

Acta Medica Okayama

Volume 12, Issue 1

1958

Article 4

APRIL 1958

Two cases of acute basophilic leukemia, with a special reference to basophiloblasts

Kiyoshi Hiraki*

Tamotsu Sibata[†]

Saburo Nabeshima[‡]

*Okayama University,

[†]Okayama University,

[‡]Okayama University,

Two cases of acute basophilic leukemia, with a special reference to basophiloblasts*

Kiyoshi Hiraki, Tamotsu Sibata, and Saburo Nabeshima

Abstract

The two rare cases with a high fever and anemia as the chief complaints were confirmed to be acute basophilic leukemia on the basis of the following findings, namely, 1) Numerous basophiloblasts and immature basophilocytes were found in the peripheral blood and bone marrow picture, but there were few neutrophils. 2) By the culture of bone marrow in cover-slips the growth type to acute leukemia, these basophilocytes appearing in the growth zone were clearly distinguishable from neutrophils, eosinophils or monocytes by the modus of their movement and cellular structure. 3) In vitro fluid medium culture revealed that blasts decreased in number along with lapse of time whereas immature and mature basophilocytes increased in inverse proportion. Having encountered these two rare cases of acute basophilic leukemia and being able to autopsy one of them, the authors report their case findings and confirm the distinction of basophiloblasts. Judging from these findings, the authors are of the opinion that some modification seems to be in the offering as regard the Naegeli's myeloblast theory.

Acta Med. Okayama 12, 42—50 (1958)

TWO CASES OF ACUTE BASOPHILIC LEUKEMIA, WITH A SPECIAL REFERENCE TO BASOPHILOBLASTS

Kiyoshi HIRAKI, Tamotsu SIBATA and Saburo NABESHIMA

*Department of Internal Medicine, Okayama University Medical School
Okayama, Japan (Director Prof. Kiyoshi HIRAKI)*

Received for publication on November 22, 1957

In the past three years, 67 cases of leukemia were treated in our clinic, and two of them proved to be the cases with acute basophilic leukemia which is extremely rare and interesting but verified by various examinations, especially with tissue culture^{5,6,7} of the bone marrow. By the tissue culture of the bone marrow and the peripheral leucocytes drawn from the two patients, immature cells were confirmed patho-physiologically to be basophiloblasts distinguishable morphologically and from the so-called myeloblasts (Naegeli).

From these findings we believe that the time has come to rescrutinize the theory of granulocyte formation.

CASE REPORT ON Y. Y.

This patient is a 10-year-old boy without any noteworthy past history in his family. Since February 1955, his face became markedly pale and in the beginning of May he began to complain of fever, cough and sweating at night and on X-ray examinations he was diagnosed as suffering from right exudative pleurisy. From the early part of June he complained of high fever, toothache, unsustainable watery diarrhea, radiating pain in the left thigh and attacks of slight nausea and vomiting. Blood examinations revealed leukemia and he was admitted to our clinic on the third of July but he had no hemorrhagic diathesis till that time.

Findings at admission : He was small for his age, under-nourished, and extremely anemic in the skin as well as in mucous membrane. No bleeding or tumor, but slight hemorrhages in the fundi of the eye. There were neither tonsillar swelling nor bleeding in the gum. The lung and heart were normal but with a little rasping sound. No pain of the sternum on tapping and the liver palpable one finger breadth in the mamillary line, spleen was also palpable. Three lymphnodes were as large as a pea and palpable in the right neck and the left axillary fossa, but not

This investigation was supported by a research grant from the Leukemia Society, Inc.

in other parts.

CASE REPORT ON S. K.

This is an 18-year-old girl without any special past history, but her grandmother died of cancer of the uterus. In March 1957, lymphnodes had swollen in the right neck but were reduced by streptomycin injections. In the beginning of June she had temperature as high as 38°—40°C and petechia in the chest; and agranulocytosis was her diagnosis. She was given blood transfusion and cortisone with no appreciable therapeutic effects. She was admitted to our clinic on the twenty-fifth of July.

Findings at the time of admission : She was of medium height and relatively well nourished and conscious. Extremely anemic in the skin and the mucous membrane and submucous bleeding in the mouth. Pharyngeal tonsils swollen and hyperemic. No abnormalities in the lungs and heart. The liver and spleen were not palpable. She showed no pathologically palpable lymphnodes.

RESULTS OF EXAMINATIONS

Blood picture (Table 1) : Basophiloblasts and immature basophilocytes are found considerably in a large proportion as shown in Table 1;

Table 1 Blood Picture

		Case 1				Case 2	
Date		July 4	July 11	July 17	July 22	July 26	Aug. 4
Hb (%)		38	36	48	49	26	22
Erythrocyte count (unit : 10,000) per c.c.		197	176	209	230	118	115
Leucocyte count (unit : 1,000)		219	230	384	324	2.7	1.5
Leucocyte in per centage	Basophiloblast	81.4	79.0	80.0	84.4	24	22
	Immature basophilocyte	2.0	2.8	4.0	4.4	19	16
	Mature basophilocyte	10.6	14.4	11.0	6.4	0(+)	0(+)
	Neutrophil and eosinophil	1.2	1.4	2.4	2.4	4	12
	Lymphocyte	4.8	2.4	2.6	2.4	50	44
	Monocyte	0(+)	0(+)	0(+)	0(+)	3	6
Thrombocytes (unit : 10,000)		6.3	7.5	17.3	15.6	0.35	0.69
Peroxidase reaction (Mc Junkin's method)		57.5% Positive in blasts				2% Positive in blasts 6% as a whole	
		Polychromasia, anisocytosis and poikilocytosis of erythrocytes				A slight anisocytosis and poikilocytosis of erythrocytes	

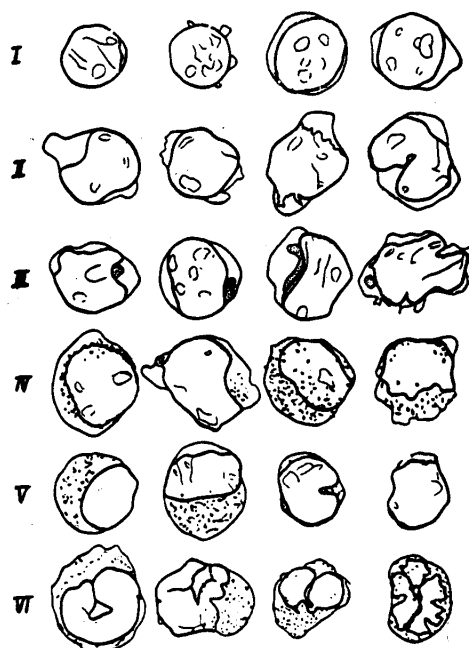


Fig. 1. Various forms of cells of basophilic system

- I blasts of small size
- II large blasts having protoplasmic process like monocytes
- III blasts with Azur substances
- IV immature basophilocytes (corresponding to promyelocytes)
- V immature basophilocytes (corresponding to myelocytes)
- VI mature basophilocytes

and basophiloblasts appear to be far smaller than the so-called myeloblasts, the neutrophiloblasts. The cell bodies are rather slender and stained deep with basophilic staining, while the periphery of cells is not stained so deep and the majority of these cells show irregular, lingual-shape protrusions. Their nuclei are round or with indented surface and their chromatin nets are faint and undistinguishable, and most nucleoli are not sharply defined. Cells of the basophilic system not like those of the neutrophilic system are in reality difficult to classify the maturity because the shape of nuclei are not distinct owing to granules as well as because the nuclei have a tendency to lobulate irregularly in the younger stages. Therefore, we distinguished the cells with more or less basophilic cytoplasm and the cells with no basophilic color but with round or kidney-shaped nuclei as the immature type while the others as the mature type. The cells of the immature type, being larger than the blasts, are clearly in the intermediate stage between the basophiloblasts and mature basophilocytes and most of them possess lingual pseudopodia.

In the early stages, granules begin to appear around the nucleus, and in the extremely immature cells granules are rather small but uniform size and resemble the Azur granules observable in neutrophilic promyelocytes. These granules are almost completely washed away by Giemsa and/or Wright staining. These mature cells are identical with the

basophilocytes observable in the peripheral blood of normal person.

Bone marrow picture (Table 2) : Most of the cells are either basophiloblasts or immature basophilocytes as shown in Table 2.

Table 2 Myelogram

		Case 1	Case 2
Date		July 8	July 28
Numbers of nucleated cells (unit : 10,000) per c.c.		25.1	9.85
Leucocyte in per- centage	Basophiloblast	89.0	24.8
	Immature basophilocyte	2.0	21.2
	Mature basophilocyte	5.0	18.6
	Neutrophil and eosinophil	0.4	1.8
	Lymphocyte	3.6	27.6
	Monocyte	0	0.2
	Others	0	5.8

Blood picture by supra-vital staining (case 1) : By neutral red and Janus green staining, the majority of mature cells are readily stained diffusely with neutral red ; and in their movement nuclei precede, followed by cell body containing fairly large granules stained deep by neutral red, and their movement gives a picture resembling a moving scorpion. The cells believed to be basophiloblasts are well stained with Janus green and present a change in shape by projecting pseudopodia slightly out.

Bone marrow findings by culture in cover-slips (hanging drop-culture) : By the simplified culture of bone marrow in cover-slips, the method⁵ devised in our laboratory, the border of growth zone is sharply defined, presenting a picture of typical acute leukemia^{5,6,7}. The growth zone is occupied almost completely by immature basophilocytes, and along with the lapse of time they grow into mature basophilocytes. These mature cells (Fig. 2) are clearly different from monocytes or neutrophils

Fig. 2. Finding in the bone marrow culture

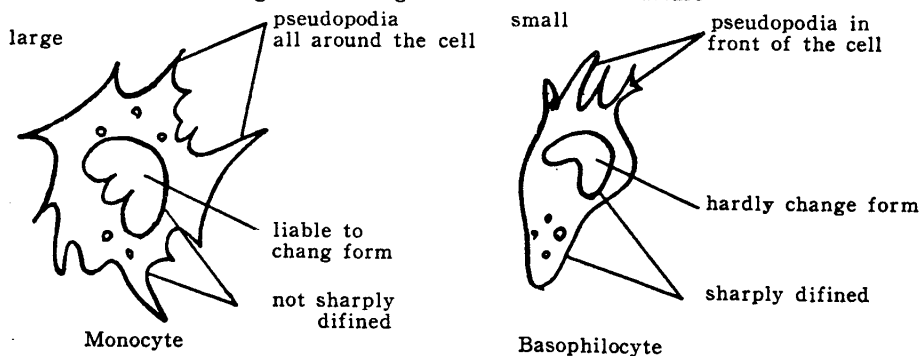


Table 3. Fluid medium culture of blood and the bone marrow (h. = hours)

Time period	Case 1										Case 2									
	Blood										Bone marrow									
	Before the culture	1 h.	3 h.	5 h.	6 h.	7 h.	8 h.	9 h.	10 h.		Before the culture	1 h.	3 h.	5 h.	7 h.	8 h.	9 h.	10 h.	11 h.	12 h.
Leucocyte count ($\times 1000$)	363	381	376	422	420	425	447	449	426		4.65	3.90	5.70	5.85	7.50	8.85	6.85	7.40	8.25	8.75
Basophiloblast	89.2	88.4	85.6	81.4	81.6	77.7	81.2	79.6	80.6		45.6	40.8	38.4	39.2	32.8	30.4	31.2	25.6	25.6	28.0
Immature basophilocyte	1.0	28	4.6	4.2	5.8	7.2	6.0	4.8	4.2		25.6	38.4	46.4	48.0	48.8	53.6	53.6	53.2	54.4	52.8
Mature basophilocyte	7.2	5.6	6.8	9.0	8.6	9.7	8.2	9.4	9.0		9.6	8.8	11.2	11.4	12.0	12.8	12.0	14.4	12.6	12.0
Neutrophil and eosinophil	0.2	0.4	0.6	0.2	1.8	0.9	1.6	1.0	0.6		2.4	1.6	0.8	0.8	1.6	1.6	0.8	1.6	3.2	1.6
Lymphocyte	2.2	2.2	2.2	4.0	2.0	2.0	1.2	1.6	1.6		16.8	6.4	2.4	1.6	3.2	0.8	1.6	2.4	3.2	4.0
Monocyte	0 (+)	0(+)	0(+)	0(+)	0(+)	0(+)	0(+)	0(+)	0(+)		0 (+)	0(+)	0(+)	0(+)	0(+)	0(+)	0(+)	0(+)	0(+)	0(+)
Others	0.2	0.6	0.2	1.2	1.2	2.5	1.8	3.6	4.0		2.4	4.0	0.8	0	1.6	0.8	0.8	1.6	0	1.6

and are classified as basophilocytes, judging from their mode of movement and from their nuclear structure as revealed by the motion picture.

In addition, these mature basophilocytes show a fairly strong phagocytic power to carbon particles, resembling much to monocytes in this particular aspect.

Findings of the peripheral blood and bone marrow by culture in fluid medium : Leucocyte count reaches its maximum after 8—9 hour incubation but along with the lapse of time the immature basophilocytes increase in number inversely proportionate to the decrease of the blasts; and this fact seems to be due to the maturation of the blasts.

Other clinical examinations : The results of other clinical examinations are shown in Table 4.

The course of illness and treatments (Fig. 3) : The case 1 had responded transiently to cortisone therapy for a time but death ensued twenty days after the admission due to brain hemorrhages. In the 2, general symptoms likewise had apparently subsided temporarily after the administration of predonisolone; and on reverting again to the pre-treatment conditions soon af-

Acute Basophilic Leukemia

47

Table 4. Clinical examinations

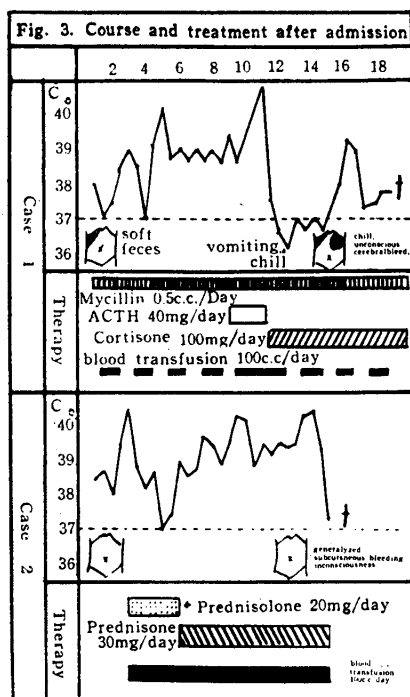
	Case 1	Case 2
Bleeding time	10min. 30sec.	66min.
Coagulation time { begin. end	1min. 30sec. 6min. 30sec.	5min. 30sec. 11min. 20sec.
Capillary resistance { positive pressure method negative pressure method	(-) (-)	(±) (-)
Serum protein (g/al)	6.95	6.24
Serum iron copper (γ%)	164	175 215
Seroreaction for syphilis	(-)	(-)
Liver function tests	no change	no change
Urine	no change	no change
Feces	no change	no change
X-ray of breast	no change	no change
Erythrocytes sedimentation rate	80mm	310mm
Resistance of Erythrocytes { largest smallest	0.32% 0.44%	0.28% 0.42%

terwards, predonisone had been given but without success and the patient died 15 days after admission showing the sign of cerebral hemorrhages. In both cases, no improvement in their blood picture could be recognized even after the administrations of such drugs.

Autopsy findings (only on the Case 1) : The cause of death in the Case 1 seems to be attributable to cerebral hemorrhages, judging from the autopsy examinations which revealed the infiltration of leukemic cells in the whole portion of the brain and the widespread invasion of leukemic cells into bone marrow as well. In addition, leukemic cells were found to have invaded practically all organs and glands, such as bronchi, mesenterium, lymphnodes, liver, spleen, kidney, heart, lungs, digestive canals, adrenal glands, etc.

DISCUSSION

These two cases are thus diagnosed as acute basophilic leukemia. Concerning the chronic basophilic leukemia there are many articles



by various investigators^{1, -3, 8-14, 16} but as for acute basophilic leukemia only the report by GROAT et al.⁴ is available. GROAT et al. however, in their report contended the case to be acute basophilic leukemia on the basis of the fact that the course of illness was acute in nature and the blood picture had revealed numerous basophilocytes as well as immature basophilocytes, but they also conceded that the blood picture itself resembled chronic myelocytic leukemia in view of the presence of numerous neutrophils, especially the immature type. Moreover, even in those chronic basophilic leukemia cases reported by various authors, the majority of them may properly be considered as a phenomenon presenting temporarily basophilic reaction of chronic myelocytic leukemia, judging from

their findings of blood.

In this connection, it may be added that basophilocytes have long been known to increase more or less in number in the cases of chronic myelocytic leukemia.

However, in our cases, the majority of leukocytes were either blasts or immature basophilocytes, but neutrophils were scarcely observable. In tissue culture, the growth was of acute leukemic type^{5, 6, 7} and a great number of basophilocytes could be clearly differentiated from neutrophils, eosinophils or monocytes by their peculiar movement and cellular structure. Moreover, *in vitro* bone marrow culture in fluid media, it was found that the number of blasts decreased along with the lapse of time whereas the more mature basophilocytes increased in an inverse proportion. From these findings, we diagnosed these two cases as acute basophilic leukemia.

During the culture, the blasts observed in our two cases gradually matured and possessed characteristic structure by May-Giemsa staining, which should be classified as basophiblasts rather than as myeloblasts (Naegeli) and should be differentiated from neutroblasts and eosinophils. These findings coincide closely to those of Undritz¹⁵.

Pathohistologically it is interesting to know to what tissue these basophiloblasts have affinity and in what manner they grow and mature. The motility of these blasts resemble closely to that of monocytes while their structure by stained specimens resemble that of lymphoblasts; and the modus of infiltration into tissue indicates clearly that these cells are really of myelogenous in origin. The infiltration of these cells into bone marrow is of such extensive nature that the bone marrow is completely replaced by the leukemic cells. Moreover, lymphnodes are in general slightly swollen, but the follicles are atrophied owing to the infiltration of these cells into the lymph sinus. The spleen is about three times the normal size and the cell infiltration is much more marked than that of lymphnodes so that the lymph follicles are obliterated. Some splenic trabeculae are also destroyed the cell infiltration. As for the kidney, the cell infiltration is moderate in the interstitium of medulla while markedly in the glomerulus of the cortex. In the lung, the cell infiltration is observed in the alveolar septum; and the liver reveals marked infiltration in hepatic lobules and a slight infiltration in Glisson's sheath as well. In others such as the tissue around the arteries and the follicles of lymphnodes, where lymphoblasts are apt to congregate, no striking affinity can be detected; and neither there is any tendency of tumor formation as is genenally observable in monocytic leukemia. Thus the infiltration processes resemble closely those of myelocytic leukemia but not like those of lymphocytic and monocytic leukemia.

SUMMARY

The two rare cases with a high fever and anemia as the chief complaints were confirmed to be acute basophilic leukemia on the basis of the following findings, namely,

1) Numerous basophiloblasts and immature basophilocytes were found in the peripheral blood and bone marrow picture, but there were few neutrophils.

2) By the culture of bone marrow in cover-slips the growth type to acute leukemia^{5,6,7}, these basophilocytes appearing in the growth zone were clearly distinguishable from neutrophils, eosinophils or monocytes by the modus of their movement and cellular structure.

3) *In vitro* fluid medium culture revealed that blasts decreased in number along with lapse of time whereas immature and mature basophilocytes increased in inverse proportion.

Having encountered these two rare cases of acute basophilic leukemia and being able to autopsy one of them, the authors report their case find-

ings and confirm the distinction of basophiloblasts. Judging from these findings, the authors are of the opinion that some modification seems to be in the offering as regard the Naegeli's myeloblast theory.

BIBLIOGRAPHY

1. ASTALDI, G., RONDANELLI, E.G. et BERNARDELLI, E. : Recherches cytochimiques sur la moelle osseuse et le sang d'une leucémie à basocytes, *Rev. Hémat.*, 8, 105—118, 1953.
2. CHEVALLIER, P., et MARINONE, G. : Sur un cas de leucémie myéloïde à basophiles, *Sang*, 18, 401—405, 1947.
3. ELLIOTT and YOUNG : Myelogenous leukaemia, *M. Clin. North America*, 15, 569, 1931.
4. GROAT, W.A., WYATT, T.C., ZIMMER, S.M. and FIELD, R.E. : Acute basophilic leukemia, *Amer. J. Med. Sci.*, 191, 457, 1936.
5. HIRAKI, K. et al : The method of tissue culture (mainly of the bone marrow) and a simple method of observing living tissue, *The Acta Medicinæ Okayama*, 10, 99—109, 1956.
6. HIRAKI, K. et al : Observation of various living blood cells by tissue culture of the bone marrow, *The Acta Medicinæ Okayama*, 10, 110—129, 1956.
7. HIRAKI, K. et al : Diagnosis of leukemia and aplastic anemia by the bone marrow culture, *The Acta Medicinæ Okayama*, 10, 130—150, 1956.
8. JOACHIM, G. : Über Mastzellenleukämien, *Dtsch. Arch. klin. Med.*, 87, 437, 1906.
9. LAZARUS : *Zit. n. Joachim.*, 1906.
10. MASSA e MARINONI : Rilievi su una forma rara di mielosi leucemica e piastrinemia con emoistioblasti in orientamento basofilo, *Clin. med. ital.*, 57, 487, 1926.
11. ORDWAY, GORHAM and BEEBE : Leukemia, *Oxford Medicine*, 2, 681, 1933.
12. SABRAZES : Présence d'hémohistiblastes se différenciant en mastzellen dans un cas de myélolécémie chronique, *Gaz. hebd. Soc. méd. Bordeaux*, 46, 628, 1925.
13. TINTI : Sui derivati istiodi nelle leucemie, *Riv. clin. Med.*, 27, 365, 1926.
14. TOMASZEWSKI : Über einen Fall von Mastzellenleukämie, *Fol. haem.*, 12, 115, 1911.
15. UNDRITZ, E. : *Sandoz Atlas of Hematol.*, 1953.
16. VASATURO : La mastzellenleucemia, *Studium*, 15, 172, 1925.