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Original Article

Clinicopathological Profile of Acute Leukemia in Children

Harpani PT[1], BJ Parmar[2], Makwana AM[3]

[1]Dr. Palak Tejas Hapani, MBBS, MD, Assistant Professor, PDC Medical College, Rajkot, [2]Dr. BJ Parmar, MBBS, MD, Assocoate Professor, BJ Medical College, Ahmedabad, [3]Dr. AM Makwana, MBBS, MD, Assistant Professor, PDC Medical College, Rajkot, India.

Address for correspondence: Dr. PT Harpani, E-mail: drtejasharpani@rediffmail.com

Abstract

Introduction: Acute leukemia is the most common malignancy in children of which acute lymphoblastic leukemia accounts for majority of the cases. The objective of this study was to see the clinical profile, hematological parameters and assessment of response to chemotherapeutic agents in acute leukemia. This was an observational prospective study involving 58 children conducted over a period of two years from September 2005 to August 2007 at the department of paediatrics, B.J. Medical College, Ahmedabad. **Materials and Methods:** Leukemia was suspected in children presenting with history of prolonged fever, pallor, hepatosplenomegaly, lymphadenopathy, abnormal bleeding or history of repeated blood transfusion. A complete history, clinical examination and relevant investigations were done to diagnose leukemia. After confirmation of diagnosis, patients were treated, followed up to first remission after receiving chemotherapy. Follow up bone marrow examination was done after induction phase to confirm remission. Complete blood count and CSF cytology were done periodically during intrathecal chemotherapy. **Results:** Out of total 58 patients, 49 (84.5%) were ALL and 9 (15.5%) were AML. Pallor (87.9%), fever (82.7%) and fatigue (86.2%) were most common presenting symptoms. Pallor (86.2%), splenomegaly (89.6%) and hepatomegaly (84.5%) were the most common clinical signs. Forty two patients (74.2%) presented with moderate anemia. Remission was achieved in 51 cases (87.9%) after intrathecal chemotherapy. **Conclusion:** ALL is more common than AML in children. With detailed history and clinical examination, timely diagnosis and initiation of appropriate chemotherapy commonly leads to remission in childhood acute leukemias.

Keywords: Anemia, ALL, AML, Chemotherapy, Hepatosplenomegaly, Leukemia

Introduction

The leukemias are malignant neoplasms of the hematopoietic stem cells characterized by diffuse replacement of the bone marrow by neoplastic cells[1]. Acute leukemia is the most common malignancy in children of which acute lymphoblastic leukemia accounts for majority of the cases. Acute leukemias are a heterogenous group of disorders with identical presentation having different clinical causes. So it can mimic any disease in pediatrics. Due to this reason, this study was mainly carried out to study clinical profile, hematological parameters, cytochemical analysis of bone marrow and assessment of response to chemotherapeutic agents in acute leukemia. Even today, though the exact etiology of leukemia is not known, considerable progress has been made to achieve cure. Exposure to ionizing radiation and a number of chemicals has been linked to the development of acute leukemia. The evidence linking radiation exposure and leukemia comes in part from the long term follow up of survivors of the atomic bomb explosions in Hiroshima and Nagasaki[2,3,4,5.] The highest rates were observed in persons younger than 10 years or older than 50 years at the time of exposure. In Nagasaki, were exposed to a higher amount of gamma radiation, the incidence of AML was even greater[6]. The hallmark of success in pediatric oncology is multidisciplinary approach executed through combined modality team comprising of a pediatric oncologist, a pediatric surgeon, a radiation oncologist, diagnostic specialists & supportive.

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AML represent approximately 1.2% of all cancer deaths in the United States[7,8]. AML represents approximately 90% of all acute leukemias in adults but accounts for only 13% of all leukemia cases in children younger than 10 years. in children younger than 15 years, acute lymphoblastic leukemia(ALL) is approximately five times more common than AML[9]. Before effective anti leukemic therapy, acute leukemias were uniformly fatal, and most children survived only 2 to 3 months after the diagnosis & up to 90% were dead within the first year. Currently, approximately 60% to 70% of children with this disease achieve prolonged disease free survival[10] (5 year after diagnosis) and most of these patients are considered to be cured.

Materials and Methods

This prospective study was conducted in the paediatric department over a period of 23 months from September 2005 to August 2007. Patients of acute leukemia (first presentation only) attending the outpatient department and subsequently admitted as well as those admitted in paediatric wards and diagnosed at a later date were included in the study. A high index of clinical suspicion was maintained for patients presenting specially with prolonged fever, lymphadenopathy, hepato splenomegaly, pallor or abnormal bleeding and history of repeated blood transfusion within a short time interval before admission.

The study was conducted among 58 patients. A detailed history taking, physical examination and focused investigations were carried out in all patients. Bone marrow examination was considered the gold standard for diagnosis.

Bone marrow aspiration was done using Jamsidhi needle in all patients at posterior superior iliac spine older children and at anteromedial side of tibia in infants. About 0.2-0.5 ml of material was aspirated and slides were prepared by pathologist at site. All slides were stained by Wright's stain and when specifically indicated, special stains like Periodic Acid-Schiff (PAS) stain, Sudan Black B stain and Peroxidase stain were used for differentiation and confirmation of diagnosis.

The cases with alternative diagnosis like ITP, aplastic anemia, those patients in whom bone marrow examination was not possible due to early expiry or discharge against medical advice and patients of leukemoid reaction in which acute leukemia was ruled out were excluded from the study.

Detailed history was taken giving stress to history of current illness, history of infections in near past, history of treatment given prior to admission e.g. steroids, antituberculer treatment, blood transfusion, etc; family history of similar illness, tuberculosis or genetic abnormality like mongolism. General examination was done especially to look for weight, pallor, pyrexia, lymphadenopathy, hepatosplenomegaly, bleeding sites and bone joint tenderness.

Apart from routine investigations, renal function test, liver function tests, bleeding profile, blood grouping, bone marrow aspiration/biopsy, CSF examination were carried out to confirm diagnosis as well as typing of acute leukemias. After confirmation of diagnosis, patients were treated according to typing of acute leukemia in paediatric oncology wards. First dose of intrathecal chemotherapy was given after obtaining CSF for cytology. If cytology turned positive, dose intensification was done. Towards the end of induction, patients received cranial irradiation. Protocols used were MCP 841 for ALL and BFM 87 for AML.

All patients were followed up to the attainment of first remission. The following criteria were taken for remission. i) a normocellular bone marrow with 5% or lower blasts along with peripheral blood without lymphoblasts, and with ii) ANC > 1,000/cumm iii) a platelet count exceeding 1,00,000/cumm and iv) Hb>8gm/dl.

CBC was done periodically and CSF cytology during intrathecal therapy, blood products (PCV, platelet concentrate, FFP or whole blood) were administered whenever indicated. Neutropenic patients received special care in isolation with broad spectrum antibiotics, antifungals, optimum nursing care and administration of colony stimulating factors (G-CSF, GM-CSF) whenever indicated. Follow up bone marrow examination was done after induction phase to establish remission.

Results

Clinical features including symptoms and clinical examination findings in our patients were as shown in following Table 1.

Laboratory investigations including hematological and biochemical investigations and radiological findings of chest X-ray and abdominal ultrasound were as shown in Table 2.

Classification of our patients based on bone marrow examination was as given in Table 3.

Response to chemotherapy in our patients was as shown in Table 4.

Table 1: Clinical features of patients

Symptoms	No. of cases (n=58)	Percentage (%)
Pallor	51	87.9
Fatigue	50	86.2
Fever	48	82.7
Weight loss	38	65.5
Anorexia	35	60.3
Abdominal distension	26	44.8
Petechiae	23	39.6
Vomiting	9	15.5
Neck swelling	3	5.2
Bone pain	1	1.7
Clinical examination		
Splenomegaly	52	89.6
Hepatomegaly	49	84.5
Cardiac murmur	25	43.1
Crepitations	14	24.1
Bony tenderness	11	18.9
Meningeal signs	7	12.1
Free fluid in abdomen	6	10.3
Pleural effusion	3	5.1

Table 2: Laboratory investigations

Investigations	No. of cases (n=58)	Percentage (%)
Moderate anemia	42	72.4
Leucopenia	3	5.2
Leucocytosis	47	81
TLC > 50,000/cumm	12	20.7
Thrombocytopenia	54	93.1
Peripheral smear examination		
Blast cells	51	87.9
Band cells	3	5.1
Toxic granulation	8	13.8
Eosinophilia	6	10.3
Increased LDH	58	100
Increased serum uric acid	53	91.4
Increased SGPT	46	79.3
Chest X-ray		
Pneumonia	9	15.5
Pleural effusion	3	5.1
Free fluid in peritoneum	3	5.1
Positive CSF cytology	4	6.9
Occult blood in stool	16	27.6

Table 3: Bone marrow diagnosis

Diagnosis	Number of cases(n=58)	Percentage
Acute lymphoblastic leukemia(ALL)	49	84.5
ALL-L1	37	63.8
ALL-L2	11	19.0
ALL-L3	1	1.7
Acute Myeloid Leukemia	9	15.5
AML-M1	4	6.9
AML-M2	4	6.9
AML-M3	1	1.7

Table 4: Response to treatment

Treatment outcome	Number of cases(n=58)	Percentage
Remission	51	87.9
Refractory	1	1.7
Discharge against medical advise	3	5.2
Expired (before 1st remission)	3	5.2

Discussion

Leukemia was first recognized by Donne by doing first microscopic examination of peripheral smear from a leukemia patient in 1837[11]. Before the discovery of the first antileukemic drug (aminopterine) in the late 1940's, there was little hope for any patient to survive with acute leukemias. Since the 1960s, prognosis for children with acute leukemia has improved and most patients have prolonged disease free survival because of improved techniques and therapy.

In present study, incidence of ALL and AML comes out to be 84.5% and 15.5% respectively, comparable to the study, conducted by Young et al[12]. ALL comprised 75% and AML comprised 25% of all cases. In the present study, more patients were found with pallor (86.2%) and fever (82.7%), compared to the study done by D.G. Poplack et al[13], in which cases with pallor and fever were 43% and 61% respectively. Cases with lymphadenopathy in the study conducted by D. Mukhopadhyay et al[14] was 43.9% as compared to present study in which the case with lymphadenopathy was only 27.6%

More patients with severe anemia (Hb<7 g/dl in 72.4% cases) were seen in the present study as compared to that by D.G. Poplack et al[13] (43% of cases). Total count (TLC) more than 50,000/cumm in both studies was comparable – 20.7% in the present study as against 17%

in D.G. Poplack et al. Also the distribution of subtypes of ALL was comparable; ALL-L1, ALL-L2 and ALL-L3 consisted of 84%, 15% and 1% in D.G. Poplack et al study, while in the present study, the relative proportion (in that order) was 75.5%, 22.4% and 2.1% among 49 cases of ALL.In the study by D. Mukhopadhyay et al[14], remission could be induced in 92.9% of cases, while in the present study, 87.9% of patients achieved remission; the figures are comparable.

Conclusion

Present study reported cases of ALL more common than of AML in children. Pallor, fever and fatigue were the most common presenting symptoms, followed by weight loss and anorexia. On routine haemogram, the most common finding was anemia. In peripheral blood smear examination, presence of blast cells was a strong clue to leukemia. The most common type of ALL in our study was ALL-L1, while for AML, AML-M1 and AML-M2 was equal in numbers. Treatment with MCP 841 for ALL and BFM 87 for AML resulted in remission in more than 85% of the patients.

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