RESEARCH COMMUNICATION

Childhood Acute Leukemia in West Bengal, India with an Emphasis on Uncommon Clinical Features

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Abstract

Leukemias are the commonest childhood malignancy in West Bengal. This study was undertaken on 75 children at NRS Medical College, West Bengal to determine the distribution of signs and symptoms of leukemia and to identify unusual clinical features. After obtaining clinical history, physical examination, hematological and radiological investigations were performed. Acute lymphoblastic leukaemia (ALL, 72%) was the commonest followed by acute myeloid leukaemia (AML, 18.7%). Common symptoms and signs were fever (85.3%), pallor (64%), hepatomegaly (72%), splenomegaly (60%) and lymphadenopathy (50.7%). The uncommon signs and symptoms were abdominal pain (9.3%), joint pain (9.3%), hematemesis and malena (8%), diarrhea (5.33%), proptosis (2 cases), dysphagia, mediastinal mass and parotid swelling (1 case each). Uncommon clinical presentations lead to delay in diagnosis in some cases. Awareness of uncommon signs and symptoms of childhood leukemia together with laboratory tests may help in earlier diagnosis and proper management of the patients.

Key words: Childhood leukemia - acute lymphoblastic leukemia - acute myeloid leukemia - uncommon symptoms

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Introduction

Acute leukemias are the most common malignant disease affecting children of West Bengal, accounting for 39.2% of childhood cancers (Chaudhuri et al., 2003). Leukemia usually presents with non-specific signs and symptoms such as anorexia, fatigue and irritability (Lanzkowsky, 2005). As the disease progresses, pallor, bleeding tendency, hepatosplenomegaly and lymphadenopathy may appear. However, uncommonly, joint pain, proptosis, abdominal pain, malena, diarrhea, dysphagia etc. can also be noted as initial manifestation, which may bewilder the clinician as well as the pathologists.

Results of various investigations are decisive for the diagnosis of leukemias. However, a thorough history taking and physical examination are valuable tools in the diagnosis of any disease. Hence, one should remember both the common as well as uncommon signs and symptoms of leukemias for rapid and appropriate diagnosis and management. Studies have shown a correlation between the prognosis and various clinical and laboratory findings at the time of diagnosis such as age, sex, WBC count, organ infiltration (liver, spleen, lymph nodes) etc (Armstrong et al., 1990; Wessels et al., 1997).

The present study was undertaken to determine the distribution of signs and symptoms of leukemia in children of West Bengal, India and to identify the uncommon ones to hasten the diagnosis. Correlation of different symptomatology with the hematological profile was also evaluated.

Materials and Methods

The study population consisted of children aged between 0 to 14 years admitted to NRS Medical College, Kolkata (which caters to the population of West Bengal, India) from June 2003 to July 2005 for suspected hematological malignancy. After obtaining a thorough clinical history, physical examination was performed. Clinical features like hepatomegaly, splenomegaly, fever, upper respiratory tract infection, lymphadenopathy and gum bleeding were recorded. Rare presentations like joint pain, gastrointestinal bleeding, abdominal pain, proptosis, dysphagia were assessed. Ultrasonography was performed for detection of organomegaly and lymphadenopathy. Chest X-ray (in all cases) along with radiograph of relevant joints (in symptomatic cases) were performed.

A written informed consent was obtained for invasive procedure. FNAC was performed wherever clinically indicated e.g. lymphadenopathy, chloroma.

Clinical data was recorded including variables like age, sex, type of malignancy, signs and symptoms at the time of admission (Table 1). The diagnosis of leukemia was based on findings of complete blood count and bone marrow examination including cytochemical stains like

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Table 1. Distribution of Different Signs and Symptoms

	ALL (%)	AML (%)	Acute leukemia (%) (cytochemically unclassified)	Total (%)
No of cases	54 (72.0)	14 (18.7)	7 (9.33)	75 (100)
Fever	43 (79.6)	13 (92.9)	5 (71.4)	64 (85.3)
Pallor	33 (61.1)	8 (57.1)	5 (71.4)	48 (64.0)
Gum bleeding	11 (20.4)	6 (42.9)	0 (0.00)	17 (22.7)
Bleeding from skin	5 (9.30)	6 (42.9)	1(14.3)	12 (16.0)
Lymph-adenopathy	27 (50.0)	5 (35.7)	5 (71.4)	38 (50.7)
Hepatomegaly	36 (66.6)	11 (78.6)	5 (71.4)	54 (72.0)
Splenomegaly	36 (66.6)	4 (28.6)	3 (42.9)	45 (60.0)
Sternal tenderness	1 (1.85)	1 (7.14)	1 (14.3)	3 (4.00)

PAS and Sudan Black.

Considering the above criteria, 75 cases of acute leukemia were identified and included in the study group. These cases were further classified according to morphology and cytochemical staining pattern (FAB classification). Cases of acute leukemia showing morphological and cytochemical features of both myeloid and lymphoid differentiation or could not be classified were categorized as acute leukemia, cytochemically unclassified.

Results

Among these 75 patients, acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) comprised 54 (72%) and 14 (18%) respectively. Seven (9.3%) cases of acute leukemia were cytochemically unclassified.

In the study group, 49 were males, 26 were females (M: F = 1.9:1). ALL cases had an age range of 1.8-14 years (average 6.12 years, SD ±2.98). AML patients had an age range of 2-14years (average 5.67 years, SD ±2.62). Among the different symptoms, fever (85.33%) was commonest followed by pallor (64%). Hepatomegaly (72%), splenomegaly (60%) and lymphadenopathy (50.67%) were the frequent signs at the time of presentation (Table 1).

Gum bleeding was seen in 11 cases of ALL (20.4%) and 6 cases of AML (42.9%). Bleeding from skin manifested as purpuric spots was seen in 5 cases of ALL (9.26%) and 6 cases (42.86%) of AML.Fever is the commonest symptom occurring in average age of 5.98 years in ALL and 5.48 years in AML. Gum bleeding occurred in older age in ALL (average age of 5.73years) compared to AML (average age 4.38 years). In cases of AML and ALL, the average age of presentation with hepatomegaly and splenomegaly were similar. Lymphadenopathy was seen in older age in ALL (average age of 6.69 years) compared to AML (average age of 5.4years).

Uncommon symptoms and signs

Abdominal pain was noted in 7(9.33%) cases (5 in ALL, 2 in AML), Three patients presented with abdominal protrusion due to organomegaly. Ascites was noted in one case of ALL. Seven cases (9.33%) of leukemia (five ALL cases) presented with joint pain (one or multiple), myalgia was significant in two cases (2.67%). Bone pain was complained by 6 (8%) children. Four patients of ALL and one case of AML presented with malena (6.67%). One case each had hematuria (AML) and hematemesis (ALL). Two cases presented with proptosis and both were diagnosed as AML. Upper respiratory tract infection was seen in 4 cases of ALL (7.41%). Limb swelling was seen in one case of ALL. Prolonged diarrhea noted in 4 cases of ALL (7.41%). Parotid swelling was seen in one case of acute leukemia, cytochemically unclassified. One case presented with mediastinal mass and pleural effusion and was ultimately diagnosed as ALL.

Hematological features

Average hemoglobin (Hb) was 6.84 gm/dl in the study population. Average TLC was 19,523 and 10,250/cmm in ALL and AML respectively. TLC was less than 4,000/mm^3 in 9 cases, between 4,000 to 10,000/mm^3 in 24 cases, between 10,000 to 100,000/mm^3 in 32 cases, between 100,000 to 2,00,000/mm^3 in 7 cases and above 200,000/mm^3 in 3 cases. Average blast was 80% and 50% in ALL and AML respectively. Average platelet count was 47,000 and 10,250/cm^2 in ALL and AML respectively. The bone marrow was hypercellular comprising of sheets of blasts in most of the cases. Adequate megakaryocytes in the marrow were noted in one case of ALL and AML each.

Discussion

Acute leukemia constitutes 97% of all childhood leukemia, the majority being acute lymphoblastic leukemia (75%) followed by acute myeloid leukemia (20%) (Lanzkowsky, 2005). In the present study, similar occurrence of these leukemias was observed (72% and 18.67% respectively).

WHO classification of leukemias which was formulated in 1997 (Harris et al., 1999) requires cytogenetics and immunophenotyping. As facilities for these ancillary techniques were not available in our set-up, FAB classification, which has been widely accepted due to its objectiveness and good reproducibility, has been used in our study. It has been observed in a study conducted by a premier institute of India (Sachdeva et al., 2006) that in developing countries, FAB classification is still relevant in subcategorisation of large majority of acute leukemias. In that study, cases in which morphology as well as cytochemistry had failed to identify the lymphoid or myeloid nature of blasts were reported as

acute leukemia, cytochemically undifferentiated. In the present study, dual population of myeloid and lymphoid blasts (morphologically and cytochemically) was observed in 2 cases. 5 cases could not be classified morphologically and cytochemically. These 7 cases (9.33%) were together categorized as acute leukemia, cytochemically unclassified. In our study, ALL occurred in average age of 6.12 years (age range 1.8 to 14 years) whereas AML presented in average age of 5.67 years (age range 2 to 12 years). In the present study, the average age of occurrence of fever was 5.98 years. in ALL and 5.48 years in AML. Fever, bleeding tendency, hepatomegaly, splenomegaly and lymphadenopathy has been previously reported to occur in younger age in ALL than AML (Karimi et al., 2008). This is due to the fact that ALL was reported to be more common in the age range of 3-8 years, while this range was 10- 12 years for AML. In contrast no such age difference was noted in our patients. However, joint pain occurred in a similar age group (median age of 7 years) in both our and the study of Karimi et al., (2008). The patient who presented with mediastinal mass and pleural effusion was relatively older (10 years) similar to previous reports (Karimi et al., 2008).

Fever (85.33%) was the commonest sign followed by pallor (64%). One recent study (Karimi et al., 2008), showed similar pattern of presentation, fever (74%) being the commonest followed by pallor (42%). Patients with fever of unknown origin (FUO) should not be neglected and bone marrow aspiration should be done . Non-specific symptoms like weakness were present in 14.67% cases in the present study. Fatigue (92%) was observed to be the commonest non-specific symptoms among all patients of leukemia (Whitlock and Gaynon, 1999). The lower occurrence in the present study is due to lack of appreciation among the children about this symptom.

A child aged 10 years presented with multiple joint pain. Autoantibodies were negative and radiograph of relevant joints showed no erosive or periosteal changes. However, as the peripheral blood revealed pancytopenia, a bone marrow aspiration was undertaken. The aspiration smears revealed sheets of lymphoblasts with depression of other precursors and was ultimately diagnosed as ALL. Barbosa et al., (2002) showed 62% of pediatric patients had musculoskeletal pain but only 13% had evidence of arthritis, at the onset of leukemia; 8% of patients had been misdiagnosed with rheumatic fever or juvenile idiopathic arthritis before referral and some of these patients had already received steroids delaying the initiation of appropriate treatment. When a child develops recent onset of bone and joint complaints, the presence of subtle complete blood count changes combined with nighttime pain should lead to consideration of leukemia as the underlying cause (Jones et al., 2006). All patients of ALL presenting with joint pain showed low hemoglobin (<11gm/dl), low platelet count (<40,000/mm^3) and WBC count ranging from 3,500 to 30,000/mm^3. Literature showed that all ALL patients with joint pain present with low WBC count, low hemoglobin and low normal platelets (Jones et al., 2006). Juvenile idiopathic arthritis is characterised by severe anemia, low normal WBC count with relative lymphocytosis, thrombocytopenia (Murray et al., 2004). Children having ALL tend to present with joint symptoms rather than bone pain which may be mono or polyarticular (Chell et al., 2001). In our case, ALL patients with joint pain showed blasts in peripheral smear. Usually blast cells are not seen in ALL patients with leucopenia. When the WBC count is greater than 10,000/ mm3, blasts are usually abundant (Lanzkowsky, 2005).

Seven patients of acute leukemia (9.33%) presented with joint pain and six patients (all ALL) presented with bone pain. Joint pain was the presenting feature in 5 cases (9.26%) in our ALL cases though it was observed in 6% cases in a similar study (Karimi et al., 2008). Bone pain was observed in 11.11% of ALL in our study compared to reported incidence of 25%(Lanzkowsky, 2005). Bone pain may result from direct leukemic infiltration of the periosteum, bone infarction, or expansion of marrow cavity by leukemic cells (Lanzkowsky, 2005).

Seven cases (9.33%) presented with abdominal pain and diarrhea noted in four cases (5.33%) in the present study. Different types of gastrointestinal bleeding (hematemesis-1, malena-5) were seen in 5 cases of ALL (9.26%) and one case of AML. Abdominal pain (19.5% in ALL and 11.8% in AML), diarrhea (3.6% in ALL and 11.8% in AML), and gastrointestinal bleeding (7.9% in ALL and 9.7% in AML) have also been reported previously (Robazzi et al., 2008). All patients of malena in acute leukemia presented with low hemoglobin and decreased platelet count in the present study.

Parotid swelling was seen in one of our patients. It occurs due to infiltration of blasts into the parotid gland, which may mimic mumps.

Our study showed that chronic cough was present in 2 cases, upper respiratory tract infection in 1 case, joint pain in 7 cases, diarrhea in 4 cases and abdominal pain in 7 cases. Chronic cough, facial edema, upper respiratory tract infections, joint pain, abdominal pain, skin nodules should also be considered as rare presentations in leukemia patients (Karimi et al., 2008).

Complete blood count and bone marrow aspiration were performed for diagnosis. Thorough history taking supported by a precise physical examination of suspicious patients may prevent delayed diagnosis. Familiarity with the most common signs and symptoms along with uncommon features of leukemias, as noted among the children of this region of India, is vital for faster diagnosis and better management. This will eventually increase the survival rate of these children.

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