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A CASE OF 45, X, −Y, Ph[1] CHRONIC GRANULOCYTIC LEUKEMIA IN AN ATOMIC BOMB SURVIVOR AND A REVIEW OF THE LITERATURE

被爆者にみられた45, X, −Y, Ph[1] 慢性骨髄性白血病の一例とその文献的考察

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RADIATION EFFECTS RESEARCH FOUNDATION
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臨床血液 Rinsho Ketsueki - Jpn J Clin Hematol 19:139-46, 1978

放影研 RADIATION EFFECTS RESEARCH FOUNDATION
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SUMMARY

A case of 45, X, −Y, Ph[1] chronic granulocytic leukemia (CGL) in an atomic bomb survivor is reported and 41 other cases reported in Japan and elsewhere are reviewed. Our subject is a 60-year-old male. His seven children are in good health. The individual was exposed to the atomic bomb approximately 3000 m from the hypocenter, and he has been undergoing biennial examination at RERF since 1960. Leukocytosis and appearance of immature granulocytes were noted at the time of his examination in August 1975. In November 1975, hyperplasia of the granulocyte series was demonstrated on bone marrow. The chromosome examination presented 45, X, −Y, Ph[1] karyotype, and CGL was diagnosed. At present, 19 months after the diagnosis was established his course is satisfactory and there are no findings suggestive of blast crisis.

For these cases the survival time does not differ from that of CGL in general. Neutrophil alkaline phosphatase activity and clonal evolution are considered to be points which need to be studied on a larger number of cases in the future.

INTRODUCTION

A few score of cases of CGL with missing Y chromosome have been reported in Japan and elsewhere since this was first reported in 1962,[1] and cytogenetically it is regarded as a subgroup of CGL. Clinically, however, it is questionable whether such a CGL could be a subgroup. We have observed a case of CGL with missing Y

要 約

被爆者にみられた45, X, −Y, Ph[1] 慢性骨髄性白血病(CGL)の一例を報告し，あわせて国内外の41例について検討した．我々の症例は60歳男性，子供7人健在．約3,000m の地点で被爆し，放影研では1960年より2年に1回定期検診を受けている．1975年8月の検診時に白血球増多，幼若顆粒球の出現を認め，同年11月の骨髄穿刺で顆粒球系の過形成と，染色体検査で45, X, −Y, Ph[1] の核型を示し，CGL と診断した．確定診断より19か月後の現在経過良好で急性転化を思わせる所見は認めない．

これらの42例の生存期間は一般の CGL と変わらなかった．好中球アルカリフォスファターゼ活性，clonal evolution などは今後症例を重ねて検討すべき点と考えられた．

はじめに

Y染色体を欠失した慢性骨髄性白血病(CGL)は，1962年に初めて報告されて[1]以来，国内外で数十例の報告がなされ，細胞遺伝学的には CGL の subgroup とされている．しかし，臨床的にはこのような CGL が subgroup となり得るか否かは問題のあるところである．我々はY染色体の欠失した被爆者 CGL の1例

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chromosome in an A-bomb survivor, which is presented here with a review of the literature.

CASE REPORT

Patient. Male aged 60, MF [redacted]

Medical History. The individual has been examined here biennially since 1960, but except for the finding of anemia (hemoglobin: 10-11g/100ml) in 1965, 1969, and 1973, his condition has been unremarkable. White blood cells (WBC) were increased to a count of 28,100 and immature granulocytes, from promyelocytes to metamyelocytes, appeared at the time of his examination in August 1975 and CGL was suspected (Table 1). The diagnosis of CGL was made because a bone marrow puncture performed in November 1975 (Table 1) showed hyperplasia of the granulocyte series, the ratio to the erythroid series being 6:1 in the May-Giemsa stain specimen, and chromosome examination showed 45, X, −Y, Ph^1 karyotype in all cells which were examined. At this time, the spleen was palpated two fingerbreadths; the peripheral blood showed a red blood cell count

を経験したので症例を提示し，文献的考察を行う．

症　例

患者． 60歳，男性，MF No. [redacted]

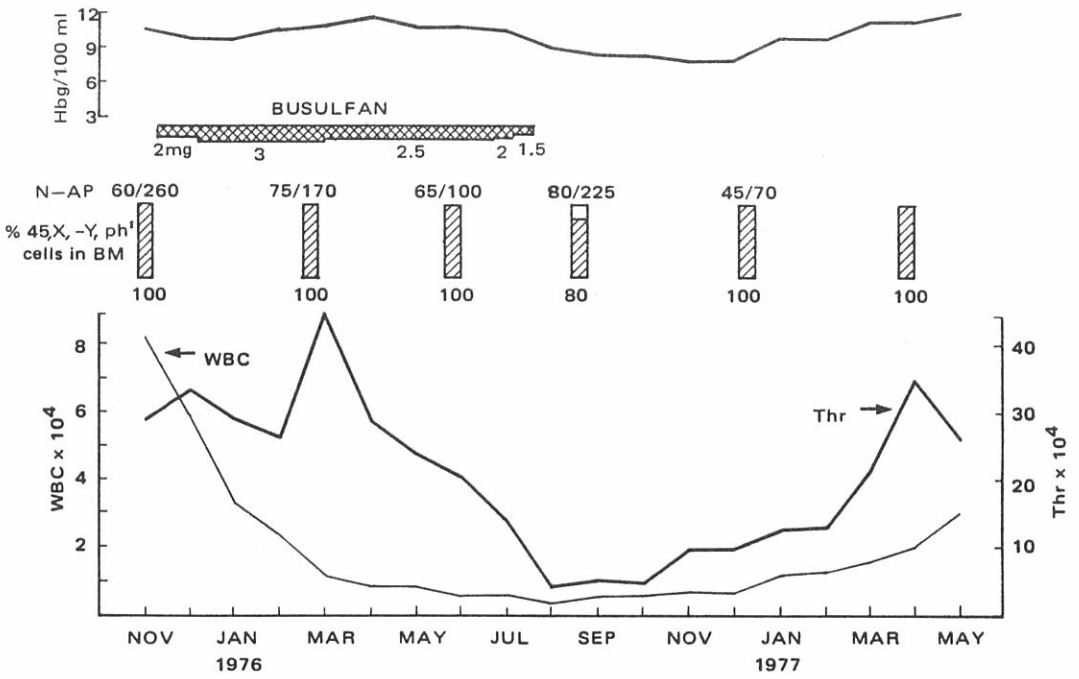
病歴． 放影研では1960年から２年に１回の周期で定期検診を受けているが，1965年，1969年，1973年に貧血（ヘモグロビン10—11ｇ／100ml台）を指摘された以外には特記すべきことはなかった．1975年８月の検診時に白血球数が28,100と増加しており，前骨髄球から後骨髄球までの幼若顆粒球が出現し，CGLが疑われた（表１）．1975年11月に骨髄穿刺を行い（表１），メイ・ギムザ標本で顆粒球系対赤芽球系の比が６：１と顆粒球系の過形成を示し，染色体検査で45，X，−Y，Ph^1 の核型を100％の細胞に認めたためCGLと診断した．なお，このとき脾臓は２横指触知し，末梢血所見は赤血球数348×10^4，ヘモグロビン

TABLE 1 HEMATOLOGICAL DATA

表１　血液学的所見

	28 Aug. 1975	24 Nov. 1975	15 Mar. 1976	21 June 1976	13 Sept. 1976	10 Jan. 1977	18 Apr. 1977
Peripheral Blood							
WBC	28,100	83,500	19,250	5,300	4,000	11,900	20,700
RBC	370	348	394	407	290	367	390
Hb.	11.0	10.8	10.9	10.9	8.6	10.0	11.2
Thr.	250,000	295,000	375,000	205,000	50,000	125,000	352,500
St.	4.0	9.5	2.0	0.0	0.5	0.0	5.0
Seg.	46.0	44.5	44.5	47.0	47.5	44.0	33.0
Ly.	21.0	10.5	20.0	27.5	33.0	33.0	21.0
Mo.	4.0	7.0	16.0	18.0	11.0	15.0	14.0
Eo.	2.5	1.5	2.0	2.5	1.5	1.0	2.0
Ba.	1.0	2.0	7.0	3.0	1.5	1.0	3.0
M.B.	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Pro.	11.0	1.5	0.0	0.0	0.0	0.0	1.0
My.	13.0	12.5	5.0	1.5	0.5	2.0	7.0
Met.	7.5	11.0	3.5	0.5	4.5	4.0	14.0
E.Bl.	0.5	0.0	0.0	0.0	0.0	0.0	0.0
N-AP	-	60/260	75/170	65/100	80/225	45/70	
Bone-Marrow							
N.C.C.	-	-	-	137,400	20,500	80,800	582,000
Mgk.	-	-	-	0	0	0	100
M.B.	-	0.2	0	0	0.5	0	0.5
G:E	-	6:1	11.3:1	7.3:1	1.2:1	4.7:1	14.2:1

FIGURE 1 CLINICAL COURSE
図1　臨床経過



(RBC) of 348 × 10^4, hemoglobin 10.8g/100ml, hematocrit 33.5%, platelet count 295,000, WBC 83,500 (differential: promyelocytes 1.5, myelocytes 12.5, metamyelocytes 11.0, band cells 9.5, segmented cells 44.5, lymphocytes 10.5, monocytes 7.0, eosinophils 1.5, basophils 2.0); and neutrophil alkaline phosphatase (N-AP) was normal with a rate of 60 and a score of 260, showing no abnormally low values which are regarded as characteristic of CGL.

Course. Administration of 2 mg of busulfan was commenced on 8 December 1975 under the diagnosis of CGL, but the WBC count did not decrease as expected. The dosage was therefore increased to 3 mg from 5 January 1976, and this brought about satisfactory decrease and the spleen was no longer palpable on 16 February. Administration of busulfan was discontinued on 12 August 1976 and his course is being followed subsequently without medication. At present, 21 months after the estimated date of onset and 19 months after establishment of the diagnosis, his course is satisfactory with no drastic increase in the WBC count, nor findings suggestive of blastic crisis (Figure 1).

10.8 g／100ml，ヘマトクリット33.5%，血小板数295,000，白血球数83,500（分類：前骨髄球1.5，骨髄球12.5，後骨髄球11.0，杆状核細胞 9.5，分葉核白血球44.5，リンパ球10.5，単球 7.0，好酸球1.5，好塩基球 2.0）であり，好中球アルカリフォスファターゼ（N— AP）は rate 60，score 260と正常値を示し，CGL の特徴とされる異常低値は示していなかった．

経過. CGL の診断のもとに1975年12月 8 日よりブスルファン 2 mgの投与を開始したが，白血球の減少が思わしくないため1976年 1 月 5 日より 3 mgに増量したところ白血球は順調に減少し，2月16日には脾臓を触れなくなった．1976年 8 月12日よりブスルファンを中止し，以後無治療で経過を観察しているが，推定発病より21か月，確定診断より19か月後の現在，白血球数の急激な増加もなく，また急性転化を思わせる所見もみられず良好に経過している（図 1 ）．

TABLE 2 CHROMOSOME NUMBER DISTRIBUTION IN CELLS FROM BONE MARROW AND PERIPHERAL BLOOD OF A PATIENT WITH CHRONIC GRANULOCYTIC LEUKEMIA

表 2　慢性骨髄性白血病患者の骨髄および末梢血液の細胞における染色体数の分布

Date sampled	Sample	Culture time (days)	PHA	Chromosome number						Total	% of L-cell**
				≦43	44	45	46	47+	End*		
24 Nov. 1975	B.M.	0	−	−	1	10	−	−	−	11	100
8 Dec. 1975	P.B.	1	−	1	7	22	−	−	−	30	100
	〃	2	+	−	2	7	8	−	−	17	41
18 Dec. 1975	P.B.	4	+	−	3	7	30	1	−	41	2
	〃 (a)	7	−	−	1	5	2	−	−	8	50
	〃 (b)	7	−	−	2	10	−	−	−	12	100
15 Mar. 1976	B.M.	0	−	−	2	17	−	−	−	19	100
	P.B.	1	−	−	5	25	−	−	−	30	100
	〃	3	+	−	1	5	34	2	14	56	0
21 June 1976	B.M.	0	−	−	−	10	−	−	−	10	100
	P.B.	1	−	−	−	5	−	−	−	5	100
	〃	3	+	−	−	6	13	−	1	20	0
13 Sept. 1976	B.M.	0	−	−	−	9	1	−	−	10	80
	P.B.	2	+	−	−	1	9	−	−	10	0
10 Jan. 1977	B.M.	0	−	−	2	38	−	−	−	40	100
	P.B.	2	+	−	−	3	17	−	−	20	0
18 Apr. 1977	B.M.	0	−	−	−	10	−	−	−	10	100

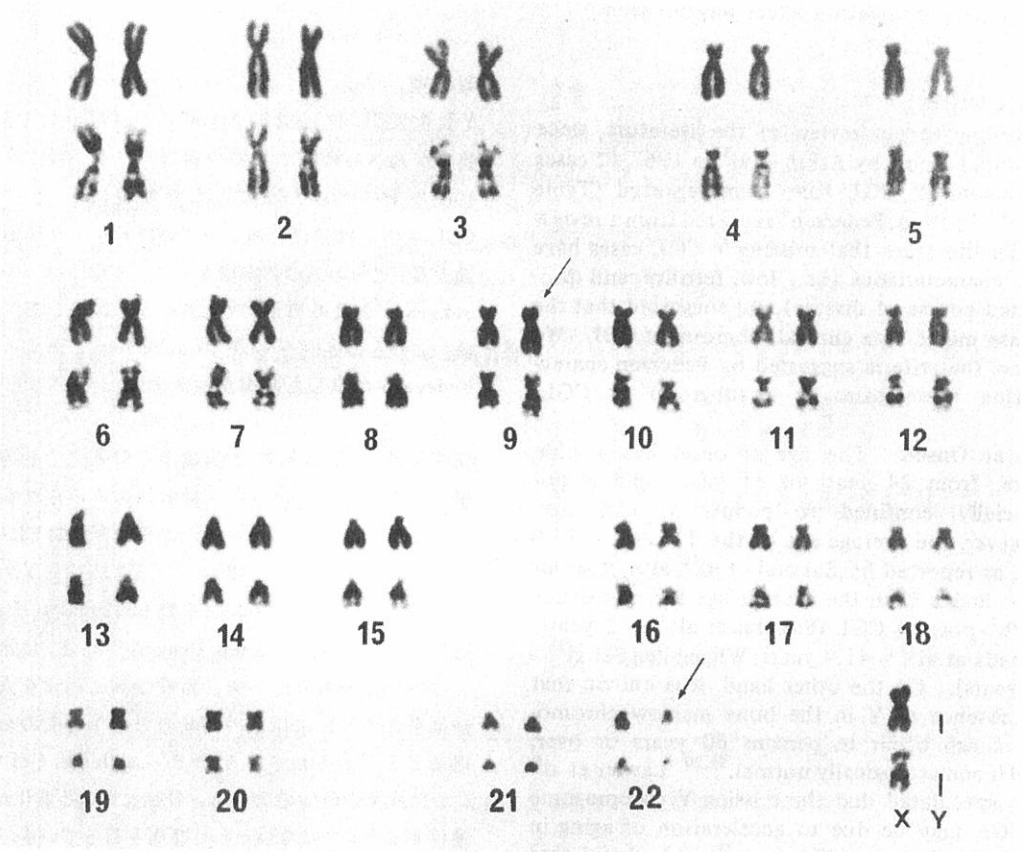
*Endoreduplication

**Leukemic cell characterized by presence of Ph^1- chromosome and missing Y chromosome

Results of Chromosome Analysis. From direct bone marrow preparations the chromosomes of bone marrow cells numbering 45 with missing Y chromosome, and Ph^1 chromosomes characteristic of CGL were found. By the Q- and G-banding technique, the absence of the Y chromosome was confirmed and it was noted that Ph^1 chromosome was derived from a translocation between chromosomes No. 9 and No. 22. Therefore, the karyotype of leukemic cell may be expressed as 45, X, −Y, t (9q + 22q −) (Figure 2). By direct bone marrow preparations, this karyotype was found in 100% of cells up to June 1976, whereas in the examination made in September, it was found in 8 of the 10 karyotyped cells (80%), while one had a normal male karyotype with 46 chromosomes and the other, 45 normal chromosomes, including those of the Y and G groups, but with a missing chromosome of the F group. However, the 45, X, −Y, Ph^1 karyotype was again seen in 100% of cells in January and April 1977. Further, the karyotype of lymphocytes derived from a 3-day culture of peripheral blood (PHA added) was that of a normal male (46, X, Y) (Table 2).

染色体分析結果. 骨髄直接法による骨髄細胞の染色体は45本でY染色体を欠失しており，CGL に特徴的な Ph^1 染色体を認めた．QおよびG分染法を用いてY染色体の欠失を確認し，染色体 No. 9 と No. 22の転座から Ph^1 染色体が得られることを認めた．したがって，白血病細胞の核型は45，X，−Y，t（9q +22q −）と表現される（図２）．この核型を有する白血病細胞は骨髄直接法で1976年６月までは100%に認められたが，９月の検査では10個の核型分析中８個（80%）に認められ，１個は染色体数46で正常男性の核型を有し，残る１個は正常染色体数45でYおよびG群は有していたがF群の１個が欠失していた．しかし，1977年１月と４月には再び45，X，−Y，Ph^1 の核型を有する細胞が100%に認められた．なお，末梢血３日間培養（PHA 添加）によるリンパ球の染色体は，正常男性の核型（46，X，Y）を示していた（表２）．

FIGURE 2 KARYOTYPE OF A BONE MARROW CELL
図 2　骨髄細胞の核型分析



Family History. Unremarkable. His seven children are in good health.

Past Illnesses. Injured left eye at the age of 21 and has artificial eye at present. Experienced liver disease when 49 years old.

Occupational History. Has been a painter since the age of 34.

A-bomb Exposure History. Was exposed at 3000 m from the hypocenter (estimated dose 0 rad). Acute radiation effect was not seen.

DISCUSSION

According to our review of the literature, since the initial report by Atkin et al[1] in 1962,42 cases of missing Y CGL have been reported (Table 3).[2-17] In 1968, Pedersen[5] reported from a review of the literature that missing Y CGL cases have two characteristics (i.e., low fertility and protracted course of disease) and suggested that the disease might be a clinical subgroup of CGL. We review the criteria suggested by Pedersen characterizing these cases as a subgroup of CGL.

Age at Onset. The age at onset has a wide range, from 24 years to 81 years, and is not especially confined to people of high age. However, the average age of the 42 cases is 53.0 and, as reported by Sakurai et al[12] also, it seems to be higher than the average age for no missing Y, Ph[1]-positive CGL (Sakurai et al[12] - 42 years; Kamada et al[14] - 41.9 years; Whang-Peng et al[18] - 45 years). On the other hand, it is known that the absence of Y in the bone marrow chromosomes can occur in persons 60 years or over, even if hematologically normal.[19,20] Lawler et al[8] have speculated that the missing Y chromosome in CGL may be due to acceleration of aging in the bone marrow. However, it is doubtful that this is merely an aging phenomenon.

Survival Time. The survival time is probably the most important point in deciding whether or not this could be clinically a subgroup of CGL. Ever since the reports by Lawler[8], and Pedersen[5], it had been generally believed that the survival time of the missing Y CGL cases was long. However, with the subsequent increase in the number of cases, some were found to have developed blast crisis early,[10,12] and Furusawa et al[16] and Shiffman et al[10] maintain that no

家族歴. 特記することなし．子供７人健在．

既往歴. 21歳のとき左眼外傷で現在義眼．49歳のとき肝疾患．

職業歴. 34歳のときから今日まで塗装業に従事している．

被爆歴. 3,000m の地点で被爆（推定線量は０rad）．急性放射能症状は認めていない．

考　察

Y欠失 CGL は1962年 Atkin ら[1]が報告して以来，我々が調べた範囲で42例の報告[2-17]がある（表３）．1968年 Pedersen[5] はそれまでの報告から，Y欠失 CGL 症例では子供に恵まれないこと，また病気の経過が長いことの二つの特徴を有し，臨床的に CGL の subgroup となり得るのではないかと報告した．我々は，これらの症例を CGL の subgroup であるとする Pedersen の示した基準を検討する．

発病年齢. 発病年齢は24歳から81歳までと各年齢層にわたっており，特に高齢者にのみみられる現象ではない．しかしながら42例の平均年齢は53.0歳となり，Sakurai ら[12]も述べているように，Y欠失のない Ph[1] 陽性 CGL の平均年齢（Sakurai ら[12] 42歳，鎌田ら[14] 41.9歳，Whang-Peng ら[18] 45歳）に比べると高いようである．一方，血液学的に正常な人の骨髄染色体でも60歳以上の高齢者ではY欠失のおこり得ることが知られている．[19,20] Lawler ら[8]は CGL におけるY染色体の欠失は，骨髄における老化が早く進行するためではないかとの推測を行っている．しかしこの点に関しては，まだ簡単に老化現象のみでかたづけてしまうのは問題があるように思われる．

生存期間. 臨床的に CGL の subgroup となり得るか否かを決める最も重要な点は生存期間にあると考えられる．Lawler[8]，および Pedersen[5] の報告以来，Y欠失 CGL は生存期間が長いと一般的に信じられてきた．しかしその後，症例が増加するに従い，早期に急性転化をおこした例もあり，[10,12] 古沢ら，[16] Shiffman ら[10]は現段階でははっきりとは言えないとしている．

TABLE 3 CASES OF 45, X, −Y, Ph[1] CHRONIC GRANULOCYTIC LEUKEMIA

表 3　45, X, −Y, Ph[1] 慢性骨髄性白血病

Case	Year	Principal Investigator	Age	No. of Children	% of −Y cells	Condition at the 1st time of Chromosome examination	Cause of death	Survival (Mo.) C. phase	Survival (Mo.) A. phase	Survival total	Chromosome analysis in acute phase	N-AP	Source of Reference
1	62	Atkin	53	0	(P.B.[1])63	C.[2]	Alive	10+	-	10+	-	?	1
2	63	Tough	60	?	37	〃	〃	1+	-	1+	-	?	2
3	〃	〃	?	?	100	〃	?	?	?	?	?	?	〃
4	65	Engel	61	N.M.[3]	100	〃	Alive	3+	-	3+	-	⇩	3
5	67	Elves	57	?	30	〃	〃	102+	-	102+	-	?	4
6	68	Pedersen	45	0	(P.B.) 50	〃	〃	46+	-	46+	-	?	5
7	72	Garson	58	5	45	〃	M.I.[4]	32	0	32	-	?	6
8	〃	〃	53	2+	100	〃	Alive	25+	-	25+	-	4(N.10-100)	〃
9	〃	〃	47	2	100	〃	〃	17+	-	17+	-	10(〃)	〃
10	73	Grozdea	?	?	?	〃	〃	?	-	?	-	21-42% (CML.0-5%)	7
11	〃	〃	?	?	?	〃	〃	?	-	?	-		〃
12	〃	〃	?	?	?	〃	〃	?	-	?	-		〃
13	74	Lawler	27	?	100	〃	Blastic crisis	90	3	93	Change in −Y cell	?	8,9
14	〃	〃	43	?	100	〃	〃	15	5	20	100% X, −Y	?	〃
15	〃	〃	59	4	100	〃	〃	87	4	91	100% X, −Y	?	〃
16	〃	〃	57	?	99	〃	〃	16	5	21	Not done	?	9
17	〃	〃	74	?	100	〃	Anemia	22	0	22	-	?	〃
18	〃	〃	78	?	100	〃	Alive	27+	-	27+	-	?	〃
19	〃	〃	52	?	100	〃	〃	82+	-	82+	-	?	〃
20	〃	〃	69	?	50	〃	〃	28+	-	28+	-	?	〃
21	74	Shiffman	43	3	100	〃	Blastic crisis	29	2	31	Not done	0	10
22	〃	〃	64	0	100	〃	〃	5.5	0.5	6	P.B. only	?	〃
23	〃	〃	81	+	?	〃	Alive	3+	-	3+	-	?	〃
24	76	Nigam	58	1	92	A.[5]	Blastic crisis	-	5	5	92% 45, X, −Y	17(N.40-120)	11
25	76	Sakurai	45	?	100	C.	Alive	27+	-	27+	-	?	12
26	〃	〃	69	?	100	〃	〃	39+	-	39+	-	?	〃
27	〃	〃	52	?	100	〃	〃	38+	-	38+	-	?	〃
28	〃	〃	43	?	100	〃	Blastic crisis	6.5	20.5	27	47,46,45+Y 46,XY	?	〃
29		de Grouchy	32	N.M.	?	?	?	?	?	120	?	?	10
30		Tanzer	?	?	?	?	Blastic crisis	?	?	24	?	?	〃
31		Bauters	64	1	?	C.	GI bleeding	180	-	180	-	?	〃
32		〃	55	2	?	〃	Alive	96+	-	96+	-	?	〃
33		〃	55	1	?	?	Blastic crisis	?	?	18	?	?	〃
34		Serra	45	N.M.	?	?	Strongyloidiasis	?	?	48	-	?	〃
35		Meisner	72	?	?	?	?	?	?	120	?	?	〃
36	70	Miyata	24	?	80	A.	Blastic crisis	-	7	7	80% 45, X, −Y, Ph[1]	⇩	13
37	72	Kamada	29	N.M.	58	C.	〃	6	5	11	58% 45, X, −Y, Ph[1]	⇩	14
38	76	〃	49	3	100	〃	〃	11	5	16	100% 45, X, −Y, Ph[1]	⇩	*[6]
39	73	Motomura	27	?	75	〃	〃	7	13	20	59-64, 85+Y, Ph[1]	?	15
40	73	Furusawa	24	N.M.	100	〃	〃	49	3	52	100% X, −Y	⇩	16
41	75	Shibutani	64	?	89	〃	Alive	15+	-	15+	-	score 68	17
42	76	Mikami	60	7	100	〃	〃	19+	-	19+	-	60/260	

1 P.B.: Peripheral blood　2 C.: Chronic phase　3 N.M.: Not married　4 M.I.: Myocardial infarction　5 A.: Acute phase　6 *: Personal communication

conclusive statement can be made at the present stage. In the present estimation also, among 35 cases that presented with missing Y in the chronic stage, 8 survived for more than 40 months, but 10 died within the same period. The average survival time of 40.4 months of the 42 cases cannot be said to be longer than the periods of 40 months (Whang-Peng et al[18]) and 42 months (Kamada et al[14]) for cases of CGL in general. Because the follow-up period is short and a fairly large number of cases are living, the average survival time may become a little longer, but since the tabulation of CGL in general also includes surviving cases, there presumably will appear no remarkable difference between the two groups.

今回の集計でも慢性期からY欠失のみられた35症例中40か月以上生存したのは8例で，反対に40か月以内に死亡したものが10例あった．また42例の平均生存期間は40.4か月で，一般のCGLの40か月（Whang-Pengら[18]），42か月（鎌田ら[14]）と比べても長いとはいえない．Follow-upの期間が短かく，かつ生存中のcaseがかなりあるため平均生存期間がもう少し延びる可能性があるが，一般のCGLの集計も生存中のものを含めての集計であるため，両群の間にあまり極端な差は出てこないものと考えられる．

Fertility. Pedersen[5] reported that low fertility might also be a characteristic of missing Y CGL in view of the fact that as many as three of the four cases that had been reported had no children. However, Pedersen himself maintains that this is difficult to explain because the missing Y is confined to bone marrow cells. Low fertility cannot be considered a characteristic of missing Y CGL because in our study of the literature 12 of the 15 cases had children (our case had 7). Theoretically also, it would be appropriate to consider that the fertility is unaffected because the missing Y is an acquired characteristic that is observed only in the bone marrow cells.

妊性. Pedersen[5]はそれまでの報告で4人のうち3人まで子供がなかったことから，子供のできないこともまたY欠失CGLの特徴となるのではないかと報告した．しかしその説明については，Y欠失が骨髄系統の細胞に限られていることからPedersen自身も困難としている．我々の検索で15例中12例に子供があり（我々の例は7人の子供がある），子供に恵まれないこともまたY欠失CGLの特徴とはなり得ないものと考えられる．理論的にもY欠失は後天的なものであり，骨髄系細胞にのみみられるのであるから子供を作る能力には影響がないと考えるのが妥当であろう．

Neutrophil Alkaline Phosphatase Activity. Grozdea et al[7] reported that the N-AP rates were 21%-42% in three cases of missing Y CGL, which is high when compared with 0-5% in CGL in general. The rates of our case also ranged from normal to slightly low over his entire course so far, showing no abnormally low values which are regarded as characteristic of CGL. However, as there are reports of low values in other cases, further study should be made of a larger number of cases to determine whether or not higher N-AP rate as compared with CGL in general is a characteristic of missing Y CGL.

好中球アルカリフォスファターゼ活性. Grozdeaら[7]は3例のY欠失CGLにおいてN—APのrateが21%—42%を示し，一般のCGLの0—5%に比べて高いことを指摘した．我々の症例も今まで全経過を通じて正常ないしやや低値であり，CGLに特徴的とされる異常低値を示していない．しかし他のcaseでは低値との報告もあり，N—APが一般のCGLに比べて高いということがY欠失CGLの特徴となり得るか否かさらに症例を重ねて検討してゆくべき問題と思われる．

Blast Crisis and Clonal Evolution. Missing Y chromosome in the missing Y CGL group cannot be considered a change accompanying blast crisis because it is seen from the chronic stage in almost all cases. However, one case of Kamada et al[14] which had a 46, X, Y, Ph^1 karyotype during the chronic stage developed a missing Y clone with blast crisis, and there are

急性転化とclonal evolution. Y欠失CGL群におけるY染色体の欠失はほとんどの症例において慢性期よりみられており，急性転化に伴う変化とは考えられない．しかし鎌田ら[14]の1例は慢性期には46, X, Y, Ph^1の核型を有していたのが急性転化に伴いY欠失のクローンを生じている．また初回染

two cases of Nigam[11] and Miyata[13] which were already in blast crisis at the time of the initial chromosome examination. These three are cases which had or may have had the Y chromosome in the chronic stage and, strictly speaking, it may be inappropriate to include these in the missing Y CGL group.

色体検査時すでに急性転化を起こしていたものが，Nigam[11]，宮田[13]の2例あり，この3例は慢性期にはY染色体を有していた，あるいは有していたかも知れない症例であり，厳密にいえばY欠失CGL群には入れない方がよいかも知れない．

The causes of death are known for 19 of the 42 cases, of whom 15 died of blast crisis and 4 of other causes. Thus, the majority died during blast crisis, which is similar to the general cases of CGL. The survival time in the acute stage ranges from 0.5 to 20.5 months, averaging 6 months, but cases are noted to follow a longer course than those reported so far.

42例中19例について死因がわかっているが，うち急性転化で死亡したものが15例，その他4例となっており，一般のCGLと同じくほとんどが急性転化を起こして死亡している．急性期の生存期間は0.5か月から20.5か月で平均6か月となり，今までいわれているものより長い経過をとる例が認められる．

Chromosome examination was conducted in both the chronic and acute stages on only eight cases. These include 4 which developed no change at all in their karyotype (Case 14, 15, 38, 40), 2 which developed changes in the cells with Y (Case 28, 39), one which had Y in the chronic stage and developed missing Y in the acute stage (Case 37), and one which developed additional changes in the missing Y cells (Case 13). Sakurai et al[12] reported that 45, X, −Y, Ph^1 cells may be more resistant to the development of additional karyotypic abnormalities as compared with 46, X, Y, Ph^1 cells. To be sure, only one case developed additional changes in the missing Y cells and in Cases 28 and 39 changes developed in cells with Y in the acute stage although missing Y cells were predominant, accounting for 100% and 75%, respectively, in the chronic stage. These results support the report of Sakurai et al. However, it seems that further study of more cases is necessary before judging whether or not missing Y cells really do not readily develop clonal evolution.

慢性期と急性期の両期に染色体検査がなされているのは8例にすぎないが，その内訳は核型に全く変化を来さなかったものが4例(Case 14, 15, 38, 40)，Yを伴う細胞に変化を来したものが2例(Case 28, 39)，慢性期にはYがあり急性期にY欠失を来したものが1例(Case 37)，Y欠失細胞に新しい変化をきたしたものが1例(Case 13)となっている．Sakuraiら[12]は，45, X, −Y, Ph^1の細胞は46, X, Y, Ph^1の細胞に比して新しい核型異常の発生に対し抵抗性があるのではないかと報告している．たしかに，Y欠失細胞に新しい変化を来したのは1例のみであり，Case 28, 39においては慢性期にはY欠失細胞の方が100%, 75%とそれぞれ優位であったにもかかわらず，急性期にはYのある細胞に変化が起こっている．これらの結果はSakuraiらの報告を支持している．しかし，Y欠失細胞がほんとうにclonal evolutionを起こしにくいのかどうかを判定するにはよう少し症例を重ねる必要があると思われる．

REFERENCES
参考文献

1. ATKIN NB, TAYLOR MC: A case of chronic myeloid leukaemia with a 45-chromosome cell-line in the blood. Cytogenetics 1:97-103, 1962

2. TOUGH IM, JACOBS PA, COURT BROWN WM, BAIKIE AG, WILLIAMSON ERD: Cytogenetic studies on bone marrow in chronic myeloid leukemia. Lancet 1:844-6, 1963

3. ENGEL E, JENKINS DE, TIPTON RE, MCGEE BJ: Ph^1-positive chronic myeıogenous leukemia with absence of another G chromosome in a male. N Engl J Med, 273:738-42, 1965

4. ELVES MW, ISRAEL MCG: Cytogenetic studies in unusual forms of chronic myeloid leukemia. Acta Haematol, 38:129-41, 1967

5. PEDERSEN B: Males with XO Ph1-positive cells: A cytogenetic and clinical subgroup of chronic myelogenous leukemia? Acta Pathol Microbiol Scand 72:360-6, 1968

6. GARSON OM, MILLIGAN WJ: The 45, XO, Ph1 subgroup of chronic granulocytic leukemia. Scand J Haematol 9:186-92, 1972

7. GROZDEA J, KESSOUS A, COLOMBIES P: Leukemia and loss of Y chromosome. Lancet 2:506, 1973

8. LAWLER SD, LOBB DS, WILTSHAW E: Philadelphia-chromosome positive bone marrow cells showing loss of the Y in males with chronic myeloid leukemia. Br J Haematol 27:247-52, 1974

9. LAWLER SD, GALTON DAG: Chromosome changes in the terminal stages of chronic granulocytic leukemia. Acta Med Scand (Suppl) 455:312-8, 1966

10. SHIFFMAN NJ, STECKER E, CONEN PE, GARDNER HA: Males with chronic myeloid leukemia and the 45, XO, Ph1 chromosome pattern. Can Med Assoc J 110:1151-4, 1974

11. NIGAM R, DOSIK H: Chronic myelogenous leukemia presenting in the blastic phase and its association with a 45, XO, Ph1 karyotype. Blood 47:223-7, 1976

12. SAKURAI M, SANDBERG AV: The chromosomes and causation of human cancer and leukemia. 18. The missing Y in acute myeloblastic leukemia (AML) and Ph1-positive chronic myelocytic leukemia (CML). Cancer 38:762-9, 1976

13. MIYATA H, SHINOHARA T, YAMADA K, KAMIYAMA R: Chromosome aberrations observed in chronic myelogenous leukemia during blast crisis. Rinsho Ketsueki-Jap J Clin Hematol 11:181, 1970

14. KAMADA N, OGUMA N, SATO M, TSUCHIMOTO T, ISHII, Y, UCHINO H: Cytogenetic study of 55 cases of chronic myelogenous leukemia, including 17 cases following blast crisis. Nihon Naika Gakkai Zasshi-J Jap Soc Intern Med 61:70-77, 1972

15. MOTOMURA M, OGI K: Cytogenetic analysis of cellular evolution in leukemia. Rinsho Ketsueki-Jap J Clin Hematol 14:142-9, 1973

16. FURUSAWA S, ADACHI Y, KOMATSU F, YAMADA K: Missing Y chromosome in bone marrow cells - on the diversity of hematopoietic pathology and significance of missing Y. Nippon Ketsueki Gakkai Zasshi- Acta Haematol Jap 36:120-8, 1975

17. SHIBUYA T, NAKAO I: A case of chronic myelogenous leukemia with concomitant missing Y chromosome and a unique translocation of Ph1 chromosome. Rinsho Ketsueki-Jap J Clin Hematol 16:372, 1975

18. WHANG-PENG J, CANELLOS GP, CARBONE PP, TJIO JH: Clinical implications of cytogenetic variants in chronic myelocytic leukemia (CML). Blood 32:755-66, 1968

19. O'RIORDAN ML, BERRY EW, TOUGH IM: Chromosome studies on bone marrow from a male control population. Br J Haematol 19:83-90, 1970

20. PIERRE RV, HOAGLAND HC: Age-associated aneuploidy: Loss of Y chromosome from human bone marrow cells with aging. Cancer 30:889-94, 1972