Hematological malignancies diagnosed by bone marrow examination in a tertiary hospital at Uttarakhand, India

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Abstract

Introduction Hematological malignancies are quite common and affect all ages and genders. The diagnosis involves a multiparameter approach. The geographical distribution of various types of hematological malignancies has been provided by various authors but no such data have been published regarding the State of Uttarakhand in India.

Aim To study the hematological malignancies at Uttarakhand in India based on age, sex and the type of malignancy with further sub typing wherever possible.

Settings and design A total of 220 cases of hematological malignancies were worked up from the Reference Laboratory of Himalayan Institute of Medical Sciences over an eight year period (1998–2005).

Materials and methods Diagnosis was mainly based on morphological examination of peripheral blood and bone

marrow smears stained by Leishman's stain and MPO, Sudan Black and PAS stain as and where required. Distribution of cases was studied based on age, sex and the type of malignancy with further sub typing wherever possible.

Results The most common hematological malignancy was found to be Leukemia 129/220 (58%) followed by Lymphoma 33/220 (14.8%), Multiple Myeloma 55/220 (24.7%) and Metastatic Lesions 3/220 (1.3%). These malignancies were seen to be distributed throughout all ages with a peak at 11–20 years age group 39/220 (17.5%) and another peak at 51–60 years age group 41/220 (18.4%). We found an overall male preponderance with a M:F ratio of 2.3:1.

Conclusions The commonest haematological malignancy in our series was Leukemia. Other diagnoses were Multiple Myeloma, Lymphoma and Secondaries. Multiple Myeloma which turned out to be the second most common diagnosis was an unusual finding.

Keywords Hematologic malignancies · Distribution · Bone Marrow

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Introduction

Hematological malignancies are quite common and affect all ages and genders. The diagnosis involves a multiparameter approach including morphologic examination and phenotypic or genotypic studies [1].

The geographical distribution of various types of hematological malignancies has been provided by various authors but no such data have been published regarding the State of Uttarakhand in India.

Material and methods

A total of 220 cases of hematological malignancies were collected at Himalayan Institute of Medical Sciences over an eight year period (1998–2005). All routine hematological investigations, including peripheral smear study, were performed. Bone marrow aspiration was done and smears were prepared. Smears of blood and bone marrow were stained by Leishman's stain before light microscopy. Cytochemical stains like Myeloperoxidase (MPO), Sudan Black and Periodic Acid Schiff (PAS) stains were done where required. Only those cases where bone marrow aspiration was done, were included in the study group. If a malignancy was not evident on bone marrow aspiration or if bone marrow aspirate was not performed, such cases were not included in the study. Distribution of cases was studied based on age, sex and the type of malignancy, with further sub-typing wherever possible.

Observations

The records were accessed for cases of hematological malignancies based on the bone marrow aspirations performed between 1998 and 2005. We found 220 such cases which were mainly grouped as Leukemia 129/220 (58%), Lymphoma 33/220 (14.8%), Multiple Myeloma 55/220 (24.7%) and Metastatic Lesions 3/220 (1.3%). These malignancies were seen to be distributed throughout all ages with a peak at 11–20 years age group 39/220 (17.5%) and another peak at 51–60 years age group 41/220 (18.4%). We found an overall male preponderance with a M: F ratio of 2.3:1. Even when considered individually for each diagnosis, males always outnumbered females.

Leukemias Acute leukemia were more common than chronic leukemia. AML was the commonest 49/129 (37.7%) followed by CML-35/129 (26.95%) This was followed by ALL-33/129 (26.46%) and CLL was the least common-2/129 (1.54%). There were some cases 10/129 (7.7%) which were categorized as undifferentiated Acute Leukemia. The cases of acute leukemia were found to peak at 0–20 years while chronic leukemias were maximally seen in 31–50 years age group. M: F ratio was 2.2: 1

AML AML constituted 49/220 (22.0%) cases and 49/129 (37.7%) cases of all leukemias. It was the most common type of leukemia in our study. It was commonly seen upto 50 years of age. Males were found to predominate with a M: F ratio of 1.45:1.

ALL ALL was seen in 33/220 (14.8%) of all cases and 33/129 (25.4%) cases of all leukemias. It was mainly seen up to 20 years of age. Two cases were seen in 21–30 years age group. M: F ratio was 3.7:1.

CML CML was seen in 35/220 (15.7%) of all cases and 35/129 (26.9%) cases of all leukemias. It was seen to have a peak at 31–50 years of age. M: F ratio was 2.9:1.

CLL Only 2 cases of CLL were seen at 60 and 82 years of age. M: F ratio was 1:1.

Lymphoma The incidence of lymphoma was 33/220 (14.8%) and the main age groups were 11–20 years and 51–60 years. M: F ratio was 3.7:1.

Multiple myeloma There were 55/220 (24.7%) cases of multiple myeloma. It showed a peak at 51–60 years age group. M: F ratio was 1.8:1.

Metastasis Metastatic deposits were seen in 3/220 cases (1.3%). The three cases showed metastasis from an epithelial tumor, a small cell carcinoma and a round cell tumor. Patients presenting with metastasis were from 51–70 years age group. All the three patients were females.

Discussion

Hematological malignancies constitute a substantial portion of all bone marrow aspirations done for hematological disorders. In our study, only those cases were included that were diagnosed on bone marrow aspiration. If a malignancy was not evident on bone marrow aspiration or if bone marrow aspirate was not performed it was not included in the study. Al Ghazaly et al [2] have studied 627 cases of hematological diseases and reported that leukemia was the most common diagnosis on bone marrow examination. We found 129 / 220 (58.05%) cases of leukemia and thus leukemia was found to be the commonest diagnosis on bone marrow examination in our series as well. The next common diagnosis in our series was multiple myeloma 55/220 (24.75%). This is an unusual finding as very few available studies show such high incidence of multiple myeloma. Besson C et al [3] have reported multiple myeloma to be the commonest (34%) among all hematological malignancies in Martinique, French West Indies. Brown LM et al [4] also reported a high incidence of multiple myeloma among Afro Americans in the USA and suggested a genetic predisposition. Bhutani M et al [5] have compiled information on hematological malignancies in India and have reported that multiple myeloma in young individuals (<40 years) is higher in India (12%) than in the west. They have also reported that in India all hematological malignancies are commonest in Delhi followed by Mumbai. Rural areas have least incidence of these malignancies. They have also observed that all cancers occur one decade earlier in India.

Leukemias We found a very high distribution of acute leukemias –92 / 129 (71%) cases of leukemias compared to

Table 1 Type of hematological malignancies and their prevalence

Type	Total No.	%	Males	Females	Adults (>10 yrs)	Children (<10 yrs)
Leukemia	129	58.05	89 (40.0%)	40 (18.0%)	103 (46.35%)	26 (11.70%)
Lymphoma	33	14.85	26 (11.7%)	7 (3.15%)	32 (14.40%)	1 (0.45%)
Multiple Myeloma	55	24.75	36(16.2%)	19(8.5%)	55 (24.75%)	–
Metastasis	3	1.35	3 (1.35%)	–	3 (1.35%)	–
Total	220	100	154 (69.3%)	66 (29.7%)	193 (86.85%)	27 (12.15%)

Table 2 Type of leukemias and their prevalence

Type	Total No.	M	F	Adult (>10 yrs)	Children (<10 yrs)
AML	49 (37.73%)	29 (22.33%)	20 (15.40%)	43 (33.11%)	6 (4.62%)
ALL	33 (25.41%)	26 (20.02%)	7 (5.39%)	15 (11.55%)	18 (13.86%)
Acute leukemia-Undifferentiated	10 (7.77%)	7 (5.39%)	3 (2.31%)	8 (6.16%)	2 (0.90%)
CML	35 (26.95%)	26 (20.02%)	9 (6.93%)	35 (26.95%)	–
CLL	2 (1.54%)	1 (0.77%)	1 (0.45%)	2 (0.90%)	–
Total	129	89	40	103	26

Table 3 Year wise distribution of haematological malignancies

	No. of cases	%	Leukemia	Lymphoma	Multiple Myeloma	Metastasis
1998	10	4.5	4	4	1	1
1999	17	7.6	14	1	2	0
2000	21	9.4	15	2	4	0
2001	34	15.3	22	5	6	1
2002	31	13.9	17	5	9	0
2003	29	13.0	14	9	6	0
2004	24	10.8	13	4	6	1
2005	54	24.3	30	3	21	0
Total	220	100	129	33	55	3

chronic leukemia 37/129 (28.5%). Similar high incidence of Acute leukemia has been reported by Kwiatkowski A [6], C Besson et al [3], Idris M [7], Al Ghazaly et al [2], Pradhan PK et al [8] and Chatterjea et al [9]. However Hansen NE et al [10] found more cases of chronic leukemias in their study (60%) as compared to acute leukemias. Similarly Rani S [11] from Delhi, India also reported more chronic leukemias (51.1%) as compared to acute leukemia. Acute and chronic leukemias have been reported to be seen with equal frequency by Advani et al [12]. We found a male preponderance in our study. This has also been reported by Rani S et al [11], Pradhan P et al [8], Bhutani M et al [5], Yeolle B B et al [13], Kushwaha et al [14] and Advani et al [12]. Increased incidence of all leukemias in males seems to arise as males are comparatively more exposed to occupational and environmental carcinogens as has been suggested by Bhutani M et al [5].

The commonest type of leukemia in our study was AML followed by CML and then ALL and CLL. Myeloid leukemias have been reported as being more common also by Pradhan PK et al [8], Rani S et al [11], Bhutani M et al [5] and Yeolle BB et al [13]. The fact that we got more cases of AML than CML in our study may be explained by the fact that Bone Marrow Examination was the basis of case collection in our study and some cases of CML diagnosed only on peripheral smear might have been missed. Studies of Idris M et al [7] and Al Ghazaly et al [2] match our findings of AML being the most common form among all leukemias.

Birch JM et al [15] found that among all the malignant diseases in childhood, one third of the cases were leukemia and it was the most common malignant disease in children in their series. Pradhan P et al [8] found that among children, Acute leukemias were more common (97.3%) and Chronic leukemias were only 2.7% of all cases. Among acute

leukemias in children, they found 70.3% cases of ALL. Similarly, higher incidence of ALL among acute leukemias has been reported by Van Steensel-Moll HA et al [16], Monge P et al [17], Coeberg JW et al [18] and D Costa G et al [19]. Similarly, we too found a higher incidence of ALL in children. However Laurent Roda et al [20] have reported a high non lymphoblastic / lymphoblastic acute leukemia ratio in childhood and have stressed it as a peculiar finding in French Polynesia between 1990 and 1995.

Among adults in our series the commonest leukemias were myeloid – 78/129 (60%). Of these AML were more common – 43 (33.11%). Pradhan P et al [8] also got more cases of myeloid leukemia. However, in their series, cases of CML (38.3%) were more than AML (29.0%). A higher incidence of CML has also been reported by Chatterjea et al [9] and Advani et al [12]. This difference could be attributed to geographical variation or to the fact that our cases had been selected from bone marrow records only. Kasthuri AS et al [21] have reported that Adult leukemias comprise 2.56% of all admissions due to malignancies. They have also reported AML as the most common (61/121) among leukemias in adults in Pune, India.

Among lymphoid leukemias in our series, ALL was far more common 33/129 (25.41%) than CLL 2/129 (1.54%) in our series. Similar findings have been reported by many authors like Roda L et al [20], Pradhan P et al [8], Rani S et al [11], Kasthuri S et al [21], Kushwaha et al [14], and D'costa G et al [19]. A markedly high incidence of CLL has been given by Kwiatkowski A [6], Hansen NE et al [10] and Brincker H [22] who reported CLL as being more common than CML in Poland, Denmark and Scandinavia respectively. We found maximum cases of ALL upto 4 years of age as has also been reported by Van Steensel Moll NA et al [16], Clavel J et al [23] and Monge P et al [17].

Lymphoma

In our study 33/220 cases (14.85%) were diagnosed as Lymphoma. Idris M et al [7] have reported 15.39% cases of haematological malignancies as lymphoma in Abbotabad. However RA Tasleem et al [24] have reported lymphoma only in 2/318 bone marrow examinations. Bhutani et al [5] have reported that occurrence rates of lymphomas are highest in the United States, Europe and Australia and the lowest rates are seen in Asia.

Multiple myeloma

We found a high incidence of multiple myeloma 55/220 (24.75%) cases in our study. Besson C et al [3] have reported multiple myeloma as the most common (34%) haematological malignancy in their series. A similar high

incidence of multiple myeloma has been reported among Afro Americans in the USA by Brown LM et al [4]. Idris M et al [7] found a 4.61% incidence of multiple myeloma in their study.

Metastasis

We found metastatic deposits in 3/220 (1.35%) cases. Other studies on metastasis have reported 8/319 cases Tasleem RA [24] et al, 19/5420 cases – Ozkalemkas F et al [25], 25/11,820 cases – Ringenberg QS et al [26], 5/1569 cases Atac B et al [27] and 2/627 cases Al Ghazaly et al [7].

Conclusions

The commonest haematological malignancy in our series was leukemia. Other diagnoses were multiple myeloma, lymphoma and secondaries. Multiple myeloma which turned out to be the second most common diagnosis was an unusual finding. More studies are required to determine the cause of such geographical variation to ascertain whether genetic or environmental factors are involved. Involvement of bone marrow by lymphoma or metastasis from distant tumours constitute a small but important share of all haematologic malignancies.

References

1. John B (2004) Cousar Hematopoietic-Lymphoid Neoplasms: Principles of diagnosis-In Greer JP, Rodgers GM, Foerster J, Paraskevas F, Lukens JN, Glader B, editors Wintrobe's Clinical Hematology. Vol 2. 11th ed. Philadelphia USA: Lippincott Williams & Wilkins, 1914
2. Al Ghazaly J, Al Selwi AH, Abdullah M, Al-Jahafi AK, Al-Dubai W, Al-Hashdi A (2006) Pattern of Hematological diseases diagnosed by bone marrow examination in Yemen : a developing country experience. Clin Lab Haematol 28(6): 376–381
3. C Besson, C Gonin, A Brebion, C Delaunay, G Panelatti, Y Plumelle (2001) Incidence of hematologic malignancies in Martinique, French West Indies, over representation of multiple myeloma and adult T cell leukemia / lymphoma. Leukemia 15:828–831
4. Brown LM, Linet MS, Greenberg RS, Silverman DT, Hayes RB, Swanson GM, Schwartz AG, Schoenberg JB, Pottern LM, Fraumeni JF Jr (1999) Multiple myeloma and family history of cancer among blacks and whites in the US. Cancer 85:2385–2390
5. Bhutani M, Vora A, Kumar L, Kochupillai V (2002) Lymphohematopoietic malignancies in India. Medical Oncology 19(3):141–150
6. Kwiatkowski A (1994) Trends in the incidence of leukemia in Poland, 1963–1990: an epidemiologic study. Eur J Cancer Prev 3(3):277–283

7. Idris M, Shah SH, Fareed J, Gul N (2004) An experience with sixty cases of haematological malignancies; J Ayub Med Coll Abbottabad 16(4):51–54
8. Pradhan PK, Tiwari SK, Dabke AT, Agarwal S ((1982)) Pattern of leukemia in Raipur (Madhya Pradesh) – An Analysis of 162 cases. Indian J of Cancer 19:20–23
9. Chatterjea JB, Ghose S and Ray RN (1972) Incidence of Leukemia. An analysis of 544 cases studied in Calcutta. J Assoc Phy Ind 10:673–376
10. Hansen NE, Karle H, Jensen OM (1983) Trends in the incidence of leukemia in Denmark, 1943–1977: An epidemiologic study of 14,000 patients. J Natl Cancer Inst 71(4):697–701
11. Rani S, Beohar PC, Mohanty TK, Mathur MD (1982) Leukemic Pattern in Delhi – A Ten year study of 490 cases. Indian J of Cancer 19:81–86
12. Advani SH, Jussawala DJ, Nagaraj Rao D, Gangadharan P and Shetty PA (1979) A study of 1226 leukemia cases – Epidemiologic and end result analysis. The Indian J of Cancer 16:8–17
13. Yeolle BB, Jussawalla DJ, Advani SH (1998) Descriptive epidemiology of leukemias in Greater Mumbai. Natl Med J India 11(3):116–119
14. Kushwaha MRS, Bagchi M and Mehrotra RML (1978) Leukemia at Lucknow-a study of 200 cases. Ind J Cancer 15:28–34
15. Birch JM, Marsden HB, Swindell R (1980) Incidence of malignant disease in childhood: a 24 year review of the Manchester Children's Tumor Registry data. Br J Cancer 42(2):215–223
16. Van Steensel-Moll HA, Valkenburg HA, Van Zanen GE (1983) Incidence of childhood leukemia in The Netherlands (1973–1980) Br J Cancer 47(4):471–475
17. Monge P, Wesseling C, Rodriguez AC, Cantor KP, Weiderpass E, Reutfors J, Ahlbom A, Partanen T (2002) Childhood leukemia in Costa Rica, 1981–1996 Paediatr Perinat Epidemiol 16(3):210–218
18. Coebergh JW, Reedijk AM, deVries E, Martos C, Jakab Z, Steliarova Foucher E, Kamps WA (2006) 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 42(13): 2019–2036
19. D'Costa GG, Siddique HM, Pradhan RM, Gupte SS (1989) Pattern of leukemias: a ten year incidence study of 242 cases. J Postgraduate Med 35:191
20. Laurent Roda, Florent de Vathaire, Bernard Rio, Agnes Le Tourneau, Patrice Petidier, Francois Laudon, Robert Zittoun (1999) Incidence of hematological malignancies in French Polynesia between 1990 and 1995. Leukemia Research 23(4):349–355
21. Kasthuri AS, Jaiprakash MP, Panicker NK, Gupta MM, Rajoor GS, Basu SK, Sambandam S, Bhalla IP (1991) A clinical study of adult leukemias. J Assoc Physicians India 39(3):291–292
22. Brincker H (1982) Population based age and sex specific incidence rates in the 4 main types of leukemia. Scand J Haematol 29(3):241–249
23. Clavel J, Goubin A, Auderc MF, Auvrignon A, Waterkeyn C, Patte C et al (2004) Incidence of childhood leukemia and Non Hodgkin's lymphoma in France: National Registry of childhood leukemia and lymphoma, 1990–1999. Eur J Cancer Prev 13(2):97–103
24. Tasleem RA, Chowdhary ND, Kadri SM, Chowdhary QA (2003) Metastasis of solid tumors in bone marrow: a study from Kashmir, India. J Clin Pathol 56(10):803
25. Ozkalemkas Fahir, Ali R, Ozkocaman V, Ozcelik T, Ozan U, Ozturk H et al (2005) The Bone Marrow Aspirate and biopsy in the diagnosis of unsuspected non hematologic malignancy: A clinical study of 19 cases BMC Cancer 5: 144:1471–2407
26. Ringenberg QS, Doll DC, Yarbrow JW, Perry MC (1986) Tumors of unknown origin in the bone marrow. Arch Intern Med 146(10):2027–2028
27. Atac B, Lawrence C, Goldberg SN (1991) Metastatic tumor: the complementary role of the marrow aspirate and biopsy. Am J Med Sci 302(4):211–213