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Myelonecrosis in Acute Leukemia

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Myelonecrosis or Bone Marrow Necrosis (BMN) is defined as "necrosis of the myeloid tissue and medullary stroma in large areas of hematopoietic bone marrow," and has been reported in a wide range of malignant and non-malignant diseases(1). It is a

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rare antemortem finding and has received scant attention from clinicians and hematologists due to its uncertain clinical significance(2). Most of the reports on myelonecrosis in acute leukemias are post mortem studies(3-6), and the antemortem studies lack the specific analysis of clinical correlation(7-9). With the increasing awareness about this entity it is now noticed more commonly than previously suspected(1). There is paucity of related reports in Indian context; we discuss here the three cases recently encountered by us.

Case Reports

In a series of 45 consecutive cases of acute leukemia admitted at the Maulana Azad Medical College and Associated LNJP Hospital, New Delhi, three cases with BMN were identified.

All the cases of acute leukemia were diagnosed and classified on peripheral blood and bone marrow aspiration smears. A detailed record of their clinical findings, investigations, treatment and subsequent day to day follow up was recorded. Bone marrow biopsy was obtained pretherapy, during therapy and post therapy from the posterior iliac crest using modified Westerman Jensen Needle.

TABLE I-Hematological Data in Three Cases of Myelonecrosis

Investigations	Case 1	Case 2	Case 3
<i>Pretherapy</i>			
Hb (g/dl)	2.0	7.0	2.8
TLC(/cu mm)	48,000	4,000	36,000
DLC (%)	Blasts 69, monocytes-16, polymorph 8, lymphocytes 3, metamyelocytes 1	No blast cells	Blasts 70, promyelocytes 13, myelocytes 6, metamyelocytes 2, polymorph 6, monocytes 3
Bone marrow aspirate	86% blasts with reduced erythro-myelo and megakaryopoiesis. Blasts were large with anopenlacy chromatin of nucleus with folding of nuclei and prominent nucleoli	87% blasts with high N/C ratio and similar morphology	Blasts 78%, promyelocytes 15%, myelocytes 4%, polymorph 3%
<i>Intratherapy</i>			
Hb (g/dl)	(Day 6) 4.8	(Day 28) 5.4	(Day 60) 5.2
TLC(/cu mm)	700	1,200	1,800
DLC (%)	Not possible	Few lymphocytes seen	P 18, L 92
Platelets (/cu mm)	20,000	45,000	40,000
Bone marrow biopsy	Marrow cells were seen only as ghost cells and bony trabeculae lacked osteocytes. Complete marrow necrosis	Areas of marrow necrosis with persisting blast cells 35% and few megakaryocytes and erythroid cells	Alternate viable and necrosed areas (seen as ghost outlines only). Viable areas showed blast cells

Bone marrow biopsy was fixed in buffer formalin for 6-8 hours and decalcified overnight in formal citrate solution. It was embedded in paraffin and 5-6/m thick sections were cut which were stained with hematoxylin and eosin stain for reticulin. Myelonecrosis was diagnosed with salient features as described by Cassileth *et al.*(2).

There were three cases of BMN, the details of which are described below.

Case 1: A 2-year-old female, was hospitalized with 15 days history of fever. Examination revealed severe pallor, hepatomegaly (4.5 cm) and spleen palpable 3 cm below costal margin. The hematological findings are summarized in *Table I*. She was diagnosed as acute non lymphocytic leukemia (ANLL-M5). Pretherapy bone marrow biopsy showed a 92% cellularity. She was treated with adriamycin and cytosar. An intratherapy bone marrow biopsy on day-6, was done to assess the response to chemotherapy. The biopsy demonstrated a complete marrow necrosis. There was in-

fraction of bony trabeculae with lack of osteocytes in the lacunae and no osteoblasts linking the trabeculae (*Fig. 1*). Hemogram at this time revealed pancytopenia (*Table I*). The child died 7 days later despite intensive supportive therapy.

Case 2: A 10-year-old male was a follow up case of ALL(L1). He developed an inguinal mass after 8 months of first remission, despite being on maintenance therapy with intermittent intensification. Fine needle aspiration cytology from the local site showed immature cells. The hemogram (*Table I*) did not show any blasts but bone marrow aspiration revealed 87% blasts and was diagnosed as ALL(L1).

He was treated with vincristine, prednisolone and leunase, but did not attain remission. The therapy was, therefore, changed to adriamycin, cytosar, prednisolone and etoposide. At the end of one cycle he developed pancytopenia. Bone marrow biopsy at this stage revealed areas of marrow necrosis with persistent blasts (35%), and a few islands of erythroid and megakaryocytic elements. In view of the presence of my-

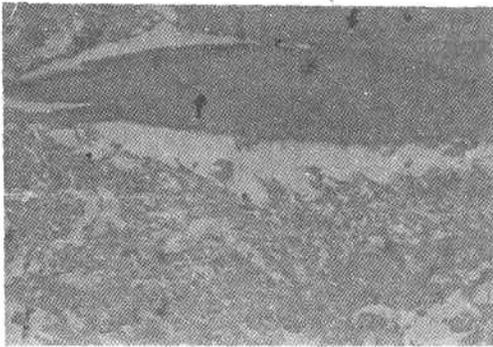


Fig 1. Bone marrow necrosis showing ghost outline of marrow cells and lacunae (↑) in the bony trabeculae lack osteocytes. Complete marrow necrosis.

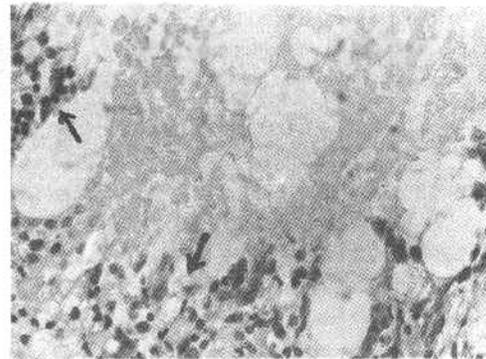


Fig 2. Alternate viable (↑) and necrosed areas in the marrow cavities. Partial marrow necrosis.

elonecrosis, further chemotherapy was withheld. However, the patient succumbed to infection and bleeding after 10 days.

Case 3: A 12-year-old male, presented with fever of 2 months duration and protrusion of the right eye for one week. He had pallor, generalized lymphadenopathy and moderate hepatosplenomegaly. His blood and bone marrow findings are given in *Table I*. He was diagnosed an ANLL-M2. -The patient was put on cytosar and adriamycin chemotherapy. At the end of two months he developed pancytopenia. A bone marrow biopsy at this stage revealed alternate areas of necrosis and viable marrow showing blasts (*Fig. 2*). The patient, however, left against medical advise.

Discussion

Myelonecrosis in acute leukemia is a rare antemortem finding and its clinical significance is uncertain(2). Its association has been noticed more frequently in ALL than ANLL(9,10). We observed myelonecrosis in one of the 22 ALL and two of the 23 ANLL patients. The incidence of myelonecrosis on bone marrow biopsy in patients of acute leukemia undergoing therapy has been reported to be 6/40 and 0/14 patients in ALL(7,11) and 0/2, 4/19 and 0/10 patients in ANLL(7,11,12).

Bone pain which is considered to be the most important presenting symptoms in patients of myelonecrosis(1), was not noticed in any of our patients. Occurrence of leukopenia and/or thrombocytopenia with myelonecrosis, as reported in other series(9,10) was however also observed in our patients.

The exact pathogenesis of myelonecrosis is unclear. It is not caused by chemotherapy as it has been seen even before administering

chemotherapy. Ischemic infarction of bone marrow due to infiltration of medullary nutrient vessels by blasts could be a probable cause(2).

In cases of leukemia developing pancytopenia with or without chemotherapy and not responding to supportive measures, a possibility of myelonecrosis should be considered. It is suggested that a marrow trephine biopsy be carried out in such cases for assessment of response to chemotherapy and early detection of myelonecrosis.

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Phantom Hernia—An Unusual Manifestation of Hypokalemia

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Phantom hernia is a term used to describe unilateral bulging on either side of the abdomen due to weakness or paralysis of abdominal wall muscles. This term was first used by Achar based on his observations in

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cases of anterior poliomyelitis(1). The word "Phantom" is derived from the word "Phantasm" which means the mental imagery produced by fantasy(2).

We observed this unusual phenomenon of phantom hernia with generalized paresis in six cases* of gastroenteritis complicated by hypokalemia which rapidly disappeared with intravenous potassium therapy.

Case Reports

Six cases of phantom hernia were seen over a period of 2 years at Sri Ramachandra Hospital, Porur, Madras. All the cases (Table I) were primarily admitted with acute gastroenteritis and one of them had phantom hernia as a presenting symptom. *Vibrio cholera* was proved to be the etiological factor in 2 of these 6 cases.

The common features among these cases were undernutrition, hypokalemia, phantom hernia, generalized hypotonia with paresis, and a complete rapid recovery over a period of 12 to 24 hours with intravenous potassium administration. All of them had been appropriately immunized with oral polio vaccine. ECG changes of ST segment