TECHNICAL REPORT
2-69
業 績 報 告 書

ACUTE GRANULOCYTIC LEUKEMIA TERMINATING IN ERYTHROBLASTIC PROLIFERATION, CASE-REPORT

末期に赤芽球増殖を呈した急性顆粒球性白血病症例報告

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ATOMIC BOMB CASUALTY COMMISSION

国立予防衛生研究所－原爆傷害調査委員会

JAPANESE NATIONAL INSTITUTE OF HEALTH OF THE MINISTRY OF HEALTH AND WELFARE

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Departments of Medicine[1] and Pathology[2]
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INTRODUCTION

It has been reported that marked proliferation of megaloblastoid cells in the bone marrow is occasionally observed during the course of acute leukemia. In such cases, the problem is whether or not these cases should be classified as erythroleukemia. In erythroleukemia, the disease generally and usually progresses through three phases, namely, erythremic, erythroleukemic, and leukemic, in that order.[1-3] The possibility of reverse progression from preponderant myeloblastic proliferation to dominant erythroblastic proliferation has been mentioned,[4] but case reports are rare. This report deals with a case with an initial picture compatible with acute granulocytic leukemia which terminated in erythroblastic crisis.

CASE REPORT

A 20-year-old day laborer (MF 475633) began to complain of general fatigue, vertigo and dyspnea on exertion in December 1960. Facial pallor was noted. He developed abdominal pain and underwent surgery for suspected appendicitis. Postoperative course was uneventful.

In February 1961, he had an episode of fainting while at work. He was found to be extremely anemic and given blood transfusions as well as hematinics without effective response. In mid-March 1961, he developed gingival and nasal bleeding. He was first seen as a referral patient (ME-Z) at the ABCC clinic on 4 April 1961.

His family history was noncontributory. He had had typhoid fever during childhood. He had been an occupational blood donor for 2 years and 2-4 liters of blood per year were drawn until 6 months before the onset (around August 1960). He was not in Hiroshima at the time of the atomic bomb and had no history of exposure to medical or industrial X-rays or chemicals.

Physical Examination The patient was a well developed and moderately well nourished male. Body weight was 52 kg, temperature 36.3 C, and pulse 84. Skin and visible mucous membrane were markedly pallid without icterus. Eye grounds were not remarkable. No petechiae, ecchy-

緒　言

急性白血病の経過中，時おり骨髄に著しい巨赤芽球性細胞の増殖をみることがある．このような場合，赤白血病との鑑別診断が問題となる．赤白血病は通常三つの時期，すなわち赤血性，赤白血性および白血性の順で経過するといわれる．[1-3] この逆の経過，すなわち骨髄芽球の増殖の著しい時期から赤芽球の増殖の優勢な時期へと移行する可能性も論じられているが，[4] 症例の報告はきわめて少ない．本報告は，発病時急性骨髄性白血病の病像を示し，末期に著しい赤芽球の増殖をみた症例に関するものである．

症　例

20歳の日雇い労務者（MF ＃475633），昭和35年12月全身倦怠，労作時めまいおよび呼吸困難を訴え始めた．顔面は蒼白となった．このころ腹痛があり，虫垂炎の疑いで外科手術を受けた．術後の回復は正常であった．

昭和36年２月作業中に，意識を喪失したことがあった．強度の貧血が認められ，輸血および増血剤の投与を受けたが効果は認められなかった．同年３月中旬歯齦出血，鼻出血があり，４月４日ABCC診察室で紹介患者（ME－Z）として初診を受けた．

家族歴に特記すべきものはなかった．少年のころ，腸チフスに罹患した．昭和33年ごろから２年間供血者として年間２－４１の売血をしており，発病半年くらい前まで続けていた．原爆時，広島にはおらず，医療用または工業用X線照射を受けたことも，また，化学薬品にさらされたこともない．

診察所見　体格・栄養ともに中等度で，体重52kg，体温36.3C，脈拍数84，皮膚および粘膜は著しく蒼白，黄疸はない．眼底に著変はない．点状出血，斑状出血またはリンパ腺腫脹などいずれも認めない．呼吸音は正常．心

moses, or lymphadenopathy were noted. The breath sounds were normal. Cardiac dullness was within normal range, although a systolic murmur of grade II/VI was heard at the apex. Neither the liver nor spleen was palpable. The recent appendectomy operation scar was noted in the right lower abdominal wall. The extremities were not remarkable and neurologic examination was negative.

Laboratory Findings Urinalysis and stool examination were negative. The red blood cell sedimentation rate was 8mm in 1 hour. The serologic reaction for syphilis was negative. Both direct and indirect Coombs' test gave no reaction. The serum total bilirubin was 1.2mg/100ml and direct bilirubin was 0.6mg/100ml. CCF test was 2+ and thymol turbidity test was 5.1. Alkaline phosphatase 4.12, serum GOT 50.0, GPT 74.2, and BSP retention was 9.5% in 30 minutes. The total serum protein was 6.6g/100ml with 3.8g albumin and 2.8g of globulin. Serum iron was 187μg/100ml. Chest X-ray was negative.

The hematologic findings at the first examination revealed marked anemia and a normal white blood cell count with appearance of myeloblasts and promyelocytes as shown in Table 1 and Figure 1. Aspirated bone marrow was hypercellular. As shown in Table 2, approximately half of the total nucleated cells were myeloblasts and promyelocytes with frequent presence of Auer rods. Erythroid cells showed a hypoplastic picture with slight maturation disturbance. Megakaryocytes, both mature and immature forms, were markedly increased in number and mature forms showed excessive platelet production (Figure 2).

Clinical Course The patient was immediately treated with 6MP 100mg and prednisone 50mg daily (Figure 3). In approximately 2 months, the immature myeloid cells disappeared from the peripheral blood and the patient's general condition improved although anemia persisted and he gradually developed thrombocytopenia. Then, 6MP was discontinued and prednisone was tapered downwards. Four months after initiation of the therapy, myeloblasts again appeared in the peripheral blood. Bone marrow study then revealed a marked increase of myeloblasts which had large nuclei containing very fine chromatin network. These cells were thought to be more immature than those on admission (Table 2, Figure 4). Prednisone was increased to 100mg daily combined with 50 to 125mg of 6MP daily. This was followed by a marked increase in platelets and disappearance of myeloblasts from the peripheral blood. Because of persistent severe anemia he was given blood transfusions also for the following 3 months. Anemia and thrombocytopenia improved rapidly with a good remission as indicated by return to a normal value of the red blood cell count and hemoglobin.

尖部に第Ⅱ度／第Ⅵ度の収縮期雑音を聴取するが，心濁音界は正常．肝脾はともに触れない．右下腹部に新しい虫垂切除術痕を認める．四肢に著変なく，神経学的検査に異常を認めない．

臨床検査所見 検尿および検便に異常を認めない．血沈値は1時間8mm．血清梅毒反応は陰性，Coombs 直接および間接試験はともに陰性．肝機能検査では総ビリルビン値1.2mg／100ml，直接ビリルビン値0.6mg／100ml，CCF（＋），チモール混濁5.1．アルカリフォスファターゼ4.12，血清GOT 50.0，GPT 74.2，およびBSP 30分値9.5%．血清総蛋白量は6.6g／100ml，アルブミン値3.8g／100ml，グロブリン値2.8g／100ml，血清鉄187μg／100mlであった．胸部X線検査で異常を認めなかった．

初診における血液学的所見では，表1および図1に示すように著しい貧血があり，白血球数は正常で，骨髄芽球および前骨髄球の出現を認めた．骨髄像では有核細胞がきわめて多く，表2に示すようにその約半数が骨髄芽球と前骨髄球で占められ，Auer 小体も多数認められた．赤血球系細胞では軽度の成熟障害を伴う低形成像があり，巨核球は，成熟型および幼若型ともにその数が著明に増加し，成熟型では過形成像がみられた（図2）．

臨床経過 ただちに6MP 100mgとプレドニソン50mg各1日量の投与を行なった（図3）．約2か月後に末梢血液から幼若骨髄細胞が消失した．患者の一般症状は好転したが，貧血は持続し，またしだいに血小板数が減少してきたので，6MPを中止しプレドニソンを漸減した．治療を開始してから約4か月後再び末梢血液に骨髄芽球が出現した．その時の骨髄検査で，骨髄芽球が著しく増加し，この芽球にはきわめて繊細な染色質を有する大型の核網が認められ，初診時のものに比較してさらに幼若のようであった（表2，図4）．プレドニソンを1日量100mgに増量し，6MP 1日量50－125mgを併用した．この結果，血小板数は著しく増加し，骨髄芽球は末梢血より消失した．強度の持続性貧血があるので，その後3か月間輸血も行なった．貧血および血小板減少症は急速に回復し，赤血球数やヘモグロビン値は正常に達し寛解にはいった．

TABLE 1 PERIPHERAL BLOOD PICTURE

表 1　末梢血液像

		1961			1962	
		4 April 4月	29 May 5月	7 September 9月	8 January 1月	1 May 5月
RBC	赤血球	1.47	2.01	2.41	4.89	2.50
Hgb	血色素	4.4	5.4	6.4	15.7	6.9
MCHC	平均血球血色素濃度	29.9	26.9	26.6	32.1	27.6
Retic.	網状赤血球	0.1%	0	0	2.3	1.6
Plate.	血小板	197.5		162.5	102.5	10.0
WBC	白血球	5.350	5.350	8.400	4.800	2.100
Diff. Count	白血球分類像					
Myeloblast	骨髄芽球	16.5%				2
Promyelocyte	前骨髄球	3.5				7
N-Myelocyte	N一骨髄球					6
N-Metamyelocyte	N一後骨髄球					4
N-Band.	桿状好中球	0.5		1.0	2.0	4
N-Seg.	分葉好中球	47.5	69.0	66.0	69.0	34
Eosinophil.	好酸球	0				
Basophil.	好塩基球	0.5				
Monocyte	単球	3.5	1.0	1.0	3.0	9
Lymphocyte	リンパ球	28.0	30.0	18.0	24.0	33
Proerythroblast	前赤芽球					36/100 WBC
Erythroblast baso.	赤芽球，好塩基性					11/100 WBC
poly.	多染性					5/100 WBC
Normo.	正染性					42/100 WBC

TABLE 2 BONE MARROW PICTURE

表 2　骨髄像

		1961		1962
		4 April 4月	27 July 7月	1 May 5月
Myeloblast	骨髄芽球	26.8%	30.0	0
Promyelocyte	前骨髄球	28.8	10.0	0.4
N-Myelocyte	N一骨髄球	6.8	22.4	3.2
N-Metamyelocyte	N一後骨髄球	3.2	4.4	0.8
N-Stab.	桿状好中球	8.4	4.8	1.2
N-Seg.	分葉好中球	10.4	4.0	2.0
Eosinophil.	好酸球	0	0	0
Basophil.	好塩基球	0	0	0
Monocyte	単球	0.4	0.4	0.4
Lymphocyte	リンパ球	7.6	15.6	4.8
Plasma cell	形質球	0.4	1.2	0.4
Reticulum cell	細網球	0	0.4	1.2
Megakaryocyte	巨核球	(+)	(+++)	(−)
Mitosis	有糸分裂	0	0.4	1.2
Proerythroblast	前赤芽球	0.4	0	52.4
Macro baso.	大赤血球好塩基性	1.2	1.2	6.4
poly.	多染性	0.4	0.8	7.2
Normo.	正染性	0.4	0	2.0
Normo baso.	正常赤血球,好塩基性	0.8	2.0	1.6
poly.	多染性	3.6	2.4	8.0
Normo.	正染性	0.4	0.8	8.0

FIGURE 1 MYELOBLASTS IN THE PERIPHERAL BLOOD SMEAR, 4 APRIL 1961
図 1　末梢血塗抹標本における骨髄芽球（1961年 4 月 4 日）

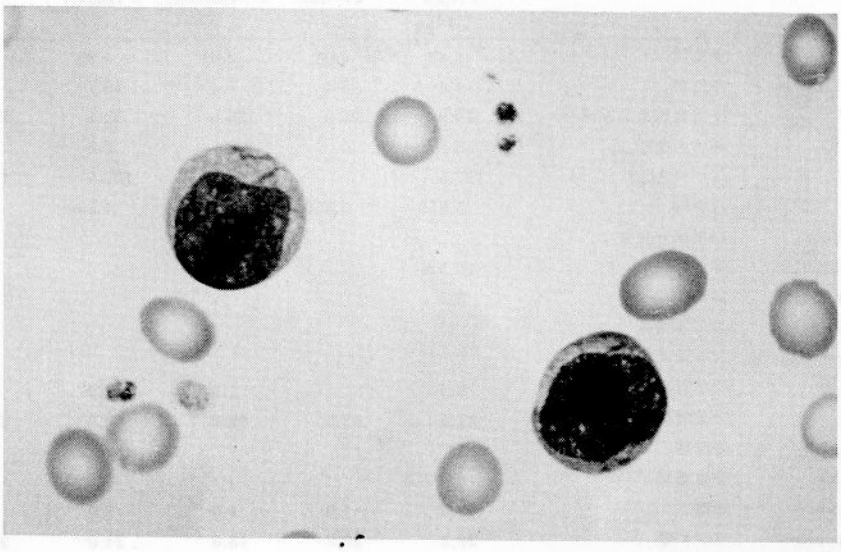


FIGURE 2 BONE MARROW SMEAR, 4 APRIL 1961
図 2　骨髄液塗抹標本（1961年 4 月 4 日）

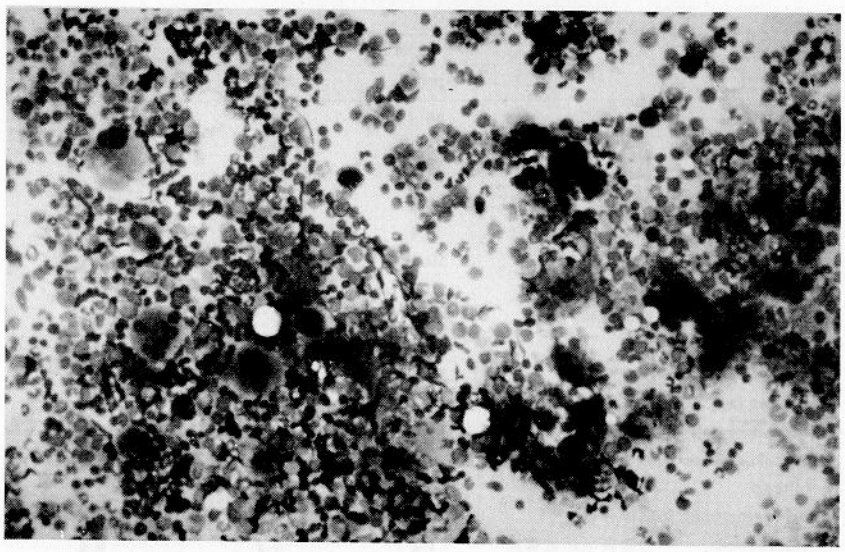


FIGURE 3 CLINICAL COURSE
図3　臨床経過

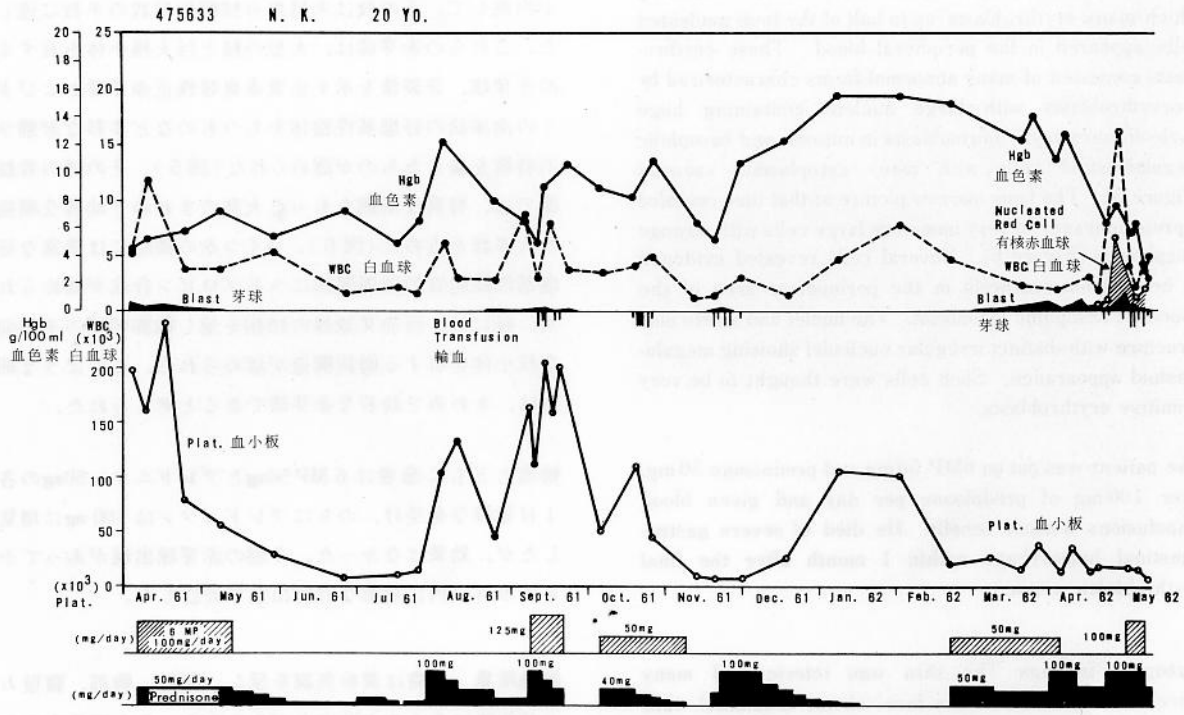
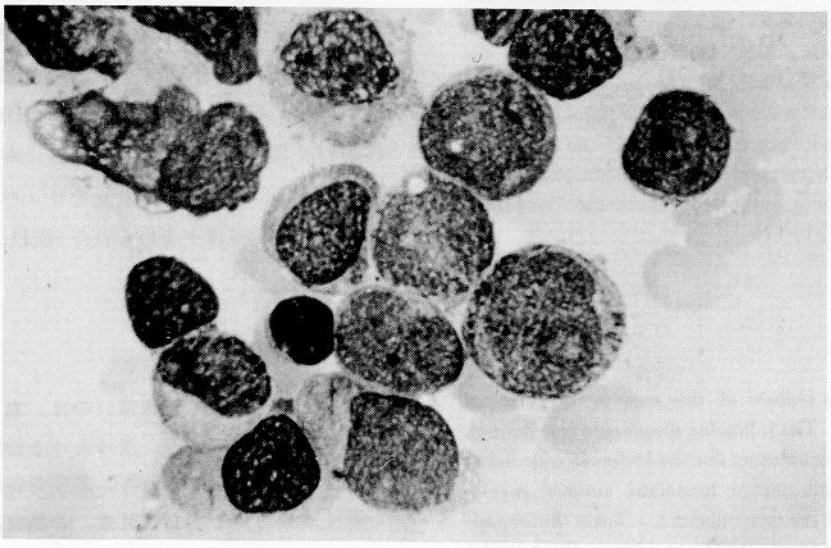


FIGURE 4 BONE MARROW SMEAR, 27 JULY 1961
図4　骨髄液塗抹標本（1961年7月27日）



A year after hospitalization, relapse was noted, with reappearance of myeloblasts in the peripheral blood. Anemia became progressively more severe following which many erythroblasts (up to half of the total nucleated cells) appeared in the peripheral blood. These erythroblasts consisted of many abnormal forms characterized by proerythroblasts with large nucleus containing huge nucleoli, normocytic normoblasts in mitosis, and basophilic megaloblastoid cells with many cytoplasmic vacuolei (Figure 5). The bone marrow picture at that time revealed a preponderance of very immature large cells with strange morphology (Figure 6). Several cells revealed evidence of hemoglobin synthesis in the perinuclear area of the abundant basophilic cytoplasm. The nuclei had a reticular structure with distinct irregular nucleolei showing megaloblastoid appearance. Such cells were thought to be very primitive erythroblasts.

The patient was put on 6MP 50 mg and prednisone 50 mg, later 100 mg of prednisone per day and given blood transfusions without benefit. He died of severe gastrointestinal hemorrhage within 1 month after the final erythroblastic crisis.

Autopsy Findings The skin was icteric and many petechiae were seen on the face, chest, abdominal wall, and extremities. The bone marrow of the mid-portion of the left femur was cloudy reddish brown and slightly firm. The bone marrow of ribs, sternum, and vertebra was reddish brown. The histology sections of bone marrow showed moderate diffuse proliferation of erythroid and myeloid cells with several megakaryocytes (Figure 7, 8). The spleen weighed 700 g, leukemic cells filled the sinusoids and the lymphoid follicles were atrophic (Figure 9). The liver was also enlarged and weighed 2100 g. Leukemic infiltrations were chiefly seen in the periportal areas (Figure 10). Lymph nodes and the kidneys, each of which weighed 250 g, showed moderate leukemic infiltration (Figures 11, 12).

DISCUSSION

The most interesting feature of this case is the terminal erythroblastic crisis. The following diagnostic possibilities must be considered: acute granulocytic leukemia associated with pernicious anemia and/or hemolytic anemia, myelophthisic anemia, and erythroleukemia. Since the examinations of the erythroblasts were not done in this case by means of phase-contrast microscopy, PAS stain, and chromosome analysis, differential diagnosis depended chiefly on the morphological features of the blasts with ordinary Romanowsky's stain.

入院1年後に再燃をみて，末梢血に骨髄芽球が再び出現した．貧血が漸次悪化し，続いて末梢血に多数の赤芽球が出現して，その数は末梢血有核細胞総数の半数に達した．これらの赤芽球は，大型の核と巨大核小体を有する前赤芽球，分裂像を示す正常赤血球性正赤芽球および多くの泡沫状の好塩基性胞体をもつものなど多彩な形態学的特徴を備えたものが認められた（図5）．その時の骨髄像では，特異な形態をもった大型のきわめて幼若な細胞が大多数を占めた（図6）．いくつかの細胞には豊富な好塩基性細胞質の核周囲部にヘモグロビン合成が認められた．核には，巨赤芽球様の様相を呈し輪郭明瞭の不規則な核小体を有する網状構造が認められた．このような細胞は，きわめて幼若な赤芽球であると考えられた．

輸血とともに患者は6 MP 50mgとプレドニソン50mgの各1日量投与を受け，のちにプレドニソンは100 mgに増量したが，効果はなかった．今回の赤芽球出現があってから1ヵ月以内に重篤な胃腸出血で死亡した．

剖検所見 皮膚は黄疸色調を呈し，顔面，胸部，腹壁および四肢に多くの点状出血がみられた．左大腿骨中央部の骨髄は，濁った赤褐色で，やや堅かった．肋骨，胸骨および脊椎の骨髄は，赤褐色であった．骨髄組織標本では，赤芽球および骨髄芽球の中等度の瀰漫性増殖と数個の巨核球が認められた（図7，8）．脾臓は重量700 gで，洞は白血性細胞で充満され，リンパ濾胞の委縮がみられた（図9）．肝臓も肥大し，重量は2100 gであった．白血性細胞浸潤は主として門脈周囲部にみられた（図10）．両腎臓の重量はそれぞれ250 gでリンパ節とともにかなりの白血性細胞浸潤が認められた（図11，12）．

考　察

本症例において最も興味深いのは，末期における異常な赤芽球系の増殖である．次にあげる診断の可能性を考慮する必要がある．すなわち，急性骨髄性白血病と合併した悪性貧血ないし溶血性貧血，骨髄癆性貧血および赤白血病が考えられる．位相差顕微鏡検査，PAS染色および染色体検査を行なっていないので，鑑別診断は，主として通常のロマノウスキー染色法によるこれらの赤芽球の形態学的特徴に依存した．

FIGURE 5 PERIPHERAL BLOOD SMEAR SHOWING VARIOUS ERYTHROBLASTS, 1 MAY 1962

図5　末梢血塗抹標本における各種赤芽球（1962年5月1日）

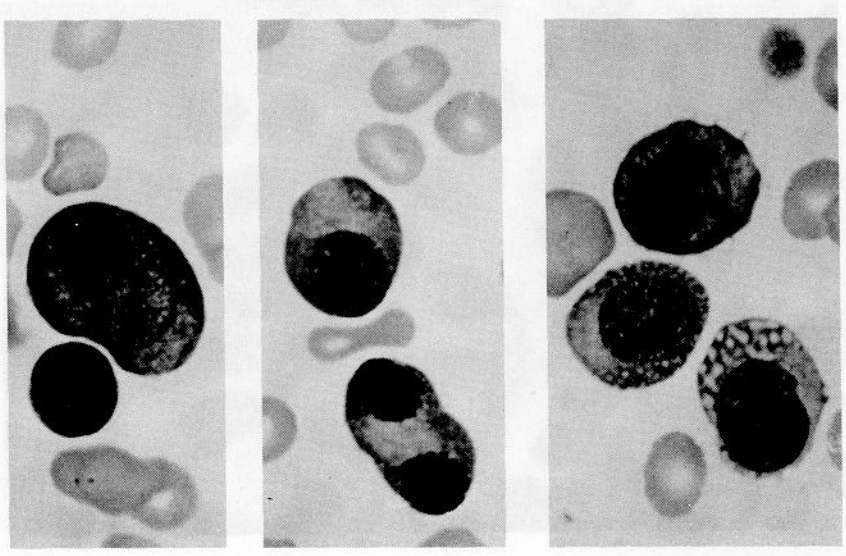


FIGURE 6 BONE MARROW SMEAR SHOWING EXCESSIVE ERYTHROBLASTIC PROLIFERATION, 1 MAY 1962

図6　顕著な赤芽球増殖を示す骨髄液塗抹標本（1962年5月1日）

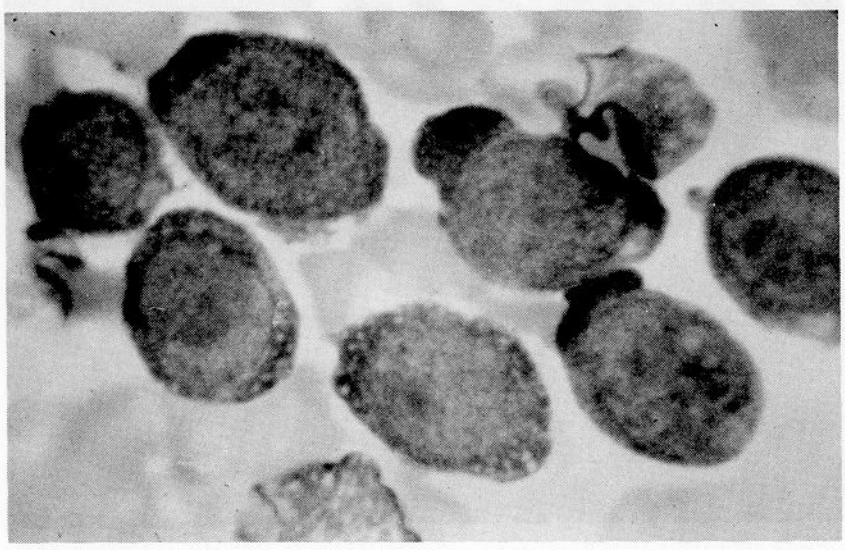


FIGURE 7 BONE MARROW
図 7　骨髄

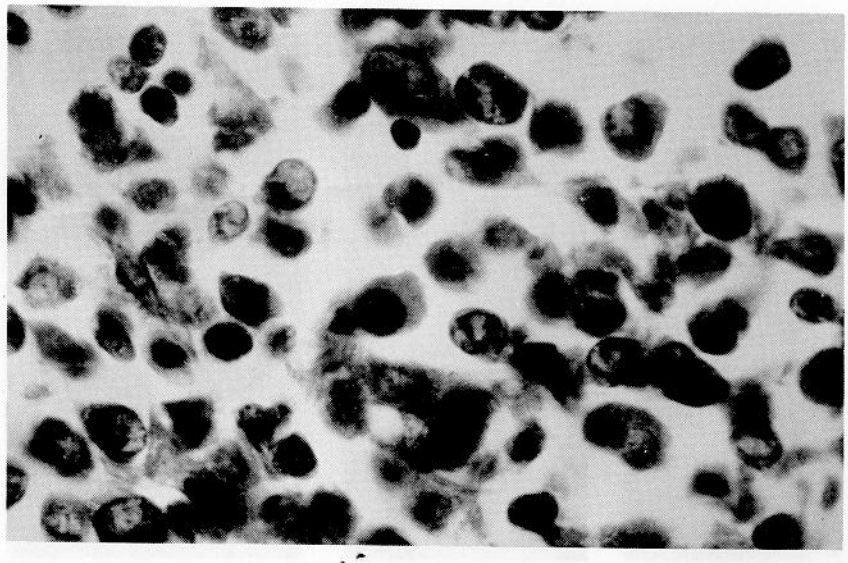


FIGURE 8 BONE MARROW
図 8　骨髄

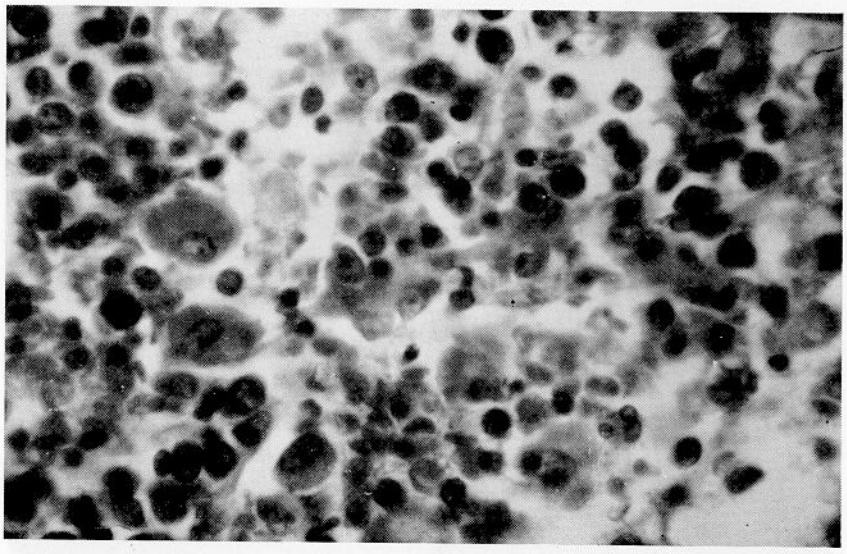


FIGURE 9 SPLEEN
図 9　脾臓

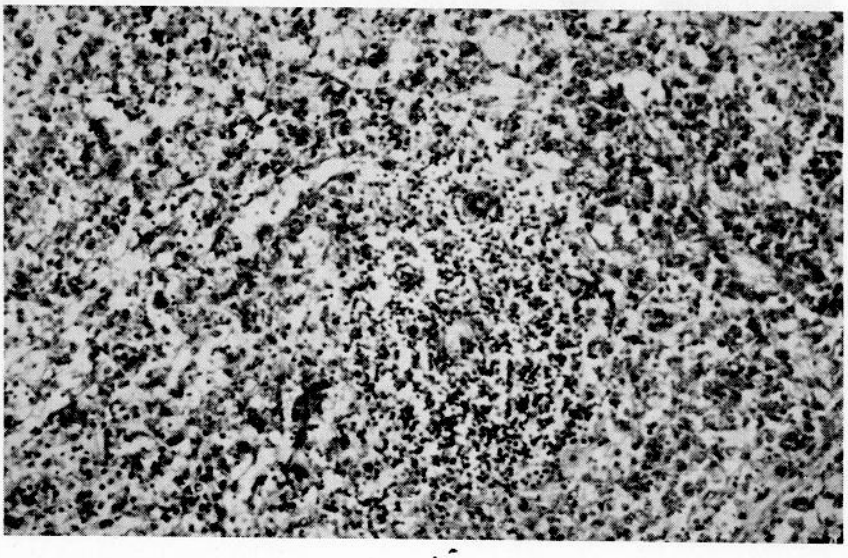


FIGURE 10 LIVER
図10　肝臓

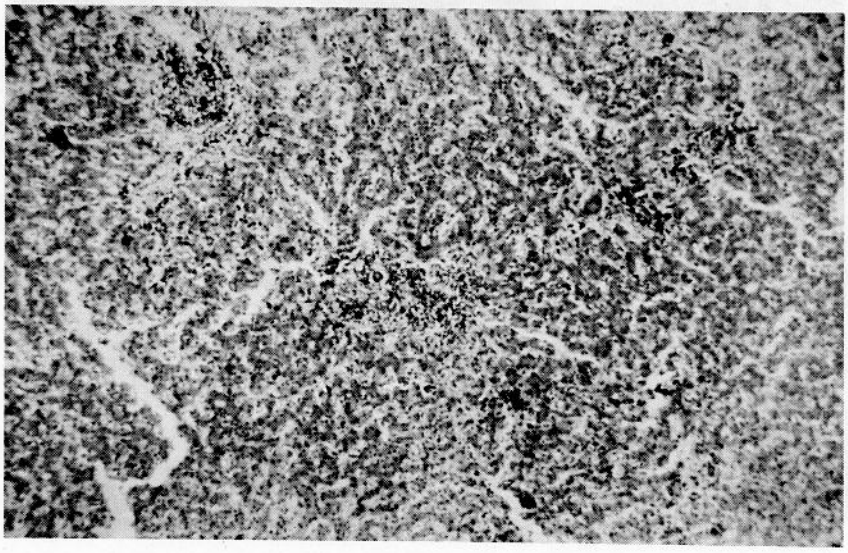


FIGURE 11 LYMPH NODE
図11　リンパ節

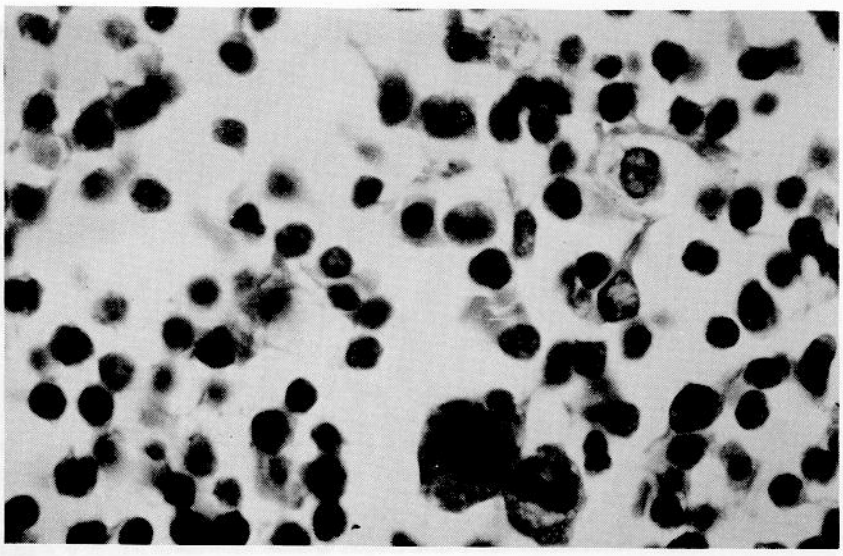
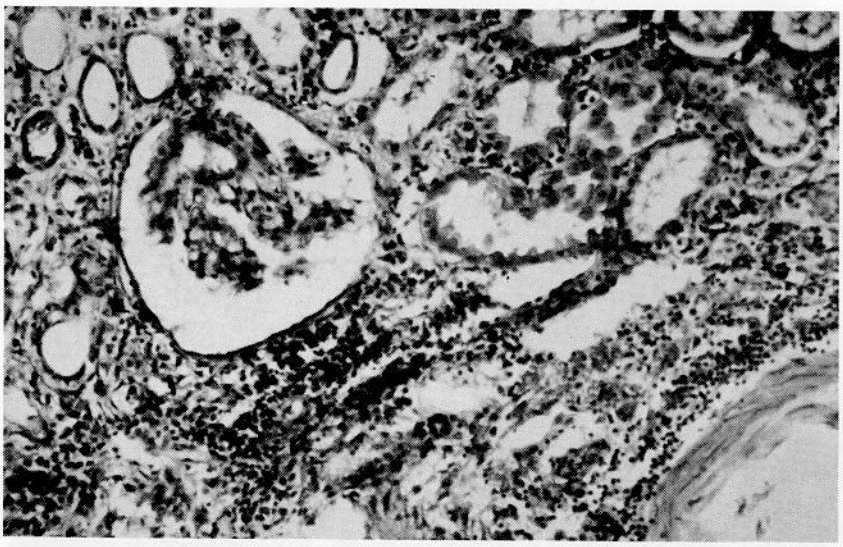


FIGURE 12 KIDNEY
図12　腎臓



Pernicious anemia associated with acute granulocytic leukemia is ruled out because hematological data revealed hypo- or normochromic anemia and none of the clinical symptoms usually attributable to pernicious anemia were noticed throughout the course. Hemolytic anemia associated with acute granulocytic leukemia is also ruled out because of the atypical appearance of the erythroblasts and a negative Coombs' test. In this case serum bilirubin, both direct and indirect, increased in the terminal stage, but reticulocyte counts remained less than 2.3% throughout his course and even in the terminal stage were 1.6%. The elevated serum bilirubin is therefore considered to represent exacerbation of the liver damage which had been found at the first examination. Since no tumor cells were seen in the bone marrow specimen and no primary or metastatic focus was apparent on clinical and pathological examinations, the possibility of metastasis of malignant tumor into bone marrow tissue is excluded.

As to the diagnostic criteria of erythremia and erythroleukemia, Komiya [5] and Kawakita [6] pointed out the following features: marked proliferation of erythroblasts, especially the appearance of megaloblastoid cells in the bone marrow and peripheral blood; morbid findings such as presence of ultramacrocytic erythroblast, hiatus erythremics, or pycnosis in erythroblasts; positive PAS reaction of erythroblasts; and hematologic findings characterized by acute or subacute leukemia. All of these, except the PAS reaction, were found in the terminal stage in this case. Furthermore, infiltration of basophilic erythroblasts and myeloblasts in various organs observed in the histological specimens suggest excessive proliferation of the erythroid series along with that of the myeloid series. According to Hashimoto, [7] among 38 cases of acute granulocytic leukemia, marked proliferation of the erythroblasts was observed in 6 cases, and this phenomenon was noted in accordance with one of the following: association of acquired hemolytic anemia; recovery from anemia at remission produced by antileukemic agents; and early phase from the onset of leukemia. However none of these is apparently applicable in this case as the cause of the erythroblastic proliferation. It seems justifiable, then, to consider that this case is an example of erythroleukemic change in the terminal phase following an initial leukemic phase.

It has been recognized that in cases of erythremia or erythroleukemia hematological findings have no consistency through the course. At one time, preponderant erythroblastic proliferation and at other times dominant myeloblastic proliferation have been observed by many investigators. [5,6,8,9] Di Guglielmo [4] mentioned that there might be various courses in a case with acute erythremia, i.e. purely erythremic course, initially erythroleukemic followed by terminal leukemic course, and possibly reverse

全経過を通じて，血液学的検査で低または正色素性貧血を認めたこと，および悪性貧血に通常起因する臨床症状が一つもみられなかったことなどから急性骨髄性白血病と悪性貧血の合併は否定できる．溶血性貧血も，赤芽球が異型性を呈したことと Coombs 試験が陰性であったことから否定しうる．本症例では，末期に直接および間接ビリルビン値の上昇をみたが，網状赤血球は全経過を通じて 2.3％以下にとどまり，末期でも 1.6％にすぎなかった．したがって，血清ビリルビン値の上昇は初診時にみられた肝障害の悪化を示すものと考えられる．悪性腫瘍の骨髄転移については，骨髄標本に腫瘍細胞がみられなかったこと，臨床的にも剖検においても原発巣や転移巣を認めなかったことから否定できる．

赤血病や赤白血病の診断について小宮，[5] 河北 [6] は次の特徴を指摘している．(1) 骨髄または末梢血に赤芽球の異常増殖を認め，特に巨赤芽球様細胞を認めること，(2) 超大赤芽球，赤血病裂孔，核型異常等の病的所見のあること，(3) PAS 反応が陽性であること，(4) 急性または亜急性白血病の所見があることなどをあげている．本症例の末期には PAS 反応を除いたこれらの特徴が認められた．さらに，各臓器の組織学的標本において観察された好塩基性赤芽球および骨髄芽球の浸潤は，骨髄系細胞の増殖とともに赤血球系細胞の過度の増殖を示唆する．橋本 [7] によれば，急性骨髄性白血病38例のうち，6例に著明な赤芽球の増殖を認め，この現象は次のいずれかに一致して起こっていたと述べている．すなわち，後天性溶血性貧血との合併，抗白血病剤による寛解期における貧血の回復時，または白血病発病の初期である．しかし，本症例では，赤芽球増殖の原因としては，これらのいずれにも該当しない．したがって，本症例は，初期には白血性を呈し，それに続いて末期に赤白血性の変化を起こした1例であると考えることが妥当であろう．

赤血病や赤白血病では血液像がその全経過を通じて一様でないことは知られている．ある時には赤芽球系細胞の増殖が優勢で，また別の時には骨髄芽球系細胞の増殖が優勢となることが，多くの研究者によって観察されている．[5,6,8,9] Di Guglielmo [4] は，急性赤血病の経過は終始赤血性の場合もあり，また赤白血病像を経て末期に白血病像に移行するものもあり，その逆もありうるという．

progression. However the reverse progression beginning with a leukemic picture and terminating in erythroleukemic as seen in this case is rare.[10] Scott et al reported a case with erythroleukemia following chronic myelocytic leukemia,[11] but no such case has yet been reported in Japan. Dameshek[1,3] had classified erythremia among the polyphasic myeloproliferative diseases and emphasized that the disease usually goes through three successive stages, namely in the order of erythremic myelosis, erythroleukemia, and acute myeloblastic leukemia.

In this case, further interesting findings, not usually observed during the clinical course of acute granulocytic leukemia, were recorded. At the first examination marked hyperplasia of megakaryocytes was noted in the bone marrow smear along with leukemic proliferation of the granulocytes. The platelet count was as high as 200,000/mm^3 at the first examination and remained at higher levels than in usual untreated acute leukemia, in contrast to extreme associated anemia. These facts may suggest involvement of megakaryocytic series as a part of myeloproliferative disorder. Furthermore, prior to the abnormal erythroblastic crisis of the terminal relapse, the previously persistent anemia recovered rapidly without transfusion and both the RBC count and hemoglobin content became completely normal. This suggests the presence of erythroid hyperplasia at that stage although the evidence was not proved by bone marrow examination. Komiya[9] described occurrence of occasional initial polyglobulia, "Polycythemische Phase" persisting transiently in early stage of acute or subacute erythremia. These findings observed in our case support the possibilities that the myeloid, erythroid, and megakaryocytic series had the unusual proliferating processes independently or in combination during the course of his disease. Administration of antileukemic agents and transfusions may have influenced the occurrence and the pattern of their proliferations.

Transfiguration of hematological pictures in leukemia, blastic crisis in chronic granulocytic leukemia and acute erythremia or leukemia from polycythemia vera have been well recognized, but interpretation of mechanisms responsible for these changes remains unsettled. It has been postulated that there is present most primitive hemocytes, hemocytoblasts, as the precursor of all blood cell elements and that malignant proliferation of these cell lines will produce either erythremia, erythroleukemia, or leukemia depending on the direction of its differentiation. However such a concept has not yet been universally accepted. If this concept is applicable to the transfiguration in erythroleukemia, the progression from a leukemic picture to an erythremic picture and the reverse should be observed with equal frequency, but as stated above a rare report has been published describing cases which showed the

しかし逆の場合，すなわち，本症例にみられたように白血性で発症し，末期に赤白血性を示す例は非常にまれである．[10] Scottら[11]は慢性骨髄性白血病でのちに赤白血病になった症例を報告しているが，このような症例は，日本ではまだ報告されていない．Dameshek[1,3]は赤血病を多相性骨髄増殖疾患（polyphasic myeloproliferative disease）の一つと考え，通常三つの段階，すなわち，赤血病性骨髄症，赤白血病を経て急性骨髄芽球性白血病へ移行すると述べている．

本症例においては，急性骨髄性白血病の臨床経過中には普通みられない興味ある所見が記録された．初診時に顆粒球の白血病性増殖とともに骨髄液塗抹標本に巨核球系細胞が著明に増殖していた．また，初診時の血小板数が約20万で未治療の急性白血病としては貧血が高度であった割りによく保たれていた．したがって，巨核球系も骨髄増殖疾患（myeloproliferative disorder）の一端を示すものとも考えられる．さらに，赤芽球が末期の再発で異常増殖をきたす前に，以前から続いていた貧血が輸血なしで急速に回復し，赤血球数と血色素量はまったく正常となった．このことは骨髄像で確かめていないが，この段階では赤血球系の過形成が起こったものと考えられる．小宮[9]によれば急性または亜急性赤血病の初期に，しばらくの間赤血球増多期"Polycythemische Phase"を認めることがあるという．本症例でこれらの所見について観察した結果，骨髄球系，赤血球系および巨核球系の細胞が経過中に単独にまたは組み合わさって異常増殖を示したものと解される．抗白血病剤の投与や輸血が各血球系の増殖の発生および形式に影響を与えたかもしれない．

白血病の血液像の変化については，慢性骨髄性白血病の急性転化を初め，真性多血球血症から急性赤血病へ，または白血病への変化等がよく知られている．しかし，その機序については定説がない．各血球系の最も幼若な血球細胞を，各血球要素の前駆細胞，すなわちhemocytoblastとして想定し，これらの血球系が悪性増殖をした場合，分化の方向により赤血病，赤白血病または白血病のいずれにもなりうると説明するものもある．しかし，このような考え方は，広く支持されるには至っていない．もしこの想定を赤白血病の変化に適用するならば，白血病像から赤血病像への変化と，その逆の変化は同じ頻度で起こるはずであるが，すでに述べたように白血病像から赤白

change from leukemic to erythroleukemic or erythremic stages. Further intensive studies are necessary in order to clarify the interrelationship of all blood cell lines and their tumorigenesis. The present case raises many interesting and provocative problems.

SUMMARY

A case of acute granulocytic leukemia in a 20-year-old male terminating in excessive erythroblastic proliferation is reported. The diagnostic problems, usual progression of the course of disease and interrelationship of hemic precursors concerning their tumorigenesis and transfiguration observed in this case are discussed in detail.

血病または赤血病像への変化を示した症例の報告はまれである．各血球系と腫瘍発生との相互関係を明確にするためには，さらに徹底的に研究を行なう必要がある．本症例は，多くの興味深い，かつ示唆に富む問題を提起する．

要　約

急性骨髄性白血病を発病し，末期に異常な赤芽球増殖を呈した20歳男性の症例を報告した．診断上の問題点，本疾患の通常の経過ならびに血球前駆細胞とその腫瘍性と病像の関係について詳細に検討した．

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