INCIDENCE AND CLINICAL PROFILE OF LEUKEMIA IN CHILDREN

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SUMMARY

To look for the incidence and profile of leukemia in hospitalized children, a two years prospective study was carried out in the Postgraduate Medical Institute, Lady Reading Hospital, Peshawar from 1st Jan, 1996 to 31st Dec, 1997. A total of 188 cases were clinically suspected as leukemias and subjected to bone marrow examination and other relevant investigations. Only 70 cases were diagnosed as leukemias. The study included 50 males and 20 females with ages ranging between 1 to 14 years. Fever (94%), palor (85.5%) and bone pains (36%) were the major symptoms, while anaemia (88.5%), hepatomegaly (77%), splenomegaly(68.6%) and lymphadenopathy (64%) were the main signs recorded. The peripheral blood smear revealed blast cells (95%), anaemia (88.5%) and low platelets in (80%) cases. The final diagnosis was based on bone marrow examination Acute lymphoblastic leukemia (93%) was the commonest diagnosis. Common-ALL (74.3%) was the major subtype, followed by Null Cell Leukemia (11.4%) and T-Cell Leukemia (7.2%). Acute myeloid leukemia accounted for 5.7% cases only. One cases was diagnosed as chronic eosinophil leukemia. The details of the study with relevant literature review is detailed in the text.

INTRODUCTION

Leukaemia is a cancer of blood forming organs with malignant proliferation of hemic precursor cells in bone marrow. It secondarily involves the peripheral blood and many other tissues, particularly those of reticuloendothlial system including lymph nodes, liver and spleen. The other major systems involved are the brain, heart, kidneys and skeleton. The bone marrow is replaced by immature cells, and the peripheral blood shows abnormal numbers and forms of immature cells.[1,2]

Leukaemia is one of the commonest of childhood cancers, and accounts for one third of total childhood malignancies. The annual incidence of leukaemia is 42.1/million white children and 24.3/million black children.[3] Approximately 20,500 new cases in adults, and 2500 in children are diagnosed annually in United Sates alone, and the disease causes about 15900 deaths a year.[4]

Like all other neoplasias, the aetiology of leukaemia also remains elusive. However, certain etiological factors like viruses, radiation's, toxic chemicals, and heredity and congenital disorders have worth mentioning roles. Epstein Barvirus and human T-lymphocytic retroviruses are known to be associated with burkitts lymphoma, and T-cell leukaemia.[3,11,12,13]

Ionising radiation's are known as a major carcinogen. Data from atomic bomb survivors and those exposed to radiations diagnostically, therapeutically or occupationally, has indicated a clear relationship with leukaemia. Prenatal exposure to radia-

tions has been linked to an increased incidence of leukaemia in later childhood. The ultrasound exposure, on the other hand, seem to be safe, as no increase in leukaemia incidence was detected in a population of children exposed to diagnostic ultrasound in utero.[5,6,7,8]

Toxic environmental chemicals like benzene are potent leukemogenic in humans.[5,9] Cytotoxic drugs like alkylating agents and immuno-suppressive agents are the most leukemogenic chemicals accounting for 74% of reported cases.[5,10]

Hereditary predisposition and certain congenital disorders also play a key role in the causation of leukaemia. Trisomy D 21 is the commonest chromosomal disorder of man. These patients are prone to develop malignancies of different types. The risk of developing leukaemia is increased by 15 folds, and they predominantly develop acute myeloid leukaemia.[14] Some of the many congenital disorders predisposing to develop leukaemia are Fanconi syndrome, Diamond Blackfan syndrome, Wiskott Aldrich syndrome, Shwachman syndrome and ataxia telangiectasia.[15] The risk of leukaemia is also augmented by 20% in an identical twin of a leukaemia patient.[16]

Leukaemias clinically present with fever, pallor, bruising, bleeding and bone pains, occurring in any combination.[17] Anaemia, petechae, bruising, echymosis, lymphadenopathy visceromegaly and bone tenderness are common signs of leukaemia. The duration of illness before diagnosis varies from 6 weeks to 6 months. The disease may, however, have a very fast course.[1]

Looking at the multidimensional picture of leukaemia, a two years prospective study was carried out in the Department of Paediatrics, Postgraduate Medical Institute Lady Reading Hospital, Peshawar from Jan., 1996 to Dec., 1997, to findout the incidence and clinical profile of leukaemia in hospitalised children.

MATERIAL AND METHODS

This study was carried out in the paediatric department of Postgraduate Medical Institute, Lady Reading Hospital, Peshawar, in collaboration with the Haematology Department of the same institute. The study period stretched over 2 years (1.1.1996 to 31.12. 1997).

The paediatric department consists of 2 paediatric wards and a unit for infectious diseases with a collective strength of 132 beds. The total number of admissions over the study period were 3168. The clinical diagnosis of leukaemia was suspected with presenting features like fever, bleeding into skin, epistaxis, malena, bone pains, jaundice, visceromegaly and lymphadenopathy.

A total of 188 cases presented with a leukaemia like picture. All these patients had a history and clinical examination recorded. The following investigations were carried out:

Peripheral blood smear

Urinalysis

Mantoux test.

X-Rays chest.

Bone Marrow Aspiration for cytology and special staining.

The bone marrow was aspirated from the medial tuberosity of tibia below 2 years age, and from the iliac crest above 2 years age, using the standard technique of bone marrow aspiration. The standard paediatric size bone marrow aspiration needles with trocar, 1.5 mm. bore, were used.

On completion of investigations, 70 patients were proved to be suffering from leukaemia, while the rest (110 cases) had other final diagnoses.

The following special stains were used for the final tying of leukaemias:

Periodic Acid Schiff Stain (PAS) shows Block positivity in Acute lymphocytic

leukaemia (ALL). It is negative in Null Cell leukaemia (N-ALL) and T-cell leukaemia (T-ALL).

Acid Phosphatase Stain (ACP) is positive in T Cell leukaemia.

Sudan Black B. Stain is positive in Acute myeloid leukaemia.

Myeloperoxidase stain is also positive in acute myeloid leukaemia.

RESULTS

A total of 188 cases were studied. On completion of investigations, 70 cases were proved to be suffering from different types of leukaemia. The rest (118 cases) had other final diagnoses, including idiopathic thrombocytopenic purpura (ITP), 47 cases, aplastic anaemia 36 cases, megaloblastic anaemia with thrombocytopenia 28 cases, and disseminated intravascular coagulopathy (DIC) 7 cases (table–I). These 118 cases were excluded from the study. The 70 cases of leukaemia were further analysed...

For the purpose of analysis, the patients were subdivided into 3 sub-groups i.e. 0-5 years (12 cases), 5-10 years (44 cases) and above 10 years (14 cases), table–II.

Amongst them 50 cases (71.4%) were males and 20 cases (28.6%) were females. The commonest symptoms were fever (94%), palor (88.5%), and bone pains (36%). Weight loss, epistaxis, malena and hematamesis were seen in decreasing order of frequency (table–III). Anaemia (88.5%), hepatomegaly (77%) splenomegaly (68.6%) and lymphadenopathy were major signs, followed by petechie, bone tenderness, joint swelling, wide mediastenum, meningeal irritation and jaundice (table–IV).

TABLE – I

DISEASE WISE BREAK UP OF 188 CASES.

Diseases	Cases	Percentage
Leukaemias	70	37.2
I.T.P.	47	25.0
Aplastic anaemia	36	19.1
Megaloblastic anaemai with thrombocytopenia	28	15.0
D.I.C.	07	3.7

TABLE – II

AGE WISE DISTRIBUTION OF 70 CASES OF LEUKAEMIA.

Age in years	Cases	Percentage
1–5 years	12	17.2
5–10 years	44	62.8
More than 10 years	14	20.0

The findings in peripheral blood at diagnosis included blast cells 66 cases (95%), anaemia 62 cases (88.5%), thrombocytopenia 56 cases (80%), leucocytosis 46 cases (65%), and neutropenia 42 cases (60%). One case showed persistently very high counts of eosinophils (table–V), and on bone marrow cytology, it was proved as a case of chronic eosinophil leukaemia.

The bone marrow aspirates were studied for cellularity, erythropoesis, myelopoesis, thrombopoesis and blast cells. The details are tabulated in Table–VI.

TABLE – III

COMMON SYMPTOMS.

Symptoms	Cases	Percentage
Fever	66	94
Palor	62	88.5
Bone pains	25	36
Weight loss	24	34.2
Epistaxis	22	31.4
Malena	15	21.4
Haematermesis	4	5.7

TABLE – IV

COMMON CLINICAL SIGNS.

Clinical signs	Cases	Percentage
Anaemia	62	88.5
Hepatomegaly	54	77.0
Splenomegaly	48	68.6
Lymphadenopathy	45	64.0
Patechae	30	42.8
Bone tenderness	25	35.7
Joint swelling	10	14.2
Wide mediastinum	5	7.1
Meningeal irritation	4	5.7
Jaundice	2	2.8

The acute lymphoblastic leukaemia emerged as the commonest of all leukaemias, 65 cases (93%). On special staining they were typed as Common- ALL, 52 cases (74.3%), Null-Cell ALL, 8 cases (11.4%), and T-Cell ALL, 5 cases (7.2%). There were 4 cases of AML (5.7%), and only one case of chronic eosinophil leukaemia, table–VII.

DISCUSSION

Leukaemia is the commonest of childhood cancers, and accounts for about 30% of paediatric malignancies in our region.[19,21] In our study, leukaemias account for 2.2% of all admissions over 2 years period.

TABLE – V

FINDINGS IN PERIPHERAL BLOOD AT DIAGNOSIS.

Findings	Cases	Percentage
Blast Cells	66	95.0
Anaemia (Hb↓8G)	62	88.5
Thrombocytopenia	56	80.0
Leucocytosis	46	65.0
Neutropenia	42	60.0
Eosinophil Leucocytosis	1	01.4

TABLE – VI

BONE MARROW CYTOLOGY.

Items	Case No.	Percentage
Cellularity		
Hyper Cellularity	51	73
Normal	7	10
Hypo Cellularity	12	17
Erythropoieses		
Normal	8	11.4
Depressed	62	88.6
Myelopoieses		
Depressed	42	60
Thrombopoieses		
Depressed	56	80
Normal	14	20
Blast Cells		
>90%	54	77
<90%	15	21.4

The peak age of incidence in our series is between 5 to 10 years (62.8%). This figure is however higher than those reported by Opitz[20] Similarly Chessels[16] has reported a peak age of incidence between 3 to 5 years.

Leukaemia dominantly affects males than females. This fact is supported by our study in which males are 71% as compared to females, 29%. An other study from the same region has reported 56% males suffering from leukaemia.[22]

The commonest presenting symptoms were fever (94%) and pallor 88.5%. Infection and septicaemia due to depressed myelopoiessis and Neutropenia, are the commonest cause of fever. Sometimes, however, no clinical or laboratory evidence of infection exists. Other causes contributing to fever include extensive disease, debility, chemotherapy, reaction to drugs and blood transfusions.

Anaemia is responsible for pallor, easy fatigability, poor exercise tolerance, lethargy, palpitation, loss of vitality, listlessness

TABLE – VII

TYPES OF LEUKAEMIAS.

Types	Cases	Percentage
Common Acute Lympho-blastic leukaemia (Common-ALL)	52	74.3
Null Cell Leukaemia (N-ALL)	8	11.4
T-Cell Leukaemia (T-ALL)	5	7.2
Acute Myeloid Leukaemia (AML)	4	5.7
Chronic Eosinophilic Leukaemia (CEL)	1	1.4

and respiratory difficulty. In extreme cases, anaemia Leads to dilatation of heart and congestive cardiac failure. Depressed erythropoesis is the main reason for anaemia. Bleeding diathesis and decreased red cell survival are other contributory factors.[19] In our series, 88.5% patients were suffering from anaemia. Even higher incidence of anaemia has been reported both in national and international medical literature.[24,25] All these patients require careful blood transfusion for correction of anaemia.

Visceromegaly is another common feature of leukaemias. In our study, Hepatomegaly and splenomegaly were reported in 77% and 68.6% cases respectively. Colebatch27 has reported nearly the same figures for Visceromegaly. In our cases, the liver was firm and tender on deep palpation.

Lymphadenopathy is another common feature of leukaemia[14] Lymphadenopathy occurred in 64% of our patients. All these cases suffered from lymphoblestic leukaemia. Three of these cases were being treated with anti-tuberculosis drugs before hospitalisation when a bone marrow examination proved the actual diagnosis. Five of our patients had a wide mediastinal shadow on chest radiogram. This widening was due to enlargement of anterior mediastinal lymphnodes.[32] Mediastinal masses are one of the poor prognostic features of leukaemia.

Bone pains and tenderness are very important features of leukaemia. They occurred in 36% of our patients. These pains are due to rapidly increasing blast cells and their subperiosteal deposition leading to Periosteal elevation and bone infarcts. Increased blood flow in the bones and increased marrow pressure further worsens these pains.[19]

Bleeding diathesis is a serious presentation of leukaemia. In our series, epistaxis (31.4%), malena (21.4%) and hematemesis (5.7%) were the major bleeding diathesis noted. In leukaemia, however, the incidence of bleeding can be as high as 90%.[23]

The main reason for bleeding diathesis is depressed thromhopoesis due to bone marrow failure.[5,28] In our series, 80% patients had depressed thrombopoesis on bone marrow examination.

Joint swelling is an uncommon feature of leukaemia. In our series 10 patients had swelling of one or two joints. Nine of these cases had swelling because of haemarthrosis while one had effusion in the knee joint.

The presence of fever with visceromegaly and lymphadenopathy rouses a strong suspicion of leukaemia, especially when associated with a progressive depression of platelets, granuloctyes and haemoglobin level in serial peripheral blood smears. Diamond CA[29] has reported leukopenia and bone marrow hypoplasia in 51% of his cases. Aplastic anaemia is, therefore, the most important differential diagnosis. Many a times the development of actual leukaemia is preceded by a phase of bone marrow hypoplasia.

Bone marrow cytology is the gold standard test to confirm the diagnosis of leukaemia. The presence of blast cells in the bone marrow is the hall mark of acute leukaemia. The French-American British

(FAB) classification of leukaemia, designates a proportion of blast cells of 30% or more as an essential criterion for the diagnosis of acute leukaemia. Similar conditions with less than 30% blast cells are classified as myclodyplastic disorders.[30] High blast cell count is quite common in paediatric leukaemia. George SL[28] has reported 65-90% blast cells count in 50% of his patients. In our series, 77% patients had more than 90% blast cells in their bone marrows. In 21.4% cases, the blast cells count was ranging between 40% and 80%.

Acute lymphoblastic leukemia is generally believed to be Predominant in the pediatric population. It represents about 75% of all cases, while acute mycloid leukemia accounts for nearly 20% of leukemias.[31] In our study, however, ALL accounts for about 93% of total leukemias, while AML is only 5.7%. This difference with the known medical literature is difficult to explain. May be our sample was not large enough to have represented the true picture.

ALL is further subdivided in to four classes.[32] These classes and their respective percentages are as follows:

Common ALL-70%.

T. Cell ALL-28%

B.Cell ALL-2%.

Null Cell ALL-Rare.

In our study common-ALL is the commonest and accounts for 74.3% of cases. Null-Cell ALL and T-Cell ALL account for 11.4% and 7.2% respectively. No case of B-Cell ALL was encountered.

Chronic eosinophic leukemia was seen in one case. This is a rare diagnosis. The patient was a 9 years old boy presenting with anaemia and visceromegaly for the last two years. He was previously investigated and he had the result of seven previous peripheral blood smears available, all revealing a very high eosinophil count ranging from 35% to 70%. He was repeatedly dewormed, and had received many anti-histmin preparations. Our clinical suspicion was lymphoma. The bone marrow, however, revealed predominent eosinophils, and the case was labelled as chronic eosinophil leukemia. On checking the record of hematology department, only one more case of CEL was diagnosed in the previous decade.

CONCLUSION

Leukemia is a very common malignancy of childhood. Patients presenting with unexplained fever, generalized bone pains, visceromegaly, lymphadenopathy and bleeding diathesis should be identified and referred to appropriate referral centres as early as possible. All paediatric units should be equipped with facilities and expertise for bone marrow aspiration. The bone marrow smears should be examined by haematologists with special interest and experience in leukemia. Special stains must be employed for final diagnosis and typing of leukemia.

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