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MEDIASTINAL TUMOR WITH BASOPHILIA TERMINATING IN ACUTE LEUKEMIA*

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Eosinophilia associated with lung cancer in adults is well-known, however eosinophils are not present in the tumor tissue in lymphomas, except in Hodgkin's disease[1]. Hypereosinophilic syndrome in association with or terminating in acute leukemia with some chromosomal abnormalities has been reported[2,3]. However, to our knowledge, a tumor with marked basophilic infiltration has not been reported in children. Although mild to moderate basophilia has been observed in chronic myelocytic leukemia (CML) in adults[4,5], and much more rarely in children[6-9], a tumor with basophilic infiltration terminating in acute leukemia is not seen in the literature. We therefore report an infant in whom this combination was observed at Hacettepe University Children's Hospital.

Case Report

A one-year-old boy was admitted to Hacettepe University Children's Hospital with a history of fever, cough, dyspnea and abdominal swelling of ten days duration. He was the eighth child of parents who were not related and had no remarkable prenatal, natal or post-natal histories. All the siblings in the family were healthy.

Physical examination on admission revealed a somewhat underweight boy (9 kg) with tachycardia (156/min) and tachypnea (48/min), but afebrile (37 °C). He had flushing and respiratory distress and his blood pressure was 100/60 mmHg. Rales were heard on both lung zones. While no murmur was present, heart sounds

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were rarely audible. The liver and spleen were very tender four to six cm below the costal margins, respectively. Other physical findings were unremarkable including the neurologic examination.

The initial and subsequent blood counts with differential and repeated bone marrow findings are shown in Tables I and II. Basophils and their precursors along with the leukemoid reaction were present on the initial peripheral blood smear (Fig. 1). Initial bone marrow examination displayed a marked increase in basophilic precursors with rare blast cells. However, morphologic examination of bone marrow obtained just prior to death showed marked infiltration with myeloblasts and lymphoblasts which were uniformly negative with myeloperoxidase, Sudan black B, and periodic acid-Schiff stain. However, metachromasia was present with toluidine blue in cytoplasmic granules. Chest X-ray revealed a huge mediastinal mass (Fig. 2). No specific T or ST changes were seen on the ECG and mild pericardial effusion was detected by echocardiogram. Three milliliters of serous fluid obtained by pericardiocentesis showed blasts on the smear. The results of urinalyses and liver function tests did not reveal any abnormalities, and the uric acid level was normal (6 mg/dl). The patient's fetal hemoglobin was 0.5% and leukocyte alkaline phosphatase 78 U (normal values 50-100 U). However urinary mucopolysaccharide was found to be markedly elevated (109.9 mg; normal 35-58 mg for 24 hours). Due to technical failure, the results of the chromosome analysis were not available.

The infant's general condition deteriorated very rapidly following admission and he died in severe respiratory distress ten days after admission despite vigorous supportive treatment. Postmortem examination revealed a huge, brown anterior mediastinal lobulated gray tumor weighing 220 g and measuring 11 x 6 cm in diameter with numerous areas of necrosis (Fig. 3). Microscopic examination of the tumoral mass showed diffuse undifferentiated blast cell infiltration, with basophilic granules in some. Although, macroscopically, the thymus could not be identified, microscopic examination of some of the sections of this mass showed atropic thymic tissue with blast cell infiltration. Diffuse infiltration of these cells was also present in the cervical lymph nodes, both lungs, trachea, liver and spleen. Focal infiltration was found in the pericardium, myocardium, kidney, pancreas and in both testes, but not in the central nervous tissue nor in the cerebrospinal fluid. Wright-stained touch preparations of the mediastinal tumor, liver and spleen showed blasts morphologically similar to those observed in the bone marrow aspiration material. Immature basophils and basophilic granules in some leukemic cells were clearly demonstrated in the bone marrow (Fig. 4), stained metachromatically with toluidine blue.

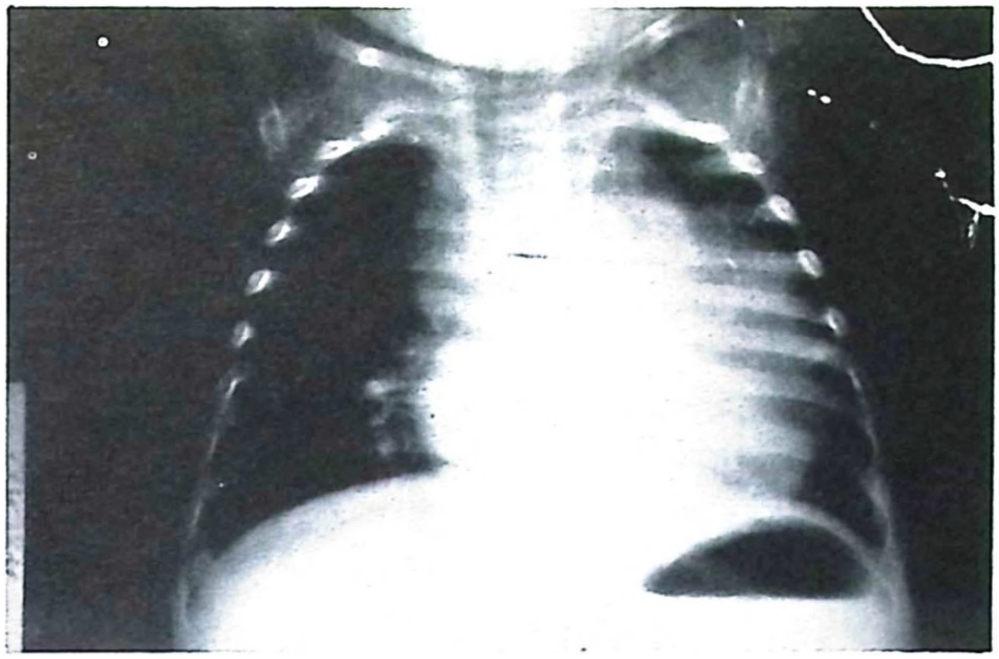

Fig. 1.: Wright stain of peripheral blood showing basophils.

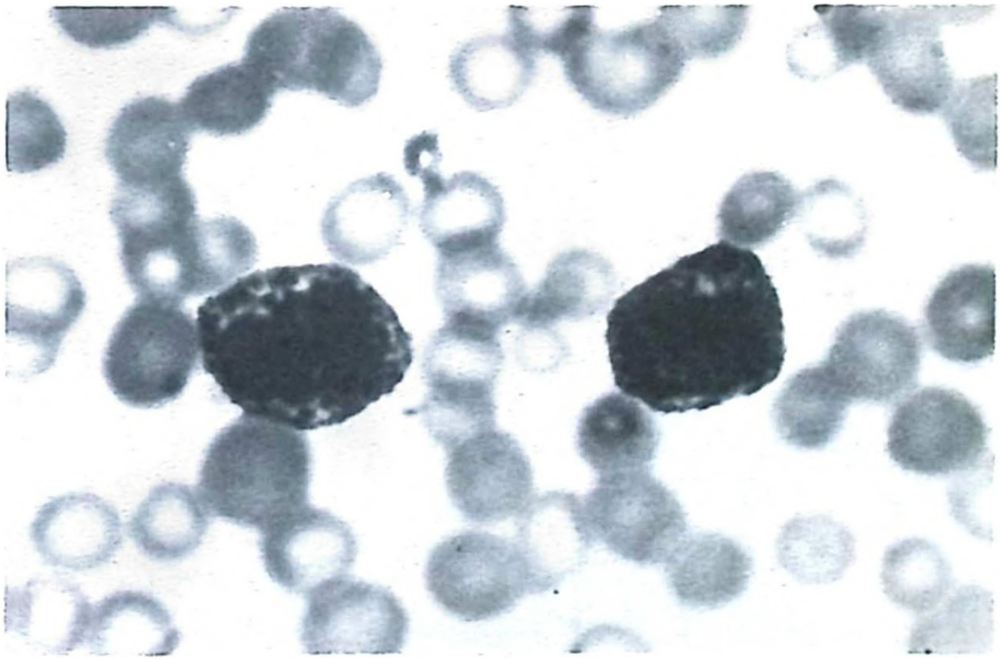

Fig. 2.: Chest roentgenogram on admission showing mediastinal enlargement.

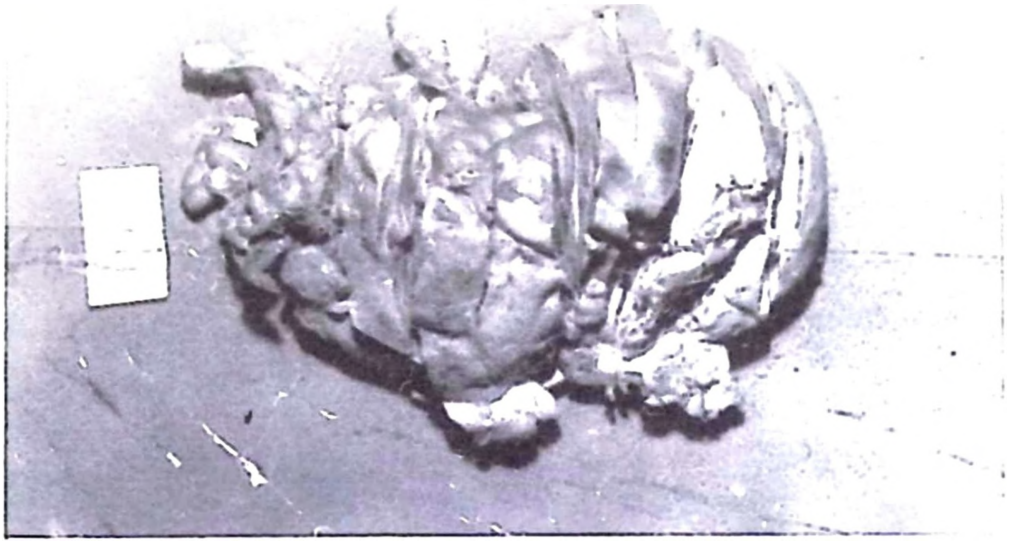

Fig. 3.: Gross appearance of the mediastinal mass.

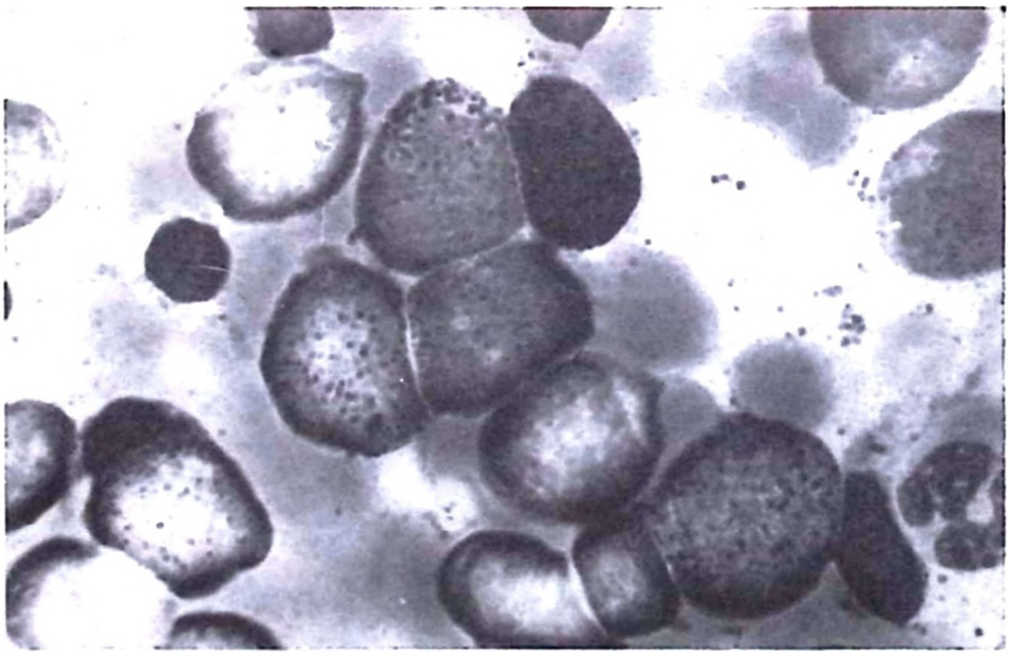

Fig. 4.: Immature basophils in the bone marrow (HE X 1000).

TABLE I: Peripheral Blood Findings

	On Admission	3rd Day	7th Day	10th Day
Hemoglobin (gm/dl)	10.7	10	9.3	9.5
WBC/mm^3	15,000	24,000	17,000	18,600
Lymphocytes (%)	29	32	40	45
Myeloblasts (%)	4	11	8	6
Promyelocytes (%)	–	–	2	–
Myelocytes (%)	10	8	14	11
Metamyelocytes (%)	2	–	3	–
Neutrophils (%)	25	31	16	18
Basophils (%)				
Myelocytes	22	12	13	13
Segmented	8	5	3	7
Normoblasts (%)	2	1	1	–
Reticulocytes (%)	–	1.8	1	–
Platelets/mm^3	260,000	240,000	180,000	16,000

WBC = White Bloods Cells

TABLE II: Bone Marrow Aspirate Findings

	On admission	7th Day	10th Day
Cellularity	Hypercellular	Hypercellular	Diffuse fatty infiltration
Blast Cells (%)	3	12	51
Myelocytes (%)	8	13	10
Neutrophils (%)	4	7	2
Basophils (%)			
Promyelocytes	20	9	
Myelocytes	17	26	11
Segmented	2	–	2
Eosinophils (%)	1	–	2
Lymphocytes (%)	35	28	17
Normoblasts (%)	10	5	5

Discussion

Although basophilia is found in association with various diseases in all age groups, it is relatively more frequently observed in adult CML in which case it is considered a poor prognostic sign[4,5]. Although there are few adult leukemia cases with prominent basophilia at the time of diagnosis[10-12], there is still a question as to whether it is true basophilic leukemia or a variant of CML. Despite this dispute, more recently Wick and co-workers[6] have reported four ANLL cases with basophilic differentiation. They assumed that their cases represented a distinctive variant of ANLL, as suggested by Groat et al[12] in 1936, for which the term basophilic leukemia was used until a complete classification could be made. Although such cases have infrequently been described in children[6-9], none were as young as this case.

In our case, leukemia was diagnosed prior to death because of the bone marrow infiltration of leukemic cells and the observation of similar blasts in the pericardial effusion. Post-mortem examination showed different organ and tissue infiltration of leukemic cells which verified the diagnosis. If ultrastructural studies had been available, some differentiation of granules could have been made in our case, but there is no doubt these granules were different from the azurophilic cytoplasmic granules of lymphoblastic leukemia[13]. Very recently Miller et al[9] described a case of acute leukemia with basophilic cytoplasmic inclusion bodies in which certain aspects suggested a lymphoblastic phenotype and others a myeloid origin. Although a morphologically mixed population of lymphoblasts and myeloblasts were present in our case, the type of leukemia is open to discussion since neither membrane phenotyping was done nor was terminal deoxynucleotidyl transferase (TDL) activity measured. We assume that the leukemia started extramedullary, most probably as a mediastinal mass, which infiltrated the thymus. However, a possible leukomogenic role of the thymus[14,15] cannot be ruled out in this case.

Although the committed basophil precursors have not been clearly defined[16], demonstration of a thymic antigen on rabbit basophils may suggest a relationship between T lymphocytes and basophils in ontogeny[17]. Some functional relationship between basophils and the thymus has also been shown by Schulte-Wissermann, et al[18]. A soluble factor from guinea pig splenic T-lymphocytes promoting basophils was demonstrated in vitro[16]. From the above information, it could be deduced that basophil production in our patient could have been related to primary or secondary infiltration of the thymus. Although Adams[14] reported a leukomogenic thymoma in a thirteen-year-old girl, basophilia was not evidenced.

Increased urinary mucopolysaccharide excretion as well as metachromasia of granules by toluidine blue staining in our patient were compatible with the high number of basophils[19].

Although other hyperhistaminemic manifestations described in some patients with increased circulating basophils[20,21] were not evident in our patient, the flushing might be related to hyperhistaminemia, but the patient's histamine level was not measured in this case.

Despite the exact origin and type of leukemia not being obvious in our patient, increased basophilia in the tissues, including the mediastinal tumor and thymus, terminating in acute leukemia with marked basophilia might be considered a new clinical entity if similar cases are observed.

Summary

Prominent basophilia at the time of diagnosis of leukemia has very rarely been reported in children. Therefore, a case of marked basophilia during diagnosis of mediastinal tumor, terminating in acute leukemia, is reported. Immature basophils and basophilic granules in some leukemic cells were present in the peripheral smear and bone marrow of our patient. Postmortem examination revealed these granules containing cells in various organs infiltrated with leukemic cells in the thymus as well as in the mediastinal mass. These granules stained metachromatically with toluidine blue but failed to stain with myeloperoxidase, Sudan black B and periodic acid-Schiff. Although the exact origin and type of leukemia could not be determined, these distinctive clinical and morphological findings in our case indicate a grave prognosis in this very rare type of clinical entity.

REFERENCES

1. Beeson, PB. Cancer and eosinophilia (editorial) *N Engl J Med* 309:792, 1983.
2. Nelken RP, and Stockman JA, 3rd. The hypereosinophilic syndrome in association with acute lymphoblastic leukemia. *J Pediatr* 89:771, 1976.
3. Chilcote RR, Pergament E, Kretschmer R, Mikuta JC. The hypereosinophilic syndrome and lymphoblastic leukemia with extra C-group chromosome and q14+ marker. *J Pediatr* 101:57, 1982.
4. Denburg JA, Wilson WE. Bienenstock J. Basophil production in myeloproliferative disorders: increases during acute blastic transformation of chronic myeloid leukemia. *Blood* 60:113, 1982.
5. Theologides A. Unfavorable signs in patients with chronic myelocytic leukemia. *Ann Intern Med* 76:95, 1972.
6. Wick MR, Li CY, Pierre RV: Acute nonlymphocytic leukemia with basophilic differentation. *Blood* 60:38, 1982.
7. Casey AE, Nettles TE, Hidden EH. Basophilic leukemia. *South Med J* 39:325, 1946.
8. Mitrakul C, Othaganonda BO, Manothai P, et al. Basophilic leukemia. Report of a case. *Clin Pediatr* (Phila), 8:178, 1969.
9. Miller DR, Ohri GL, DeHarven E. Acute inclusion-body leukemia. Case report and review of literature. *Am J Pediatr Hematol Oncol* 7:336, 1985.

10. Doan CA, Reinhart HL. Basophil granulocyte, basophilcytosis and myeloid leukemia, basophil and "mixed granule" types; experimental clinical and pathological study, with report of new syndrome. *Am J Clin Pathol* 11:1, 1941.
11. Lawlor E, McCann SR, Willoughby R, et al. Basophil differentiation in Ph-positive blast cell leukemia [letter] *Br J Haematol,* 54:157, 1983.
12. Groat WA, Wyatt TC, Zimmer SM, Field RE. Acute basophilic leukemia. *Am J Med Sci* 191:457, 1936.
13. Stein P, Peiper S, Butler D, et al. Granular acute lymphoblastic leukemia. *Am J Clin Pathol* 79:426, 1983.
14. Adams JE. Leukemogenic thymoma: report of a unique case. *Am J Clin Path* 40:173, 1963.
15. Furth J. Prolongation of life with prevention of leukemia by thymectomy in mice. *J Gerontol* 1:46, 1946.
16. Denburg JA, Davison M, Bienenstock J. Basophil production *J Clin Invest* 65:390, 1980.
17. Day RP, Singal DP, and Bienenstock J. Presence of thymic antigen on rabbit basophils. *Immunol* 114:1333, 1976.
18. Schulte-Wissermann H, Borzy MS, Albrecht R, Hong R. Functional relationship of macrophages and basophils to the thymus gland. *Scand J Immunol* 9:45, 1979.
19. Olsson I, Berg B, Fransson LA, et al. The identity of the metachromatic substance of basophilic leucocytes. *Scand J Haematol* 7:440, 1970.
20. Youman JD, Taddeini L, Cooper T. Histamine excess symptoms in basophilic chronic granulocytic leukemia. *Arch Intern Med* 131:560, 1973.
21. Denburg JA, Wilson WE, Goodacre R. Bienenstock J. Chronic myeloid leukaemia evidence for basophil differentiation and histamine synthesis from cultured peripheral blood cells. *Br J Haematol* 45:13, 1980.