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HAEMATOLOGICAL AND NON-HAEMATOLOGICAL MALIGNANCIES IN BONE MARROW: A 2 YEAR RETROSPECTIVE STUDY FROM A TERTIARY CARE CENTRE IN NORTH-EAST INDIA

Pathology

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ABSTRACT

BACKGROUND: Bone marrow is involved in a variety of haematological and non-haematological disorders. The technique of bone marrow aspiration (BMA) has been accepted and widely used. Aspiration biopsies are carried out principally to permit cytological assessment of bone marrow cells. The haematological disorders include acute leukaemia, myeloproliferative neoplasm (MPN), haemato-lymphoid neoplasm. Haematological malignancies are common, comprising approximately of 6.5% of all cancers worldwide. Bone marrow (BM) is one of the common and important sites to be involved by solid tumours. Any tumour that metastasizes via blood may deposit in BM. Bone marrow examination is a useful and cost effective diagnostic procedure in haematological practice for the diagnosis of both neoplastic and non-neoplastic haematological diseases.

METHODS: A retrospective cross-sectional study was conducted in our Institute. BMA was performed following strict aseptic precaution. BMA had been done using Salah's marrow puncture needle and 20 ml syringe from PSIS and in some patients from sternum. For paediatric patients BMA done from the medial aspect of tibial tuberosity. Leishman stain and relevant stains like myeloperoxidase and Periodic acid Schiff's were also done.

RESULTS: A total of 365 BMA was done during the study period, out of which 62 cases were turned out to be malignant. Out of 62 cases, 6 (9.7%) cases were metastatic tumours and 56 (90.7%) cases were haematological malignancies. Acute myeloid leukaemia (AML) constituting around 20 (38.9%) cases, out of which 12 (19.4%) cases were AML-M2. Acute lymphoblastic leukaemia (ALL) constituting around 12(19.4%) cases, out of which 10(16.1%) cases were ALL-L2. Of the 6 (9.7%) cases of metastatic tumour, half of the cases (three cases) were reported as metastatic adenocarcinoma.

CONCLUSION: The commonest haematological malignancy in our series was leukaemia. Majority of solid tumours metastatic to bone marrow are adenocarcinomas.

KEYWORDS

Bone marrow aspiration (BMA), Leukaemia, BM Metastasis.

BACKGROUND

Bone marrow (BM) is involved in variety of haematological and non-haematological disorders. The haematological disorders include acute leukaemia, myeloproliferative neoplasm (MPN), haemato-lymphoid neoplasm. Diseases of bone marrow present with various clinical symptoms and also involve the blood but peripheral blood picture alone does not reflect the nature of the disease process.[1] The technique of bone marrow aspiration (BMA) has been accepted and widely used. Aspiration biopsies are carried out principally to permit cytological assessment of bone marrow cells. Bone marrow examination is a useful and cost effective diagnostic procedure in haematological practice for the diagnosis of both neoplastic and non-neoplastic haematological diseases.[2]

Haematological malignancies are a group of cancers that arise from a malignant transformation of cells of the bone marrow or the lymphatic system. Even though environmental exposure to chemicals, as well as ionizing radiation and infectious agents are believed to be the causes of those malignancies, their exact cause remains unclear.[3] A bone marrow examination performed as a part of work up can reveal the underlying lympho-proliferative disorder.[4]

Haematological malignancies are common, comprising approximately of 6.5% of all cancers worldwide. It is the fourth most frequently diagnosed cancer in both men and women in developed countries of the world. They are broadly divided into two groups according to their cell lineage as myeloid and lymphoid.[5]

In majority of the cases, the diagnosis is usually made by obtaining a complete history, physical, and some basic haematological examination. But in some cases such as lymphoma, leukaemia, and tumours, bone marrow examination is required for the confirmation of disease condition.[6]

Bone marrow is one of the common and important sites to be involved by solid tumours. Presence of metastasis in bone marrow can alter the clinical course of disease by changing the stage and also hampering the clinical condition of the patient by suppressing the valuable blood components. Any tumour that metastasizes via blood may deposit in BM.[7]

Plasma cells (PC) like all other leukocytes are susceptible to transformation. Currently, there are several subtypes of PC dyscrasias including monoclonal gammopathy of undetermined significance (MGUS), asymptomatic myeloma, multiple myeloma, PC leukaemia, plasmacytoma and amyloidosis.[8]

The myelodysplastic/myeloproliferative neoplasms (MDS/MPN) are clonal myeloid neoplasms characterized, at the time of their initial presentation, by the simultaneous presence of both myelodysplastic and myeloproliferative features, which prevent them from being classified as either myelodysplastic syndrome or myeloproliferative neoplasm. The best defined entities with the group are: chronic myelomonocytic leukaemia (CMML), atypical chronic myeloid leukaemia (aCML), juvenile myelomonocytic leukaemia (JMML) and refractory anaemia with ring sideroblasts and thrombocytosis (RARS-T).[9]

The diagnosis of AML requires the presence of >20% blasts in the peripheral blood or bone marrow; in certain cases, the presence of recurrent cytogenetic abnormalities, such as the characteristic translocation (8,21) defines AML even at lower blast count.[10]

Sometimes peripheral blood show less number of blast cells or no blast cells but bone marrow fulfils criteria for acute leukaemia in those cases it is called sub-leukemic or aleukemic leukaemia respectively.[11]

French American British (FAB) classification was proposed in 1976, which was based on morphology and cytochemistry. The difference

between AML and ALL based on the positivity or negativity of the blasts for the myeloperoxidase or Sudan B Black reaction. Within AML 8 categories were discriminated (M0-M7) by morphology and the use of alpha naphthyl acetate esterase to discriminate monoblasts from myeloblasts. FAB classification of ALL into L1 and L2, merely based on the size of the blasts.[12]

The 2016 revision to the world health organization classification of myeloid and lymphoid leukaemia has been influenced by several factors including the following: 1. The discovery of recently identified molecular features has yielded new perspectives regarding diagnostic and prognostic markers that provide novel insights for the understanding of the pathobiology of these disorders. 2. Improved characterization and standardization of morphological features aiding in the differentiation of disease groups, particularly of the BCR-ABL negative myeloproliferative neoplasms (MPNs), has increased the reliability and reproducibility of diagnoses. 3. A number of clinical pathological studies have now validated the WHO postulate of an integrated approach that includes hematologic, morphologic, cytogenetic, and molecular genetic findings.[13]

AIM

To assess distribution of haematological and non-haematological malignancies in bone marrow

METHODS

A retrospective study was conducted in the Department of Pathology, Regional Institute of Medical Sciences, Imphal for a period of two years from 1st January 2018 to 31st December 2019. BMA was performed following strict aseptic precaution. In-ward patients requiring BMA were the study population. Consent was obtained from each patient before the procedure. Relevant clinical details and results of previous investigations were also reviewed. The aspirated material was smeared on clean glass slides, Leishman's stain and relevant stains like myeloperoxidase and Periodic acid Schiff's was also done. A peripheral blood film was also prepared simultaneously. Inadequate bone marrow aspirates and unsatisfactory smears were excluded from the study. In the present study, data has been entered and analysed using IBM SPSS statistics 21.

RESULTS

A total of 365 BMA was done during the study period, out of which 62 cases turned out to be malignant.

Age Group in Years	No of Cases	Percentage (%)
Haematological Malignancy		
1-10	08	12.9
11-20	04	6.5
21-30	04	6.5
31-40	04	6.5
41-50	06	9.6
51-60	12	19.3
61-70	12	19.3
71-80	06	9.6
Non-Haematological Malignancy		
41-50	01	1.6
51-60	02	3.2
61-70	01	1.6
71-80	02	3.2
Total	**62**	**100**

Table 1. Age Wise Distribution of Cases (N=62)

As shown in table 1, age group of patient spans from 1 to 80 years. The maximum number of haematological malignancy of bone marrow were seen in the age group from 51 to 70 years around 24(38.6%) cases, and all the cases of non-haematological malignancy of bone marrow were seen after 40 years of age.

Sex	No of Cases	Percentage of Cases
Haematological Malignancy		
Male	29	46.7
Female	27	43.5
Non-Haematological Malignancy		
Male	03	4.8
Female	03	4.8
Total	**62**	**100**

Table 2. Sex Wise Distribution of Cases (N=62)

As shown in table 2, of 56 cases of haematological malignancy of bone marrow 29 (51.7%) cases were males and 27 (48.2%) cases were females and of 6 cases of non-haematological malignancy of bone marrow 3(50%) cases each were seen in both males and females.

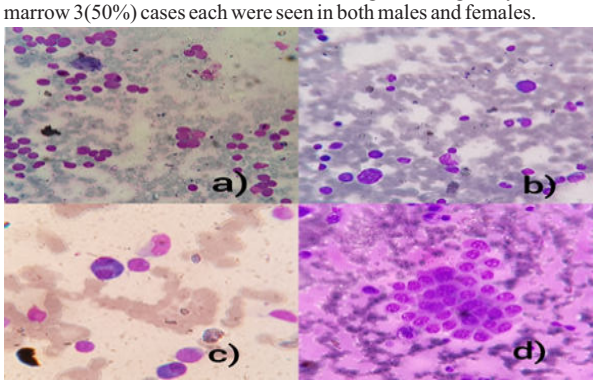

Figure 1. Photomicrograph of a) Acute Myeloid Leukaemia Showing Myeloblast having Increased N:C Ratio [Leishman,100X], b) Acute Lymphoblastic Leukaemia Showing Heterogenous Population of Lymphoblasts, ALL-L2 [Leishman, 100X], c) Plasma Cell Dyscrasia showing Binucleated Plasma Cell with Mature Plasma cell [Leishman, 400X], d) Metastatic Adenocarcinoma of Bone Marrow Showing Malignant Cells in Cluster, having Irregular Nuclear membrane with some Showing Prominent Nucleoli [Leishman,400X]

Malignancy	No of Cases	Percentage of Cases
Haematological Malignancy		
ALL-L1	02	3.2
ALL-L2	10	16.1
AML-M2	12	19.4
AML-M3	04	6.5
AML-M4	04	6.5
AML-M6	04	6.5
Myeloproliferative neoplasm (MPN)	05	8.1
Lymphoproliferative disorders	02	3.2
Plasma cell dyscrasia (PCD)	07	11.3
Myelodysplastic syndrome (MDS)	03	4.8
MPN/MDS	02	3.2
Non-Haematological Malignancy		
Metastatic adenocarcinoma	03	4.8
Metastatic undifferentiated carcinoma	01	1.6
Metastatic serous papillary carcinoma of ovary	01	1.6
Metastatic nasopharyngeal carcinoma	01	1.6
Total	**62**	**100**

Table 3. Frequency of Malignant Lesions (N=62)

As shown in table 3, out of the 62 cases, 6(9.7%) cases were metastatic tumours and 56 (90.3%) cases were haematological malignancies. Acute myeloid leukaemia (AML) constituting around 20 (38.9%) cases, out of which 12(19.4%) cases were AML-M2. Acute lymphoblastic leukaemia (ALL) constituting around 12 (19.4%) cases, out of which 10(16.1%) cases were ALL-L2. Plasma cell dyscrasias were reported in7 (11.3%) cases. Of the 6 (9.7%) cases of metastatic tumours, half of the cases (3 cases) were reported as metastatic adenocarcinoma and 1 (1.6%) case each of metastatic serous papillary carcinoma of ovary, metastatic nasopharyngeal carcinoma and metastatic undifferentiated carcinoma with unknown primary at the time of reporting. Of 6(9.7%) cases of metastatic tumours, 4(6.4%) cases were reported in males and 2(3.2%) cases were reported in females.

DISCUSSION

Out of 365 cases 56 cases (15.3%) of haematological malignancy were diagnosed during the study period which is relatively low compared to the study conducted by Kusum A et al[14], in whose study around 58% of haematological malignancy were diagnosed during the study period. Percentage of plasma cell dyscrasia reported around 11.5% in this study which is relatively low compared to the study conducted by Kusum A et al[14], Besson C et al[15] and Brown LM et al[16]. Bhutani M et al[17] in their study concluded that occurrence of PCD in individuals younger than 40 years was around 12%, which is dissimilar to the current study in which none of the cases of PCD was reported in individuals younger

than 40 years. Idris M et al[18] found a 4.61% incidence of multiple myeloma in their study.

Occurrence of acute leukaemia in the current study is around 58.2% which is relatively lower compared to the study conducted by Kusum A et al,[14] Kwiatkowski A et al,[19] Besson C et al[15], Idris M et al,[18] Ghazaly Al et al,[20] Pradhan PK et al[21] and Chatterjea et al.[22] Occurrence of chronic leukaemia in the current study is around 30.6% which is relatively lower compared to the study conducted by Hansen NE et al[23] and Rani S et al,[24] in whose study the occurrence of chronic leukaemia is around 60% and 51.1% respectively.

One case of MDS/MPN was reported in the paediatric age group in the current study. Juvenile myelomonocytic leukaemia (JMML) is the commonest subtype of MDS/MPN in children, accounting for 20-40% of paediatric MDS/MPN. Neurofibromatosis type 1 and Noonan syndrome (NS) are known to be predisposing clinical conditions for JMML.[25]

We found a male preponderance in our study, which is similar to the study conducted by Kusum A et al[14], Rani S et al,[24] Pradhan PK et al[21] Bhutani M et al[17] Yeolle BB et al[26] Kushwaha et al[27] and Advani et al.[28]

Leukaemia was the common malignant disease in children in this study, which is similar to the study conducted by Birch JM et al[29] and Pradhan PK et al.[21] Among acute leukaemia in children 85% of cases were ALL in our study. Higher incidence of ALL in children has been reported by Van Steensel Moll HA et al,[30] Monge P et al,[31] Coeberg JW et al[32] and D Costa G et al.[33] In this study most common acute leukaemia in adults was myeloid around 79.3%. Similar result was obtained by Kasthuri AS et al[34] in their study. Occurrence of non-haematological malignancy in our study is around 9.7% which is higher than the study conducted by Kusum A et al,[14] in whose study the occurrence of metastasis is around 1.35%. Subalakshmi B et al[35] in their study also concluded that the metastasis of epithelial origin were more common than mesenchymal origin

CONCLUSION

The commonest haematological malignancy in our series was leukaemia. Other diagnosis were plasma cell dyscrasia, lymphoproliferative disorders and secondaries. BMA is an effective and economical method for evaluating solid tumours metastatic to bone marrow. Epithelial tumours are more commonly metastatic then other tumour type. Hence it is concluded that aspiration of bone marrow provides an easy and quick way of detection of marrow involvement.

REFERENCES

[1] Kaur M, Rana APS, Kapoor S, Puri A. Diagnostic value of bone marrow aspiration and biopsy in routine hematology practice. JCDR 2014 Aug;8(8):13-16.
[2] Indhudara PB, Ganga H, Yenni. Role of bone marrow aspiration and bone marrow biopsy in routine practice. Int J Clin Diagn Pathol 2018;1(2):18-20.
[3] Belai N, Ghebrenegus AS, Alamin AA, Embaye G, Andegiorgish AK. BMC Hematology 2019;19:8.
[4] Sreedharanunni S, Sachdeva MUS, Malhotra P, Ahluwalia J, Naseem S, Prakash G, et al. Role of blood and bone marrow examination in the diagnosis of mature lymphoid neoplasms in patients presenting with isolated splenomegaly. Hematology;20(9):530-7.
[5] Joshi S, Wader J, Kanethkar S. Bone marrow aspiration and bone marrow biopsy in hematological disorders. Biomed. & Pharmacol. J 2020;13(2):799-804.
[6] Meenai FJ, Ojha S, Ali MA, Jain R, Sawke N. Bone marrow involvement in non-hematological malignancy: a clinic-pathological study from a tertiary hospital. APALM 2018;5(5):440-6.
[7] Khan S, Mir A, Khattak BR, Khan SN, Iqbal K, Malik SN. Pattern of adulthood hematological malignancies in Khyber Pakhtunkhwa. J Blood Discord Transfus; 10(2):424.
[8] Soh KT, Tario JD, Wallace PK. Diagnosis of plasma cell dyscrasias and monitoring of minimal residual disease by multiparameter flow cytometry. Clin Lab Med 2017 Dec;37(4):821-53.
[9] Orazi A, Germing U. The myelodysplastic/myeloproliferative neoplasms: myeloproliferative diseases with dysplastic features. Leukaemia 2008;22:1308-19.
[10] Percival ME, Lai C, Estey E, Hourigan CS. Bone marrow evaluation for diagnosis and monitoring of acute myeloid leukaemia. Blood Rev 2017 Jul;31(4):185-92.
[11] Vaghasiya VL, Parikh HS, Patel DV, Taviad DS. Transient appearance of blasts in peripheral smear in paediatric patient with acute aleukemic leukemia. NJMR 2012 Jun;2(2):234-5.
[12] Segeren CM, Veer MBV. The FAB classification for acute myeloid leukaemia- is it outdated?. Neth J Med 1996;49:126-31.
[13] 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 leukaemia. Blood 2016 May;127(20):2391-2405.
[14] Kusum A, Negi G, Gaur DS, Kishore S, Meena H, Sharma A, et al. Hematological malignancies diagnosed by bone marrow examination in a tertiary hospital at Uttarakhand, India. Indian J Hematol Blood Transfus;24(1):7-11.
[15] Besson C, Gonnin C, Brebion A, Delaunay C, Panelatti G, Plumelle Y. Incidence of hematological malignancies in Martinique, French West Indie, over representation of multiple myeloma and adult T cell leukaemia/lymphoma. Leukaemia;15:828-31.
[16] Brown LM, Linet MS, Greenberg RS, Silverman DT, Hayes RB, Swanson GM, et al. Multiple myeloma and family history of cancer among blacks and whites in the US. Cancer;85:2385-90.
[17] Bhutani M, Vora A, Kumar L, Kochupillai V. Lymphopoietic malignancies in India. Medical Oncology;19(3):141-50.
[18] Idris M, Shah SH, Fareed J, Gul N. An experience with sixty xases of haematological malignancies. J Ayub Med Coll Abbottabad 2004;16(4):51-4.
[19] Kwiatkowski A. Trends in the incidence of leukemia in Poland, 1963-1990: an epidemiological study. Eur J Cancer Prev 1994;3(3):277-83.
[20] Al Ghazaly J, Al Selwi AH, Abdullah M, Al Jahafi AK, Al Dubai W, Al Hashdi A. Pattern of hematological diseases diagnosed by bone marrow examination in Yemen: a developing country experience. Clin Lab Haematol 2006;28(6):376-81.
[21] Pradhan PK, Tiwari SK, Dabke AT, Agarwal S. Pattern of leukemia in Raipur (Madhya Pradesh)- An analysis of 162 cases. Indian J Cancer 1982;19:20-3.
[22] Chatterjea JB, Ghose S, Ray RN. Incidence of leukaemia, an analysis of 544 cases in Calcutta. J Assoc PhyInd 1972;10:673-6.
[23] Hansen NE, Karle H, Jensen OM. Trends in the incidence of leukaemia in Denmark, 1943-1977: an epidemiologic study of 14000 cases. J Natl Cancer Inst 1983;71(4):697-701.
[24] Rani S, Beohar PC, Mohanty TK, Mathur MD. Leukemic pattern in Delhi- a ten year study of 490 cases. Ind J Cancer 1982;19:81-6.
[25] Gupta AK, Meena JP, Chopra A, Tanwar P, Seth R. Juvenile myelomonocytic leukemia- a comprehensive review and recent advances in management. Am J Blood Res 2021;11(1):1-21.
[26] Yeolle BB, Jussawalla DJ, Advani SH. Descriptive epidemiology of leukemias in Greater Mumbai. Natl Med J India 1998;11(3):116-9.
[27] Kushwaha MRS, Bagchi M, Mehrotra RML. Leukemia at Lucknow- a study of 200 cases. Ind J Cancer 1978;15:28-34.
[28] Advani SH, Jussawalla DJ, Nagaraj Rao D, Gangadharan P, Shetty PA. A study of 1226 leukemia cases- epidemiologic and end result analysis. Ind J cancer 1979;16:8-17.
[29] Birch JM, Marsden HB, Swindell R. Incidence of malignant disease in childhood: a 24 year review of the Manchester children's tumour registry data.Br J Cancer 1980;42(2):215-23.
[30] Van Steensel Moll HA, Valkenberg HA, Van Zanen GE. Incidence of childhood leukemia in the Netherlands (1973-1980). Br J Cancer 1983;47(4):471-5.
[31] Monge P, Wesseling C, Rodriguez AC, Cantor KP, Weiderpass E, Reutfors J, et al. Childhood leukemia in Costa Rica, 1981-1996. Paediatr Perinat Epidemiol 2002;16(3):210-8.
[32] Coebergh JW, Reedijik AM, DeVries E, Martos C, Jakab Z, Steliarova Foucher E. Leukemia incidence and survival in children and adolescents in Europe during 1978-1997, report from the automated childhood cancer information system project. Eur J Cancer 2006;42(13):2019-36.
[33] D Costa GG, Siddique HM, Pradhan RM, Gupta SS. Pattern of leukemias: a ten year incidence study of 242 cases. J Postgraduate Med 1989;35:191.
[34] Kasthuri AS, Jaiprakash MP, Panicker NK, Gupta MM, Rajpoor GS, Basu SK, et al. A clinical study of adult leukemias. J Assoc Physicians India 1991;39(3):291-2.
[35] Subalakshmi B, Nellaiyappan B, Thanka J. Analysis of metastatic bone disease in a tertiary care centre. Ind J Pathol Oncol 2018;5(3):505-8.