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Citation	北海道大學理學部紀要, 16(1), 47-53
Issue Date	1966-12
Doc URL	https://hdl.handle.net/2115/27424
Type	departmental bulletin paper
File Information	16(1)_P47-53.pdf

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On a Familial Transmission of an Aberrant Autosome in Group 13–15[1)]

By

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(With 10 Text-figures and 1 Table)

Thanks to surprising of technical methods in cytogenetics of late years, detailed analyses of human chromosomes have been rendered possible, particularly with regard to satellite bodies, secondary constrictions, and variations in length and arm-ratio of chromosomes. Recent literature refers to many cases in which certain abnormalities of short arm or satellites of acrocentric chromosomes have occurred in association with particular developmental disorders or phenotypically normal human subjects (for reference, see Makino, 1964; Makino *et al.* 1966).

While working on a chromosomal survey of couples in relation to repeated spontaneous abortions, a woman was found by chance to carry an aberrant autosome in group 13-15. The aberrant element was characterized by an unusually elongated short arm with an enlarged satellite. The present paper reports the results of a familial survey with regard to the transmission pattern of the abnormal chromosome, its nature and origin, and its genetic significance.

The author wishes to express sincere thanks to Professor Sajiro Makino for his direction and improvement of the manuscript, and Dr. M. Sasaki for his invaluable advice and suggestion. Thanks are also due to Dr. Y. Kuroki for his friendly aid in chromosome analysis in one case and clinical examinations of the familial members, and to Dr. E. Taira for his kind cooperation in collecting blood specimens for study.

Materials and Methods: The pedigree of the family under study is presented in Figure 1. Seven members related to the propositus, 3 to 66 years of age, were subjected to chromosomal analyses: they are the propositus, her mother, two children, one of her sisters, her husband, and the husband's mother who is an aunt of the propositus.

The propositus (II–5) is a wife aged thirty-six showing no developmental disorder and mental defect. She has married with her first cousin, and had five pregnancies in the past which included three spontaneous abortions and two livebirths. The liveborn children, a 10-year-old boy (III–24) and a 2-year-old girl (III–27), are normal both physically and mentally. The three miscarriages were all terminated spontaneously in the first trimester. A similar abortion history was also noted in a sister of the propositus who is

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physically and mentally normal. She experienced six recognized pregnancies. The first pregnancy was arrested by induced abortion. This was followed by three consecutive spontaneous abortions. The fifth pregnancy ended with a healthy male child, and the last one was again lost by spontaneous abortion. All of the four abortions occurred within the first trimester. One, but not repeated, spontaneous abortion was recorded in the mother (I-2) and the female cousin (II-11) of the propositus, the former had eight livebirths and the latter had one.

Chromosome studies were carried out on the basis of short-term cultures of peripheral leucocytes from seven individuals mentioned above according to a modification of the method by Moorhead *et al.* (1960). Chromosome slides were made following the air-drying method after Rothfels and Siminovitch (1958) with Giemsa staining.

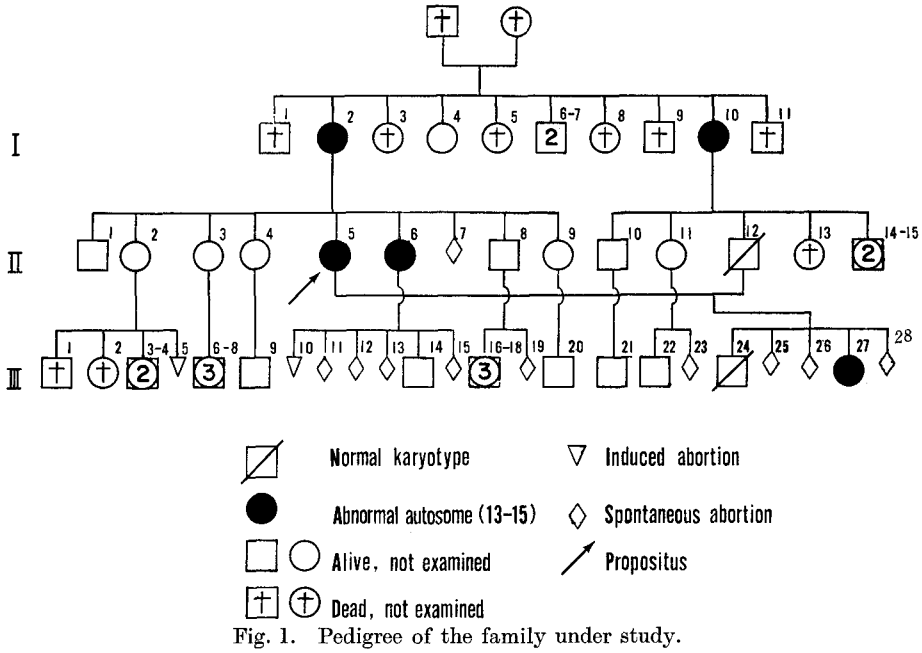


Fig. 1. Pedigree of the family under study.

Results

Table 1 provides the results of chromosomal observations undertaken in the propositus and 6 persons related to the propositus. Data indicated that they had a normal diploid number as 46. Out of cells counted six to sixteen well-spread metaphases were analyzed in each case. Figure 2 shows a representative karyotype derived from the propositus: there are five acrocentric members occurring in group 13–15, normal in appearance, leaving one chromosome which was characterized by an unusually elongated short arm and enlarged satellite with a long stalk.

The aberrant chromosome occurred in every culture specimen. It is very prominent in appearance, being easily distinguishable from the other members of group 13–15, on account of its remarkable structure and outstanding size. No morphologically anomalous element was observed in the remaining chromosomes of the somatic complement.

Table 1. Summary of chromosome studies in seven members of the family under study

Case (age)	Chromosome counts					No. of cells obs.	No. of cells anal.
	<45	45	46	47	>47		
Propositus* (36)	—	4	66	2	1	73	16
Husband (36)	—	1	29	—	—	30	7
Male child (10)	—	1	44	—	—	45	9
Female child* (3)	—	1	40	1	—	42	15
Mother* (66)	—	1	28	—	—	29	9
Sister* (35)	—	1	41	1	1	44	10
Husband's mother* (58)	1	—	23	—	—	24	6

Individuals marked with asterisks are carriers of an aberrant autosome (group 13–15).

Though several tetraploid cells were observed in this material, a pair of such abnormal elements was very prominent in occurrence.

The abnormal chromosome of similar type was found to occur in all well-spread metaphase plates from a female child of the propositus (III–27), mother (I–2), younger sister (II–6) and aunt (husband's mother) (I–10) with its outstanding feature (Figs. 3–6). In the culture specimens derived from here husband and male child, however, no such an aberrant chromosome was observed. Then it is evident that they are not the carrier of this abnormal chromosome (Figs. 7–8).

Some metaphases from the affected individuals showed that the chromosome in question was sometimes involved in a satellite-association between the aberrant element and one or more acrocentric chromosomes (Figs. 9–10).

Discussion

In the light of the results of the present chromosomal study in a family it is evident that an abnormal autosome characterized by the unusually elongated short arm and enlarged satellite with a long stalk is apparently inheritable. The aberrant chromosome is, probably, transmitted through the maternal pedigree to the propositus and to some other members of her family. Since one of the mother's sisters carried this aberrant chromosome, it seems probable that one of the parents of the propositus's mother may be a carrier of this element.

The abnormal chromosome under study resembles in every respect that reported by Chandra and Hungerford (1963). Similar abnormal acrocentric chromosomes have been described by many authors in phenotypically abnormal or normal individuals of both sexes. Very recently Makino *et al.* (1966) reported an inheritable anomalous acrocentric autosome with an enlarged short arm in group 13–15, most probably no. 15.

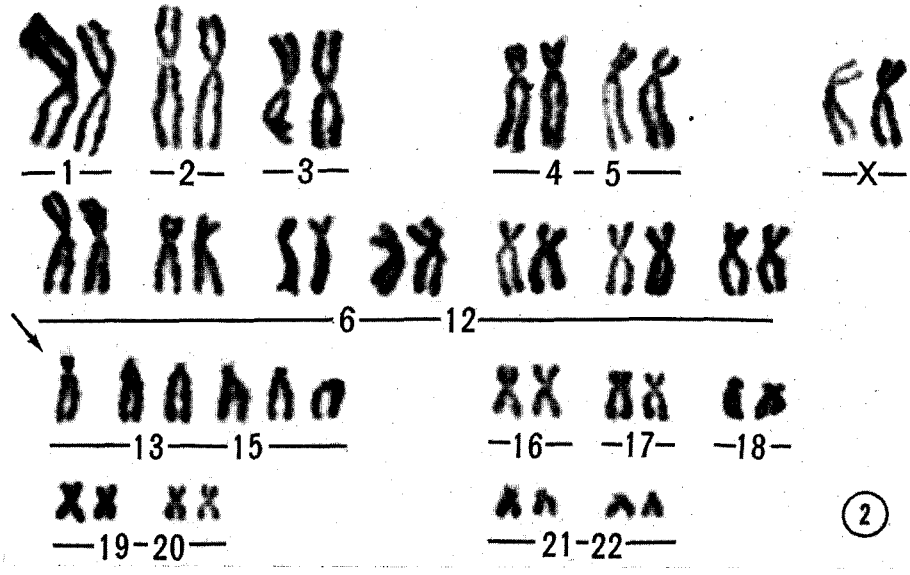
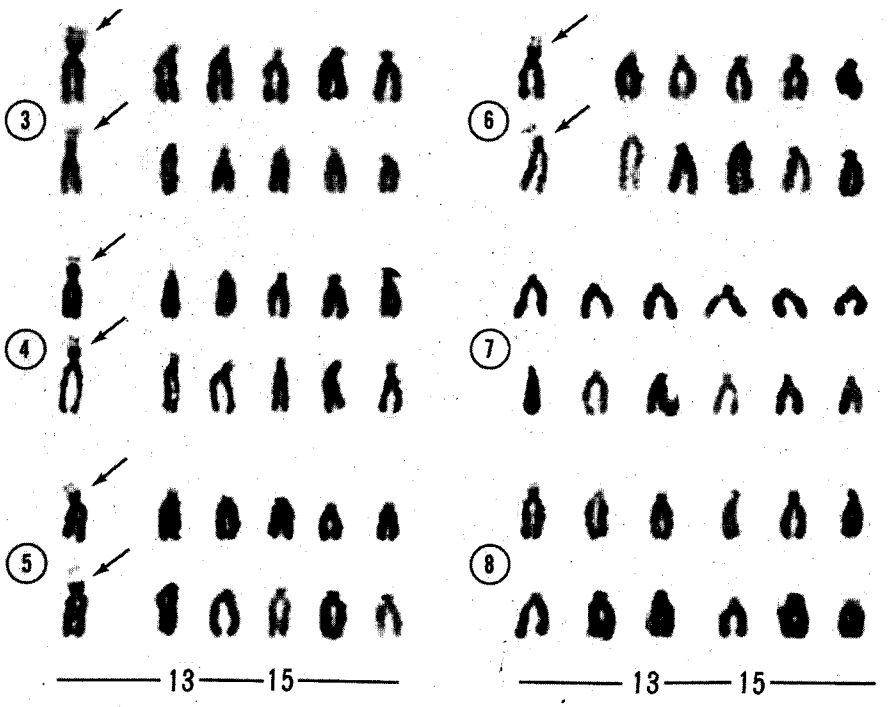


Fig. 2. Karyotype analysis of the propositus aged 36. An arrow indicates the aberrant autosome.

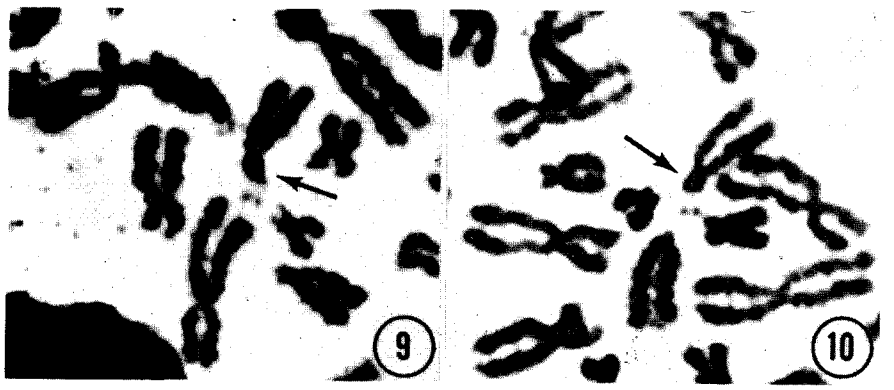
In reference to current data, the possibilities for the general interpretation on the origin of the abnormal autosome are considered in the following.

Translocation or insertion of chromosome materials to the region of the short arm and the satellite of the affected chromosome may be one of the origins for the aberrant chromosome of this nature. It is impossible, however, at the present status to identify the chromosome from which the extra chromosomal piece has been derived. An inversion seems to be rather unlikely as a cause of the present chromosomal abnormality, since in most metaphase plates the affected chromosomes are larger than every member in group 13–15.

Some other possibilities, however, such as a small duplication in the short arm and the satellite region, and an alteration of coiling structure due to unknown causes in the vicinity of the secondary constriction can not be excluded, as suggested by Cooper and Hirshhorn (1962), Therkelsen (1964) and Court Brown *et al.* (1966).



Figs. 3–8. Partial karyotype analyses of group 13–15 in two cells each from the members of the family. 3: female child aged 2. 4: mother aged 66. 5: younger sister aged 35. 6: aunt (husband's mother) aged 66. 7: husband aged 36. 8: male child aged 10. The abnormal chromosome are shown by an arrow.



Figs. 9–10. Photographs showing the abnormal chromosome in satellite-association with other acrocentric chromosomes, indicated by an arrow. 9: from the younger sister. 10: from the aunt.

At the present-day-knowledge, however, no decided statement can be made on the origin of the present chromosomal abnormality.

Recent literature refers to that parental chromosomal abnormalities may play a significant role in the etiology of recurrent abortion (Schmid, 1962; Jacobsen *et al.* 1963; Bishun *et al.* 1964; Makino *et al.* 1965; Pergament and Kadotani, 1966). A small acrocentric chromosome reported by Schmid (1962) which was regarded as a cause of repeated abortions had an extra chromatin piece translocated to its short arm. The present study detected an abnormality of similar nature in a medium-sized acrocentric belonging to group 13–15 in some members of the family. Some of its carriers had a history of repeated abortions. It seems likely that the aberrant chromosome found in the present case may not be associated with a direct cause of repeated abortions, since the propositus's mother (I-2) cast one spontaneous abortion in her nine pregnancies and her aunt (I-10) none in six pregnancies, though both are the carriers of the aberrant autosome. However, the possibility of its chance effect on abortion may not be excluded. Further, it is questionable that a chromosomal change occurring in a specific minute region of chromosomal segment occurs in association with deleterious genic unbalance which would result in spontaneous abortion.

Some authors suggested that the allied chromosomal abnormality may be associated with some disease states (Tjio *et al.* 1960; Ellis and Penrose, 1960), while some others postulated that an enlarged satellite and elongated short arm of acrocentric chromosomes was implicated in normal development. Particularly, Court Brown *et al.* (1966) reported that the allied chromosome occurred as a normal variant in the general human population at a relatively high frequency. In the family here under study, any phenotypical abnormality was not observed in all cases studied so far, except repeated abortions in some members.

Summary

A woman hospitalized due to spontaneous abortions was found to possess an abnormal autosome (group 13–15) with an unusually long short arm and enlarged satellite marked by an elongated stalk. She showed no developmental disorder and mental defect.

A familial chromosomal study undertaken in seven members related to the propositus revealed that her female child, mother, a younger sister and an aunt were carriers of the same abnormal chromosome. Except for a younger sister who are also a repeated abortor, the other members under study are clinically normal.

It appears that the abnormality of an autosome in group 13–15 may not necessarily be associated with repeated spontaneous abortions. A possible origin and the nature of the abnormal chromosome were discussed.

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