patients were males. De novo MS accounted for 12(100%) of the cases. The sites involved based on their frequency of occurrence included orbit in 8(66.7 %), zygoma 1(8.3%), gums 1(8.3%), skin in 1 (8.3%), and breast in 1(8.3%).

During de novo presentation, all the patients (100%) had bone marrow involvement. Cytogenetics findings were documented in all the cases and t(8;21) was observed in 11(91.7 %). Amongst the patients who had t(8;21); c-kit positivity was seen in 9(8.81%) patients. An aberrant expression of CD 19 and CD 7 was documented in 8(66.6%) and 1(8.3%) patients respectively.

Ten (83.33%) patients received induction with intensive therapy followed by consolidation with high-dose cytarabine (HiDAC). None of the patients had induction failure and only one patient required double induction for achieving remission. The patients who were ineligible or unwilling for intensive therapy were started hypomethylating (HMA) based chemotherapy. Patients were rigorously monitored, and they received supportive care as per the clinical requirements. After cytarabine consolidation, patients were kept on regular follow-up. However, subsequently 10(100%) patients relapsed within a median duration of 160(65–611) days. Isolated MS and combined relapse was seen in 7(70%) and 3(30%) patients, respectively. In all the patients, the MS relapsed on the same site as at baseline. However, among the patients who had relapsed, two patients had CNS involvement also. For relapsed cases, salvage chemotherapy with HAM (high dose Cytosine Arabinoside and Mitoxantrone) or ADE (Daunorubicin, Cytosine Arabinoside and Etoposide) was used to achieve CR2 and post chemotherapy reassessment was done.

At relapse along with primary therapy, two patients were given radiotherapy (24 Gray in 12 fractions) for local control of the MS but only a mild reduction in size was observed. Post radiotherapy, the size of MS increased back to its pre radiation size in 18 and 25 days respectively.

The patients who achieved remission following the post relapse reinduction therapy were planned for allogeneic transplants but due to financial constraints this therapy plan was abandoned and hence the patients were planned for HiDAC consolidation followed by hypomethylating agent maintenance. The median survival of all the patients was 299.5 days and currently only one patient is alive.

DISCUSSION

MS have been reported in 2%–10% of AML patients at presentation. In literature it has been reported that it is more common in older patients with a male–female ratio of 1.21.[1] *In a mayo clinic case series from* 96 patients with MS the median age was 53 (range 17–83 years) which was unlike our case series as we had younger age of presentation.[5] This age disparity has been frequently observed in AML cases from India.[6] In the mayo series, 67% patients were males and in our case series we had equal male and female.[5]

MS with de novo (primary) accounted for 64% but all of our patient were de-novo cases.[5] The sites involved based on their frequency of occurrence included integumentary system (skin and soft tissues) in 38% and most of our patients had orbital involvement.[5] Multiple anatomical sites are usually involved in only < 10% of cases and in our case series we had only one patient with multiple site involvement.

At initial presentation, since all our patients in this case series had bone marrow involvement, we performed either aspiration cytology or a biopsy of the extramedullary growth to confirm the malignant origin. Due to logistic issues we could not perform the immunohistochemistry on the MS lesion. Though in cases of isolated MS it becomes necessary to do the immunohistochemistry or flow cytometry to confirm the malignant origin. It is possible that in MDS or AML, the extramedullary growth is of non-malignant origin because of extramedullary

Table 1: Patients with myeloid sarcoma presentation and therapy outcomes.

Parameters	Case no. 1	Case no. 2	Case no. 3	Case no. 4	Case no. 5	Case no. 6	Case no. 7	Case no. 8	Case no. 9	Case no. 10	Case no. 11	Case no. 12
Age(years)	3	7	18	18	20	14	62	18	6	2	5	4
Sex	M	M	F	M	F	M	M	M	F	F	F	F
Risk Stratification	Favorable Risk	Inter-mediate Risk	Inter-mediate Risk	Favorable Risk	Intermedi-ate Risk	Inter-mediate Risk	Intermediate Risk	Favorable Risk	Intermediate Risk	Inter-mediate Risk	High Risk	Favorable Risk
Site of Myeloid Sarcoma	Zygoma	Gums	Eye	Orbit	Breast	Orbit	Orbit	Orbit	Orbit	Orbit	Skin	Orbit
Primary CNS Involvement	No	Yes	No	No	No	No	No	No	No	No	No	No
CD56	No	No	No	No	No	No	No	No	No	No	Yes	Yes
CD19	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	No	Yes
CD7	No	No	No	No	No	No	No	Yes	No	No	No	No
Cytogenetics	t(8;21)	t(8;21)	t(8;21)	t(8;21)	t(8;21)	t(8;21)	t(8;21)	t(8;21)	t(8;21)	t(8;21)	t(10;11)	t(8;21)
C-Kit	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes
Therapy	D+A	D+A	D+A	D+A	D+A	D+A	Azacytidine	D+A	Lost to Follow up	D+A	D+A	D+A
Remission after 1st Induction	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	NA	No	Yes	Yes
No. of HiDAC	1	3	3	3	3	3	NA	3	NA	3	2	2
Dose of HiDAC (g/m^2)	1.5	1.5	1.5	3	3	3	NA	3	NA	3	3	3
Site of Relapse	EM	EM with BM	CNS with BM	CNS with BM	EM with BM	EM	NA	EM	NA	EM	EM	EM
Bone Marrow Involvement at Relapse	No	Yes	Yes	Yes	Yes	No	NA	No	NA	No	No	No
CNS Involvement at Relapse	No	No	Yes	Yes	No	No	No	No	No	No	No	No
Relapse Free Survival (days)	70	176	150	611	334	240	NA	170	NA	65	65	121
Overall Survival (days)	449	479	220	994	497	284	291	222	27	192	315	226

Abbreviations: BM: Bone marrow; EM: Extramedullary; CNS: Central nervous system; t: translocation; NA: Not applicable; D+A: Daunorubicin (3 days) plus cytarabine (7 days)

hematopoiesis due to the effect of growth factors.[1] Performing cytogenetic, FISH and molecular studies may contribute for better delineating cases of AML with disease defining cytogenetics.[2]

Extramedullary leukemia (EML) has been reported in 10%–25% of patients with t(8;21) AML and we observed them in 11(91.7%) of our patients.[7] Various other chromosomal rearrangements; inv(16) and t(9:11) have been associated with MS.[8] In pediatric cases t(8;21)(q22;q22) was a frequent cytogenetic abnormality and similar trend was observed in our patients.

Aggressive chemotherapy therapy was given to 83% and 77% of patients with and without bone marrow involvement in the Mayo case series and the median survival in them was 17 and 20 months; with and without bone marrow involvement (P = 0.4), respectively. All the patients in our case series had bone marrow involvement at baseline and had a median survival of 299.5 days. In their series 53% of patients relapsed.[5] However, all our patients relapsed with the median relapse free survival of 160(65–611) days.

At relapse, it is common to observe an isolated MS without marrow involvement.[1,5,8] In our case series, we observed isolated BM relapse in 7(70%) patients. It has been observed in studies that isolated MS can occur in 8%–20% of patients who undergo allogenic transplant and the possible reasons for this is the graft-versus-leukemia surveillance.[1] In studies even with the patients with MS who underwent allogeneic HCT, 5-year overall survival was around 47%.[9] Considering the relapse rates and survival rates occurring after allogenic transplant, MS appears to be an entity which is difficult to treat.

Addressing CNS disease appears to important; it is reasonable for those patients to receive intrathecal prophylaxis to prevent EM (CNS) disease once in remission and in our series one patient on initial presentation and two on relapse had CNS involvement.[2]

Radiation therapy (RT) was used in the treatment of MS; however, now it is not recommended. In conditions that require debulking or rapid symptom relief because of RT or surgery may be considered in upfront followed by an aggressive chemotherapy but there is no evidence that this combined approach is superior to aggressive chemotherapy alone.[2] Two of our patients received radiotherapy at relapse but was not helpful. However, in literature low-dose RT regimen of 20–24 Gy in 12 fractions may be given to most patients with systemic therapy for local control with symptom relief and response rates of 95% and in 97%, respectively with minimal toxicity. Radiation therapy can be used to consolidate the local site because a seedling from the local site can regerminate the marrow. [2,11]

Literature shows that among patients who developed MS after transplantation, 48% occurred in the CNS and ovaries and the administration of intrathecal chemotherapy or the use of a testicular boost for men during total body irradiation (TBI) can overcome this.[2,10,12] Unfortunately, our patients were not privileged enough for the transplant.

Overall, the presence of EM disease is usually associated with a poor prognosis and shorter survival (5-year survival rates) for patients with MS range between 20% and 30%, which appear like AML.[8] Among the newer agents like checkpoint inhibitor ipilimumab and other biological therapy seems to be effective for EM manifestations of AML. However, the data is naive to prove its implications.[13]

CONCLUSION

MS are more commonly seen in young population and t(8;21) is a common cytogenetic abnormality associated with it. The treatment outcome of patients with MS seems dismal and systemic therapy remains the modality of choice. Considering radiotherapy consolidation for isolated MS needs more studies with larger sample size.

AUTHOR'S CONTRIBUTION

This work was carried out in collaboration among all authors. Authors AB, PKM, and TKD have designed the series, managed the literature searches, and wrote the first draft of the manuscript. Author PKM edited the final manuscript. Authors AB, PKM, MG, PSS, SM, AC, SB, SNB, RD, and TKD were involved in the management of the cases and all the authors read and approved the final manuscript.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Arber DA, Orazi A, Hasserjian R, Thiele J, Borowitz MJ, Le Beau MM, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood 2016;127:2391–405.
2. Bakst RL, Tallman MS, Douer D, Yahalom J. How I treat extramedullary acute myeloid leukemia. Blood 2011;118:3785–93.

3. Neiman RS, Barcos M, Berard C, Bonner H, Mann R, Rydell RE, et al. Granulocytic sarcoma: a clinicopathologic study of 61 biopsied cases. Cancer 1981;48:1426–14.
4. Yamauchi K, Yasuda M: Comparison in treatments of nonleukemic granulocytic sarcoma: report of two cases and a review of 72 cases in the literature. Cancer 2002;94: 1739–46.
5. Yui J, Mudireddy M, Patnaik MM, Gangat N, Al-Kali A, Elliott M, et al. Myeloid sarcoma: The Mayo clinic experience of ninety six case series. Blood 2016;2798.
6. Philip C, George B, Ganapule A, Korula A, Jain P, Alex AA, et al. Acute myeloid leukaemia: challenges and real world data from India. British J Hematol. 2015;170:110–7.
7. Lai YY, Qiu JY, Jiang B, Lu XJ, Huang XJ, Zhang Y, et al. Characteristics and prognostic factors of acute myeloid leukemia with t(8; 21)(q22; q22). Chinese J Hematol 2005;13:733–40.
8. Paydas S, Zorludemir S, Ergin M. Granulocytic sarcoma: 32 cases and review of the literature. Leuk Lymphoma 2006;47:2527–41.
9. Chevallier P, Mohty M, Lioure B, Michel G, Contentin N, Deconinck E, et al. Allogeneic hematopoietic stem-cell transplantation for myeloid sarcoma: a retrospective study from the SFGM-TC. J Clin Oncol 2008;26:4940–3.
10. Szomor A, Passweg JR, Tichelli A, Hoffmann T, Speck B, Gratwohl A. Myeloid leukemia and myelodysplastic syndrome relapsing as granulocytic sarcoma (chloroma) after allogeneic bone marrow transplantation. Ann Hematol 1997;75:239–41.
11. Bakst RL, Dabaja BS, Specht LK, Yahalom J. Use of radiation in extramedullary leukemia/chloroma: guidelines from the International Lymphoma Radiation Oncology Group. Int J Radiat Oncol Biol Phys 2018;102:314–9. doi:10.1016/j.ijrobp.2018.05.045.
12. Békássy AN, Hermans J, Gorin NC, Gratwohl A. Granulocytic sarcoma after allogeneic bone marrow transplantation: a retrospective European multicenter survey. Acute and chronic leukemia working parties of the European Group for Blood and Marrow Transplantation. Bone Marrow Transplant 1996;17:801–8. PMID:8733701.
13. Bakst R, Powers A, Yahalom J. Diagnostic and therapeutic considerations for extramedullary leukemia. Curr Oncol Rep 2020;22:1–7. DOI:https://doi.org/10.1007/s11912-020-00919-6

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