TECHNICAL REPORT
10-75
業 績 報 告 書

A NEW TYPE OF INVERSION OF A HUMAN Y CHROMOSOME

ヒトのY染色体にみられた新しい型の逆位について

TOSHIO SOFUNI, Sc.D. 祖父尼俊雄
KAZUMI TANABE 田辺和美
JUNSO NARUTO 鳴戸純三
AKIO A. AWA, Sc.D. 阿波章夫

ABCC

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

TECHNICAL REPORT SERIES
業 績 報 告 書 集

The ABCC Technical Reports provide the official bilingual statements required to meet the needs of Japanese and American staff members, consultants, advisory groups, and affiliated government and private organizations. The Technical Report Series is in no way intended to supplant regular journal publication.

ABCC 業績報告書は，ABCC の日米専門職員，顧問，諮問機関ならびに政府および民間の関係諸団体の要求に応ずるための日英両語による公式報告記録であって，業績報告書集は決して通例の誌上発表論文に代わるものではない．

TECHNICAL REPORT
10-75
業 績 報 告 書

A NEW TYPE OF INVERSION OF A HUMAN Y CHROMOSOME

ヒトのY染色体にみられた新しい型の逆位について

TOSHIO SOFUNI, Sc.D. 祖父尼俊雄
KAZUMI TANABE 田辺和美
JUNSO NARUTO 鳴戸純三
AKIO A. AWA, Sc.D. 阿波章夫

ABCC JNIH

ATOMIC BOMB CASUALTY COMMISSION
HIROSHIMA AND NAGASAKI, JAPAN

A Cooperative Research Agency of
U.S.A. NATIONAL ACADEMY OF SCIENCES—NATIONAL RESEARCH COUNCIL
and
JAPANESE NATIONAL INSTITUTE OF HEALTH OF THE MINISTRY OF HEALTH AND WELFARE

with Funds Provided by
U.S.A. ATOMIC ENERGY COMMISSION
U.S.A. NATIONAL CANCER INSTITUTE
U.S.A. NATIONAL HEART AND LUNG INSTITUTE
U.S.A. ENVIRONMENTAL PROTECTION AGENCY
JAPANESE NATIONAL INSTITUTE OF HEALTH

原 爆 傷 害 調 査 委 員 会
広島および長崎

米国学士院一学術会議と日本国厚生省国立予防衛生研究所
との日米共同調査研究機関

米国原子力委員会，米国癌研究所，米国心臓・肺臓研究所
米国環境保護庁および日本国厚生省国立予防衛生研究所
の研究費による

CONTENTS
目　次

Approved 承認 *31 March 1975*

A NEW TYPE OF INVERSION OF A HUMAN Y CHROMOSOME

ヒトのY染色体にみられた新しい型の逆位について

TOSHIO SOFUNI, Sc.D. (祖父尼俊雄)*; KAZUMI TANABE (田辺和美); JUNSO NARUTO (鳴戸純三); AKIO A. AWA, Sc.D. (阿波章夫)*

Department of Clinical Laboratories
臨床検査部

SUMMARY

Using chromosome banding techniques, a phenotypically normal male was found to have an abnormal banding pattern of the Y chromosome. By the constitutive heterochromatin staining method, a darkly stained band was located on the short arm and the proximal region of the long arm. The quinacrine staining method also showed a similar abnormal banding pattern: a brightly fluorescing band was seen on the short arm and the proximal region of the long arm. By the conventional Giemsa staining method, however, no specific morphological abnormality was detected in the aberrant Y chromosome. On detailed karyotype analyses no recognizable abnormality of banding patterns of any other chromosome was found aside from the abnormal Y chromosome. The abnormality was determined to be a complex inversion of the Y chromosome, which is described as 46, X, inv (Y) (pter→p11::q11→q12::cen::q12→qter).

要　約

染色体分染法によって正常男性1例のY染色体に異常なバンドパターンが見いだされた．C染色法によると濃染されるバンドは短腕と長腕の着糸点近接部に位置していた．Q染色法によっても同様の異常バンドパターンがみられた．すなわち短腕と長腕の着糸点近接部位に強く光るバンドがあった．しかし，通常のギムザ染色法では異常Y染色体に特異的な形態異常はみられなかった．詳細な核型分析によると，異常Y染色体以外のいずれの染色体にも識別できるバンドパターンの異常はみられなかった．この異常はY染色体の複雑な逆位に基づくものと判定され，命名規約に従い46, X, inv (Y) (pter→p11::q11→q12::cen::q12→qter) と表現することができる．

INTRODUCTION

Structural aberrations of the Y chromosome, such as isochromosomes,[1,2] dicentrics,[3-6] rings,[7,8] translocations,[9,10] inversions,[1,3,11] and deletions[12-14] have been found in phenotypically abnormal and normal males. Recently developed chromosome banding techniques have made it possible to identify

緒　言

Y染色体の構造異常，例えば同位染色体，[1,2] 二動原体，[3-6] 環状染色体，[7,8] 転座，[9,10] 逆位，[1,3,11] 欠失[12-14]などは，正常ならびに異常表現型の男性に発見されている．最近開発された染色体分染法により，従来の

*Hiroshima Branch Laboratory, Japanese National Institute of Health　国立予防衛生研究所広島支所

structural chromosome rearrangements with considerable accuracy, even though those are undetectable by the conventional Giemsa staining method.

The present paper deals with a male having an inversion of the Y chromosome, which was undetectable by the conventional method, but was discovered by banding techniques, the constitutive heterochromatin (C-) and quinacrine (Q-) staining methods.

CASE REPORT

The 65-year-old male (MF [redacted]) described here is a member of the ABCC-JNIH Adult Health Study sample[15] comprising A-bomb survivors and non-exposed controls residing in Hiroshima City. He was born to a 29-year-old father and a 26-year-old mother, and was the fourth of nine live-born children. His father died at 56 years of age of pneumonia, and his mother died at 66 years of age of valvular endocarditis. Of his eight siblings, three brothers died at 4, 40, and 58 years of age of Japanese B encephalitis, from injuries received in an accident, and of hepatoma, respectively, and a sister also died at 8 months after birth from an unknown cause. He married and had three daughters, the second of whom died at 11 days after birth, cause unknown. His medical history was uneventful and is not related to the chromosome finding described below. He was of average adult height and weight for his age, and no physical or phenotypic abnormality was observed on clinical examination at ABCC. He was not in Hiroshima City at the time of the A-bomb in 1945.

METHODS

Chromosome preparations were made from whole blood cultures by the routine air-dry method.[16] The C-staining study was carried out according to the method of Sumner.[17] Slides were dipped in a 0.2 N hydrochloric acid solution for 1 hour at room temperature, rinsed with deionized water, and treated with a 5% barium hydroxide octahydrate solution at 50 C for 25 minutes. After rinsing in several changes of deionized water, the slides were placed in 2 x SSC (0.3 M sodium chloride containing 0.03 M tri-sodium citrate) at 60 C for 1 hour, rinsed with deionized water and stained for 2 hours with Giemsa (2 ml to 60 ml of pH 6.8 phosphate buffer).

The Q-banding patterns in the chromosome were

ギムザ染色法で判別不可能なものをも含めて，染色体構造異常の識別がかなり正確にできるようになった．

本報では，Y染色体の逆位を示す男性1例について述べる．これは，従来の染色法では識別不可能なもので，constitutive heterochromatin (C) および quinacrine (Q) 分染法によって見いだされたものである．

症例報告

本例は65歳の男性（基本名簿番号[redacted]で，広島在住の原爆被爆者および非被爆対照者で構成されるABCC－予研成人健康調査対象群[15]の1員である．父親が29歳，母親が26歳の時に生まれ，生産児9人中の第4子である．父親は肺炎のために56歳で死亡し，母親は心臓弁膜症のために66歳で死亡した．同胞8人のうち兄弟3人は，4歳，40歳，および58歳の時にそれぞれ日本脳炎，事故，および肝癌で死亡し，姉妹の1人は生後8か月の時に原因不明で死亡した．本例は既婚で，娘が3人生まれたが，そのうちの第2子は原因不明で生後11日目に死亡した．既往歴に特記事項はなく，後述の染色体所見と関係のあるものは認められなかった．身長および体重は年齢に相応するものであり，ABCCにおける臨床診察では身体的異常も表現型異常も認められていない．本例は1945年の原爆時に広島市にはいなかった．

方　法

全血培養後に通常の空気乾燥法によって染色体標本を作成した．[16] C分染法は Sumner[17] の方法に従った．標本を0.2N塩酸溶液に室温で1時間浸してから脱イオン水で洗い，5％ barium hydroxide octahydrate 溶液で，50°C，25分間処理した．脱イオン水で数回洗浄した後に60°Cの2×SSC(0.03M tri-sodium citrate を含む0.3M塩化ナトリウム)に1時間浸し，脱イオン水で洗浄後，2 mlを60 mlのpH 6.8リン酸緩衝液に薄めたギムザ染色液で2時間染色した．

染色体のQ分染パターンは，若干の改変を加えた Caspersson

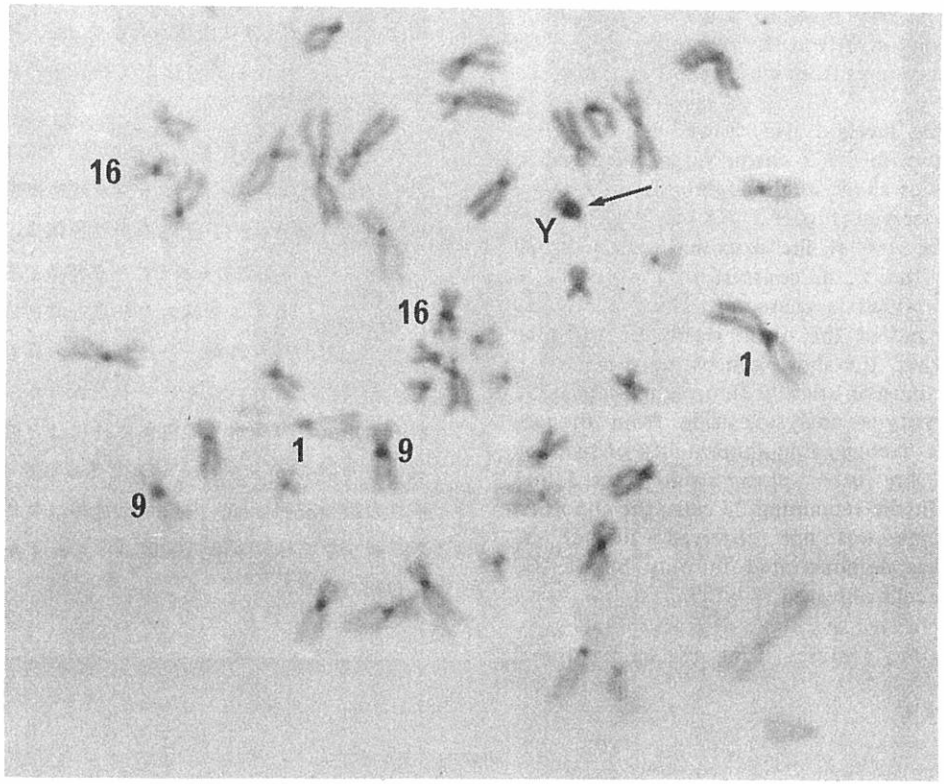

FIGURE 1. A representative metaphase showing C-bands. Arrow indicates the Y chromosome having an abnormal banding pattern.

図1. 代表的な分裂中期像におけるCバンド．矢印は異常バンドパターンを呈したY染色体．

obtained by a slightly modified technique of Caspersson et al.[18] Slides were kept in 0.005% quinacrine mustard (Polyscience Inc., U.S.A.) in MacIlvaine's citric acid phosphate buffer (pH 7.0) overnight, rinsed, and mounted in buffer for observation with a Nikon fluorescence microscope, using a BV excitor filter and Y51 and Wratten 2B barrier filters.

RESULTS

By chromosome banding analyses using the C-staining method, an abnormal banding pattern was detected in the Y chromosome, in 5 of the 10 mitoses observed (Figure 1). As previously reported for cells of normal males,[19] the C-band of the Y can be seen only at the distal region of the long arm. However, in the present case the C-band was located at the short arm and the proximal region of the

ら[18]の技法で得た．標本を0.005% quinacrine mustard（米国 Polyscience 社製）を含む MacIlvaine クエン酸リン酸緩衝液（pH 7.0）に一晩浸し，洗浄後，緩衝液内に封入してBV励起フイルターとY51および Wratten 2B 接眼フイルターを用いてニコン蛍光顕微鏡で観察した．

結　果

C分染法による染色体バンドパターンの分析の結果，観察した分裂細胞10個中の5個に異常なバンドパターンが認められた（図1）．正常男性の細胞についてはすでに報告されているように，[19] Y染色体のCバンドは，長腕の末端部にのみ見られる．しかし，本例では，Y染色体の短腕ならびに長腕の着糸点近接部にCバンドが認められ

long arm of the Y. This abnormal banding pattern was identical in five cells. In two cells the abnormality was not recognized because of ambiguous banding patterns, and the remaining three cells had 45 chromosomes from which the Y was missing.

The Q-staining method also showed the abnormal banding pattern in the Y chromosome, identical to that observed by the C-staining method, in 39 of the 62 mitoses observed (Figure 2). A brightly fluorescing band was seen at the proximal region of the long arm of the Y, in contrast to the normal Y chromosome which is characterized by a brightly fluorescing band at the distal region of the long arm.[19] Further, the short arm of the abnormal Y also had an unusual brightly fluorescing band. On detailed karyotype analyses, aside from the abnormal Y, no recognizable abnormality of banding patterns of any other chromosome was found (Figure 3). In the remaining 23 cells, the abnormal Y chromosome was not observed; further, Y-chromatin was demonstrated in only 58 of 100 mononuclear cells observed.

By chromosome analyses using the conventional Giemsa staining method which had been carried out biennially on this individual three times, between 1970 and 1974 (Table 1), no specific morphological deviation from the normal male chromosome constitution was detected in the diploid cells examined (Figure 4a).

From the above findings, it is concluded that only the Y chromosome is abnormal and that it most likely represents an inversion of the Y, rather than a reciprocal translocation between the Y and any one of other chromosomes. Since the short arm of the abnormal Y showed a brightly fluorescing band by the Q-staining method, this abnormality seems to be the result of a complex chromosomal rearrangement, rather than a simple paracentric inversion of the long arm of the Y. Two hypothetical origins are conceivable: (1) If the inverted Y chromosome is derived from a single rearrangement, three break points are necessary (Two would occur at points on both long and short arms probably almost at the centromere, and another at a site about three-quarters of the distance from the centromere into the positive C- and Q-band of the long arm, Figure 5a); and (2) If the inverted Y is derived from two consecutive rearrangements, a paracentric inversion followed by a subsequent pericentric inversion would result in an inverted Y chromosome found in the present form, or the two events could occur in reverse order (Figure 5b). According to the

た．この異常バンドパターンは細胞５個において全く同じであった．ほかの細胞２個ではバンドパターンが不鮮明であったために異常は確認されなかった．残りの細胞３個は染色体数が45でＹ染色体が欠如していた．

Ｑ分染法においても，Ｃ分染法で見いだされたものと同一のＹ染色体の異常バンドパターンが観察細胞62個中の39個に認められた（図２）．正常なＹ染色体は，長腕末端部に強く光るバンドが認められることが特徴であるのに対し，[19] 本例では，Ｙ染色体長腕の着糸点近接部に強く蛍光を発するバンドが見られた．しかも，この異常Ｙ染色体の短腕にも異常に明るい蛍光バンドがあった．詳細な核型分析の結果，この異常Ｙ染色体以外にはどの染色体にも識別できる異常バンドパターンは見られなかった（図３）．残りの細胞23個では，異常Ｙ染色体は欠如していた．なお，観察した単核細胞100個のうちわずか58個にＹ染色質が認められた．

本例については，1970年から1974年までの間に２年に１回の割合で通常のギムザ染色法による染色体分析を３回行っており（表１），分析した２倍体細胞では正常な男性染色体構成を示し特別な形態学的異常は見いだされなかった（図４ａ）．

上記の結果からＹ染色体のみが異常であり，その異常は，Ｙ染色体とその他のいずれかの染色体との相互転座というよりは，むしろ，Ｙ染色体の逆位である可能性が強いという結論に達した．Ｑ分染法でこの異常なＹ染色体の短腕に強く光るバンドが認められたので，Ｙ染色体長腕の単純な偏動原体逆位よりは，むしろ，複雑な染色体再配列の結果と思われる．この起源については，理論的に二つの可能性が考えられる．(1) このＹ染色体逆位が１回の再配列に由来するものであれば，３か所での切断が必要である．その二つは，長腕および短腕の恐らく着糸点にほとんど近接した場所に起こり，他の一つは，長腕の着糸点から約４分の３ほどの距離のＣおよびＱ濃染バンドの所で起こっている必要がある（図５ａ）．(2) Ｙ染色体逆位が二つの再配列が連続して起こったためであるとすれば，偏動原体逆位に続いて挟動原体逆位が生じた場合，または，この二つの事象が逆の順序で生じた場合に，本例にみられる形のＹ染色体逆位が起こるであろう（図５ｂ）．

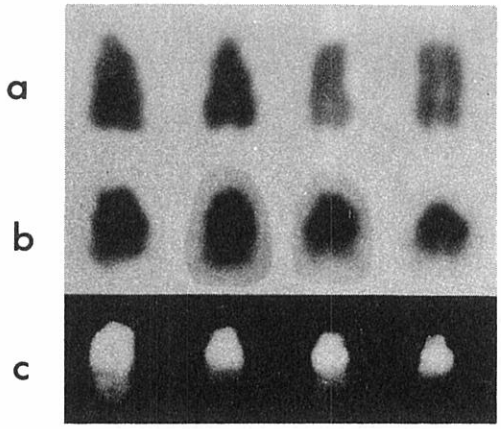

FIGURE 2. Twelve representative Y chromosomes. a: Chromosomes obtained by conventional method. b: C-banded chromosomes. c: Q-banded chromosomes.

図2. 代表的なY染色体12個. a: 通常の方法による染色体. b: C分染法による染色体. c: Q分染法による染色体.

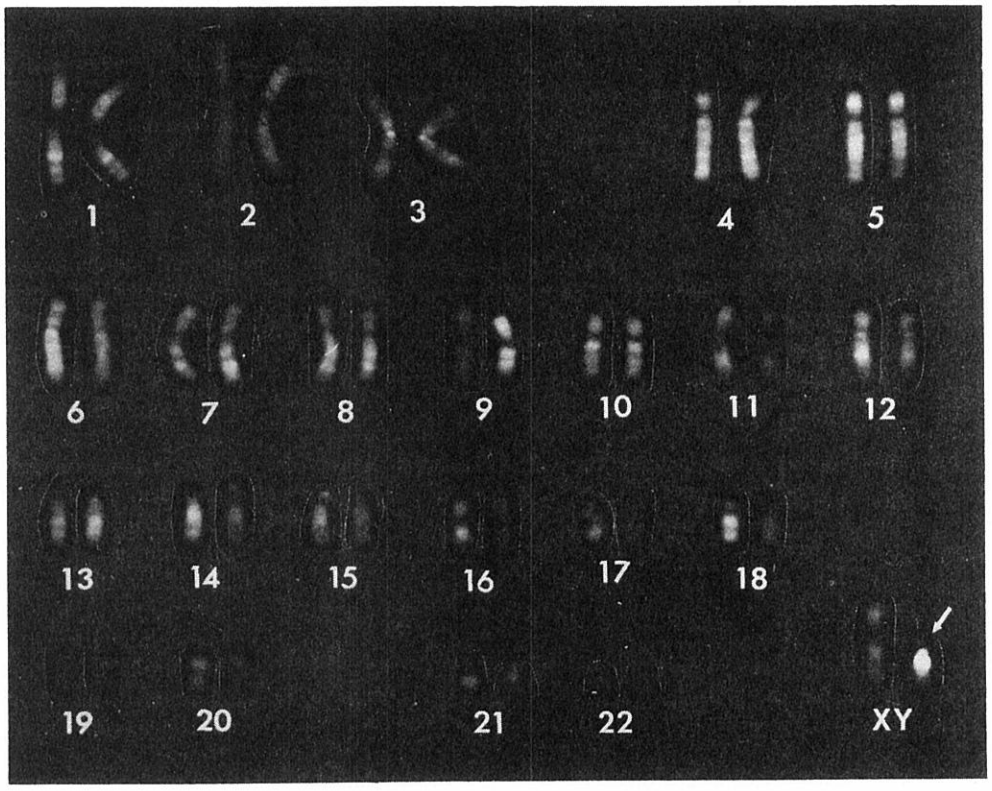

FIGURE 3. Karyotype of a metaphase stained by Q-method. Arrow indicates the abnormal Y chromosome.

図3. Q分染法による分裂中期像の核型分析. 矢印は異常Y染色体.

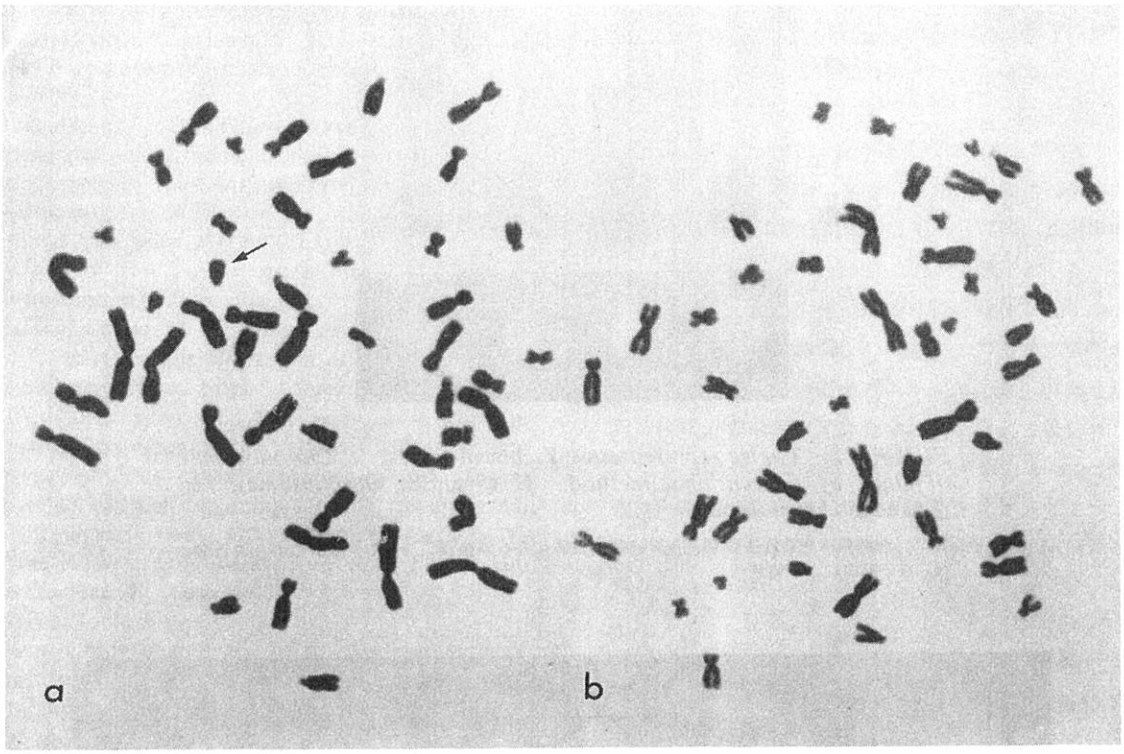

FIGURE 4. Metaphases obtained by conventional method. a: 46 chromosomes having the Y chromosome without any morphological abnormality (arrow). b: 45 chromosomes missing the Y chromosome.

図4．通常の方法による分裂中期像．a：染色体数46で，Y染色体に構造異常が全くない（矢印）．b：染色体数45で，Y染色体が欠如．

nomenclature of the Paris Conference (1971),[19] this inverted chromosome is designated as 46, X, inv(Y) (pter → p11::q11 → q12::cen::q12 → qter).

It is remarkable that a rather high frequency of aneuploid cells was found in the present case (Table 1). On detailed analysis of the aneuploid cells, it was apparent that the absence of the Y chromosome accounted for the majority of these cells (Figure 4b). This phenomenon was observed in the three samples obtained at 2-year intervals, and the frequency of Y-minus cells tended to increase with increasing age (Table 1). It was also noteworthy that in the third biennial sample a few cells had a Y chromosome with an acentric-like appearance (Figure 2).

Paris 会議（1971年）の命名規約に従い，[19] この染色体逆位を46，X，inv（Y）（pter→ p11 : : q11→ q12 : : cen : : q12→ qter）と書き表わすことができる．

本例では，異数性細胞がかなり高頻度で認められたことが注目される（表１）．異数性細胞の詳細な分析の結果，その大部分はＹ染色体が欠如していることがわかった（図４ｂ）．２年間隔で得られた３回の標本のいずれにもこの現象が見られ，Ｙ染色体の欠如した細胞の頻度は年齢とともに増加する傾向があった（表１）．第３回目の標本では，無動原体様の外観を呈するＹ染色体が少数の細胞に見られたことが注目される（図２）．

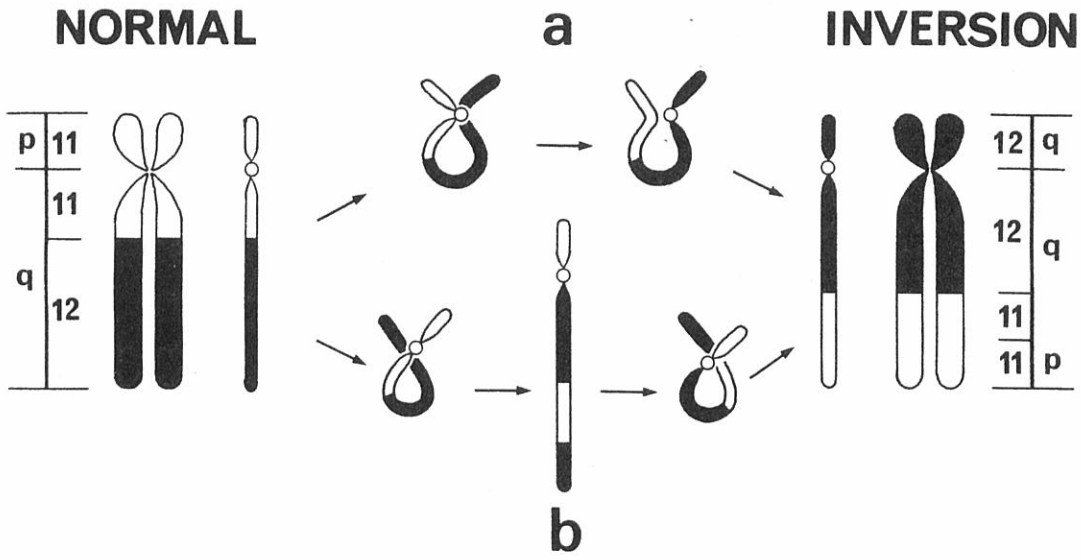

FIGURE 5. Diagramatic representation of the banding patterns of normal and inverted Y chromosome numbered according to the Paris Conference (1971). a: Inverted chromosome derived from three break points; two are at both long and short arms immediately proximal to the centromere, and another is three-quaters of the distance along the long arm into the positive C- and Q-band. b: Inverted chromosome derived from double inversions; first a paracentric inversion, followed by a pericentric inversion, or vice versa.

図5．パリ会議（1971年）の規約に基づいて示した正常Y染色体およびY染色体逆位のバンドパターンの模式図．a：染色体逆位は3か所の切断に由来；そのうちの2か所は長腕と短腕上の着糸点近接部に起こり，他の切断点は長腕の4分の3の所のCおよびQ濃染バンド内に生じたものである．b：染色体逆位が二重逆位に由来；まず，偏動原体逆位が起こり，次いで挟動原体逆位が生じた，または，この逆の順序で生じた．

TABLE 1 CHROMOSOME NUMBER DISTRIBUTION AND FREQUENCY OF MISSING AND ADDITIONAL CHROMOSOMES IN ANEUPLOID CELLS IN CULTURED LEUKOCYTES FROM THE INDIVIDUAL UNDER STUDY

表1　培養白血球における染色体数の分布および異数性細胞における染色体の欠如または過剰の頻度

Date Sampled	Age (years)	Chrom. No.	No. of Cells	Chromosome Groups											
				1	2	3	B	C	D	16	17	18	F	G	Y
6 Feb. 70	61	45	13*	-	1	-	-	1	2	-	-	-	-	1	7
		46	82												
		47	4	-	-	-	-	3	-	-	-	1	-	-	-
		4n	1												
		Total	100												
14 Jan. 72	63	45	19	-	-	-	-	2	-	-	-	-	-	3	14
		46	80												
		47	1	-	-	-	-	1	-	-	-	-	-	-	-
		Total	100												
19 Feb. 74	65	44	3	-	-	-	-	2	-	-	-	-	1	1	2
		45	26	-	-	-	1	-	-	-	-	-	1	2	22
		46	68												
		47	2	-	-	-	-	2	-	-	-	-	-	-	-
		48	1	-	-	-	-	2	-	-	-	-	-	-	-
		Total	100												

**One cell having a dicentric chromosome with two identical fragments.*

DISCUSSION

Structural abnormalities of the human Y chromosome have been reported in a certain number of instances of aberrant sexual or gonadal differentiation: isochromosomes of the long arm,[1,2] dicentrics of the long arm[3-5] and of the short arm,[4,6] rings,[7,8] deletions,[12-14] translocations,[9,10] and inversions.[1,3,11]

The Y chromosome inversion was also found in normal relatives of those with physical abnormalities,[11,20] and recent familial and population surveys[20-24] show that many phenotypically normal individuals have the Y inversion. It is now accepted that these Y inversions are neither correlated with phenotypical abnormality, an increased risk of physical disorders, nor with risk of having children with aneuploid chromosome aberrations.[25] The present case with a new type of Y inversion showed no apparent phenotypical abnormality, and it seems likely that there is no measurable effect ascribable to the presence of the inverted Y chromosome.

The recently achieved precision in chromosome banding patterns can now detect structural rearrangements which are not visible by the con-

考　察

性的あるいは性腺分化異常を有する者にY染色体の構造異常が見られることがあると報告されている．例えば，長腕の同位染色体，[1,2] 長腕の2動原体，[3-5] 短腕の2動原体，[4,6] 環状染色体，[7,8] 欠失，[12-14] 転座，[9,10] 逆位[1,3,11] などである．

Y染色体の逆位は身体的異常を有する例の正常な近親者にも認められており，[11,20] 最近の家族調査や集団調査によって，表現型の正常な者にもY染色体の逆位がかなり多いことが伴明した．[20-24] このY染色体の逆位は，表現型異常，身体的異常の危険率の増加あるいは異数性染色体異常を有する子供が生まれる危険と関連しないことが今や確認されている．[25] 新しい型のY染色体逆位を有する本例では，明白な表現型異常はなく，Y染色体逆位が存在するための識別できるような影響は恐らくないと思われる．

染色体分染法の最近の精度の向上により，従来のギムザ染色法で識別不可能である構造的再配列の発見が今や可

ventional Giemsa staining method; those include paracentric inversions, pericentric inversions where the break points are equidistant from the centromere, and reciprocal translocations where the exchanged segments are of approximately equal size. Recently, a paracentric inversion of a chromosome 7, detected only by the chromosome banding techniques, was found in this laboratory.[26] The Y chromosome inversion described here is a similar abnormality in that the conventional Giemsa staining method showed no morphological deviation of the Y chromosome compared with normal male cells, and only the chromosome banding techniques were able to detect the unusual reversed banding pattern on the Y.

The inverted Y chromosomes in all heretofore reported cases[1,3,11,20-25] were characterized by metacentric morphology as a result of a pericentric inversion occurring between the long arm and the short arm. In the inverted Y chromosome studied here, since the short arm showed a positive band by the C- and Q-method, a more complex chromosomal rearrangement than a simple pericentric or paracentric inversion must be invoked to explain its origin. As described above, there are at least two alternative mechanisms that could produce the complex inversion: one is a complex exchange accompanied by three break points occurring simultaneously, and the other is a double inversion, both a pericentric and a paracentric exchange.

A third possible mechanism for the formation of the abnormal Y is as follows: If the positive C- and Q-band in the short arm is produced as an incidental or secondary or "position" effect of a structural rearrangement in the long arm, as has been described for certain rearrangements in *Drosophila melanogaster,*[27] then this abnormal Y chromosome could be a simple paracentric inversion of the long arm. However, alteration of the banding pattern of the Y chromosome has not yet been observed in other reports of pericentric inversions of the Y[23,25] nor in cases of translocation between the Y and an autosome.[9,10] Therefore, it is less likely that this inverted Y is a simple paracentric inversion of the long arm.

Since family studies have not yet been performed, there is no evidence to indicate whether the inverted chromosome was inherited from the proband's father or was produced in a paternal gamete during meiosis.

It is interesting that in the present case, cells with 45 chromosomes which were characterized by the

能になった．例えば，偏動原体逆位，切断点が着糸点から等距離にある挟動原体逆位，交換部位がほぼ同じ大きさである相互転座などである．本研究室では，染色体分染法のみによって識別可能な第７染色体の偏動原体逆位を有する例を最近発見した．[26] その例と同様に，今回のＹ染色体逆位は，従来のギムザ染色法で正常男性の細胞に比べてＹ染色体に何らの形態学的異常が認められないのに対し，染色体分染法によってのみＹ染色体に逆転した異常バンドパターンが識別できた例である．

従来報告されたＹ染色体逆位の全例は，[1, 3, 11, 20-25] 長腕と短腕との間に生じた挟動原体逆位の結果，中部着糸型の形態を示すことが特徴であった．今回のＹ染色体逆位例では，ＣおよびＱ分染法によって短腕に濃染バンドが認められたので，単純な挟動原体逆位または偏動原体逆位よりは一層複雑な染色体再配列に基づくものと考えざるをえない．前述のごとく，この複雑な逆位が生じるには少なくとも二つの機序が考えられる：一つは，切断が３か所に同時発生して複雑な交換があった．他の一つは，挟動原体交換と偏動原体交換の二重交換があったとするものである．

この異常Ｙ染色体の形成について次のような第３の機序も考えられる：ショウジョウバエにおけるある種の染色体再配列について報告されているように，[27] 短腕のＣおよびＱ濃染バンドが長腕の構造再配列に伴った偶発性または続発性または「位置」効果として出現したものであれば，この異常Ｙ染色体は長腕の単純な偏動原体逆位であるかもしれない．しかし，Ｙ染色体の挟動原体逆位に関するその他の報告，[23, 25] また，Ｙ染色体と常染色体との間の転座を有する例[9, 10]では，Ｙ染色体にバンドパターンの変化は観察されていない．従って，このＹ染色体逆位が長腕の単純な偏動原体逆位である可能性は少ない．

家族調査は行われていないので，この染色体逆位が発端者の父親から遺伝したものか，父親の配偶子の成熟分裂の際に発生したものか不明である．

本例では，Ｙ染色体の欠如を特徴とする染色体数45の

absence of the Y chromosome were observed frequently, and that the frequency of those cells tended to increase with increasing age. This finding may be correlated with the fact that the Y chromosome in several cells showed an appearance identical to acentric fragments (i.e., the function of their centromere might have been lowered so as to produce the Y-minus cells in subsequent cell divisions).

Studies of peripheral leukocytes and bone marrow cells have indicated that the increasing hypodiploidy observed in males of advanced age was due to loss of the Y chromosome.[28-31] Higher frequency of the Y-minus cell observed in the present case thus seemed to be an aging phenomenon. However, the significance of the marked hypodiploidy in the peripheral blood and bone marrow of the aging male is not known.

細胞がしばしば見られ，この種の細胞の頻度が年齢とともに増加する傾向があったことは興味深い．この所見は，数個の細胞においてY染色体が無動原体断片に似た外観を呈したことと関係があるかもしれない．すなわち，これらの動原体の機能が低下しているために，その後の細胞分裂の過程でY染色体の欠如した細胞が発生したのであるかもしれない．

末梢血リンパ球および骨髄細胞についての研究では，高年齢男性における低2倍体細胞の増加は，Y染色体の欠如に起因していると認められている．[28-31] 今回の例にY染色体を欠く細胞が高頻度に見られたことは，加齢現象のためであろう．しかし，高年齢男性の末梢血および骨髄に見られる高頻度の低2倍体細胞の意義は不明である．

REFERENCES

参考文献

1. JACOBS PA, ROSS A: Structural abnormalities of the Y chromosome in man. Nature 210:352-4, 1966.
2. FERGUSON-SMITH MA, BOYD E, FERGUSON-SMITH ME, PRITCHARD JG, YUSUF AFM, GRAY B: Isochromosome for long arm of Y chromosome in patient with Turner's syndrome and sex chromosome mosaicism (45, X/46, XYqi). J Med Genet 6:422-5, 1969
3. MCILREE ME, PRICE WH, COURT BROWN WM, TULLOCH WS, NEWSAM JE, MACLEAN N: Chromosome studies on testicular cells from 50 subfertile men. Lancet 2:69-71, 1966
4. ANGELL R, GIANNELLI F, POLANI PE: Three dicentric Y chromosomes. Ann Hum Genet 34:39-50, 1970
5. ARMENDARES S, BUENTELLO L, SALAMANCA F, CANTU-GARZA J-M: A dicentric Y chromosome without evidence of sex chromosomal mosaicism, 46, XYqdic, in a patient with features of Turner's syndrome. J Med Genet 9:96-100, 1972
6. SIEBERS JW, VOGEL W, HEPP H, BOLZE H, DITTRICH A: Structural aberrations of the Y chromosome and the corresponding phenotype. Report of a case with the karyotype 45,X/46,X,i(Yp). Humangenetik 19:57-66, 1973
7. CHANDLEY AC, EDMOND P: Meiotic studies on a subfertile patient with a ring Y chromosome. Cytogenetics 10: 295-304, 1971
8. RUTHNER U, GOLOB E: 45,X/45,X,ace(?Yp)+/46,X,r(Y) in a phenotypically normal newborn male. Humangenetik 22:177-80, 1974
9. NOEL B, EMERIT I, LUCIANI JM, QUACK B: A familial Y/autosome translocation in man. Clin Genet 2:1-6, 1971
10. KRMPOTIC E, SZEGO K, MODESTAS R, MOLABOLA GB: Localization of male determining factor on short arm of Y chromosome. Case report of a baby with 46,X,t(Yp+;14q-). Clin Genet 3:381-7, 1972
11. SOLOMON IL, HAMM CW, GREEN OC: Chromosome studies on testicular tissue cultures and blood leukocytes of a male previously reported to have no Y chromosome. N Engl J Med 271:586-92, 1964

12. CONEN PE, BAILEY JD, ALLEMANG WH, THOMPSON DW, EZRIN C: A probable partial deletion of the Y chromosome in an intersex patient. Lancet 2:294-5, 1961

13. LANGMAID H, LAURENCE KM: Deletion of the long arms of the Y chromosome with normal male development and intelligence. J Med Genet 11:208-11, 1974

14. BENGTSSON B, GUSTAVSON K-H, REUTERSKIÖLD G, SANTESSON B, ÅHNSEN S: Male pseudohermaphroditism with 45X/46XYq- mosaicism in a pair of monozygotic twins. Clin Genet 5:133-43, 1974

15. BEEBE GW, USAGAWA M: The major ABCC samples. ABCC TR 12-68

16. HUNGERFORD DA: Leukocytes cultured from small inocula of whole blood and the preparation of metaphase chromosomes by treatment with hypotonic KCl. Stain Technol 40:333-8, 1965

17. SUMNER AT: A simple technique for demonstrating centromeric heterochromatin. Exp Cell Res 75:304-6, 1972

18. CASPERSSON T, LOMAKKA G, ZECH L: The 24 fluorescence patterns of the human metaphase chromosomes-distinguishing characters and variability. Hereditas 67:89-102, 1971

19. PARIS CONFERENCE (1971): Standardization in human cytogenetics. Cytogenetics 11:312-62, 1972

20. JACOBS PA: Structural abnormalities of the sex chromosomes. Br Med Bull 25:94-8, 1969

21. WALZER S, BREAU G, GERALD PS: A chromosome survey of 2,400 normal newborn infants. J Pediatr 74:438-48, 1969

22. SPARKES RS, MULLER HM, VEOMETT IC: Inherited pericentric inversion of a human Y chromosome in trisomic Down's syndrome. J Med Genet 7:59-62, 1970

23. GRACE HJ, ALLY FE, PARUK MA: 46,X,inv(Yp+q-) in four generations of an Indian family. J Med Genet 9:293-7, 1972

24. FRIEDRICH U, NIELSEN J: Chromosome studies in 5,049 consecutive newborn children. Clin Genet 4:333-43, 1973

25. ZEUTHEN E, NIELSEN J: Pericentric Y inversion in the general population. Humangenetik 19:265-70, 1973

26. SHIMBA H, OHTAKI K, TANABE K, SOFUNI T: Paracentric inversion of a human chromosome 7. ABCC TR 5-75

27. ZUFFARDI O, TIEPOLO L, DOLFINI S, BARIGOZZI C, FRACCARO M: Changes in the fluorescence patterns of translocated Y chromosome segments in *Drosophila melanogaster*. Chromosoma 34:274-80, 1971

28. JACOBS PA, BRUNTON M, COURT BROWN WM, DOLL R, GOLDSTEIN H: Change of human chromosome count distributions with age: Evidence for a sex difference. Nature 197:1080-1, 1963

29. HAMERTON JL, TAYLOR AI, ANGELL R, MCGUIRE VM: Chromosome investigations of a small isolated human population: Chromosome abnormalities and distribution of chromosome counts according to age and sex among the population of Tristan da Cunha. Nature 206:1232-4, 1965

30. ROWLEY JD: Loss of the Y chromosome in myelodysplasia: A report of three cases studied with Quinacrine fluorescence. Br J Haematol 21:717-28, 1971

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

ACKNOWLEDGMENT

謝　辞

We are indebted to Dr. Howard B. Hamilton, Department of Clinical Laboratories, for his advice in preparation of this report. We also thank the late Mr. Sadamaru Ichiyama for his photographic assistance.

本報告の作成に当たって助言を寄せられた臨床検査部長 Dr. Howard B. Hamilton 並びに写真作成に寄与された故市山定丸氏に対して感謝の意を表する.