

THE ASSOCIATION OF D-GROUP CHROMOSOMAL TRANSLOCATIONS AND DEFECTIVE SPERMATOGENESIS*

STEPHEN R. PLYMATE, M.D.,† WILLIAM J. BREMNER, M.D., AND C. ALVIN PAULSEN, M.D.

Department of Medicine, University of Washington School of Medicine, and United States Public Health Service, Seattle, and Department of Medicine, Madigan Army Medical Center, Tacoma, Washington 98431

It is well accepted that defective gonadal function in the male may be associated with abnormalities of sex chromosomes, as in the classic and variant forms of Klinefelter's syndrome.¹ Autosomal abnormalities, however, are less generally recognized to be associated with gonadal dysfunction. We have recently studied a family in which there was an association between a D-group chromosomal translocation and defective spermatogenesis.

MATERIALS AND METHODS

Patients. Three patients within one family had normal mental and physical development, including secondary sex characteristics (Fig. 1). The propositus, S. M., a 29-year-old white male, was evaluated because of infertility. It was learned that his brother, G. M., was also experiencing an infertile marriage. Because of this information, chromosomal studies were conducted on available family members, and parameters of testicular function were measured in all males.

Laboratory Studies. Sperm counts were made by using a Coulter counter² unless the counts were below 10 million/ml, in which case measurement was done in a Neubauer counting chamber. Sperm morphology was analyzed according to the

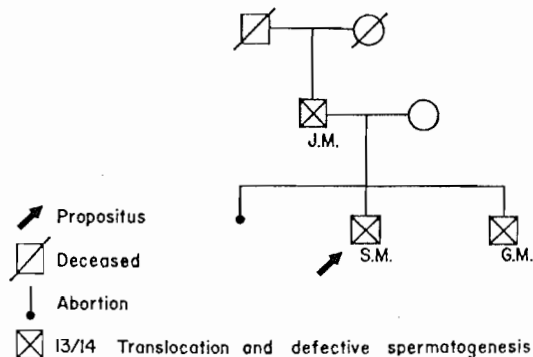


FIG. 1. Pedigree of the segregation of the D/D translocation.

system of MacLeod.³ Luteinizing hormone, follicle-stimulating hormone, and testosterone levels were measured in duplicate by radioimmunoassay.^{4,5} Chromosome studies were made by using short-term cultures of peripheral blood leukocytes⁶ and testes.⁷

Giemsa binding of leukocyte chromosomes was accomplished according to the method of Seabright,⁸ and testicular meiotic studies were performed by using the method of Luciani et al.⁹ Specimens for testicular histology were fixed in Cleland's solution and stained with iron-hematoxylin and eosin.

RESULTS

Endocrine data for the three patients are shown in Table 1. The only abnormality noted was an elevated follicle-stimulating hormone level in G. M. Seminal fluid data are presented in Table 2.

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†Reprint requests: Dr. Plymate, Chief, Division of Endocrinology, Fitzsimons Army Medical Center, Denver, Colo. 80240.

TABLE 1. *Endocrine Data in Patients with 13/14 Translocation*

Patient	Age	Follicle-stimulating hormone	Luteinizing hormone	Testosterone
		ng/ml	mIU/ml	µg/100 ml
Father (J. M.)	56	253	13.6	0.76
Propositus (S. M.)	29	320	15.7	0.44
Brother (G. M.)	31	628	22.0	0.60
Normal male range		50-450	4-25	0.3-1.4

Azoo- or oligospermia was found in each patient except the father, J. M. In J. M., although the total sperm count was normal, a marked increase in duplicate and immature forms was seen in three separate seminal fluid analyses, collected over several months. This pattern of morphologic abnormality was the same as that found in the D-group translocation patient who was oligospermic. In all cases, chromosome analyses of blood, and of testes in S. M., were carried out. These studies demonstrated the D-group chromosomal translocation (Fig. 2). Chromosome banding studies of the three family members revealed the translocation to be 45,SY,-13,-14,+t(13q14q); that is, a translocation of the long arms of chromosome 13 onto the long arms of chromosome 14, with a loss of the short arms of both. Meiotic studies of S. M. demonstrated the trivalent configuration of the translocated chromosome (Fig. 3). The testicular histology of S. M. (Fig. 4) revealed spermatogenic arrest.

DISCUSSION

The present data, in addition to those

reported by others,¹⁰⁻¹⁴ suggest an association between D-group chromosomal translocations, particularly translocations involving the 13 and 14 chromosomes, and defective spermatogenesis. Finding a familial occurrence of the spermatogenic defect together with the chromosomal abnormality in the present study makes this association appear particularly likely.

Balanced D-group translocations may occur in the normal population at a rate of 0.05%.¹⁵ The frequency with which they are being reported from male infertility clinics¹⁰⁻¹⁴ suggests a higher rate of occurrence of the translocation in infertile males. However, the possibility of fortuitous coexistence of the translocation and the defect in spermatogenesis is raised because of reports of many families which carried the translocation but in which male fertility apparently was normal.¹⁶ Testicular function was not studied in these families beyond a simple assessment of the average number of offspring of affected members. In nearly all male D-group translocation carriers in whom testicular function has been carefully studied, including seminal fluid analyses and testicular biopsies, defects in testicular function have been found.¹⁰⁻¹⁴ It is apparent that simple analyses of fertility may not be adequate to detect defects in spermatogenesis, since these defects may not be severe enough to produce sterility. An illustration of this point is J.M., in the present study, who is a fertile male with a spermatogenic de-

TABLE 2. *Seminal Fluid Data in Patients with 13/14 Translocation*

Patient	Age	Sperm count	Chromosome group						
			O	L	S	T	A	D	I
Father (J. M.)	56	million/ml							
		82	48	0	1	17	7	20	7
		128	44	0	1	16	14	19	6
Propositus (S. M.)	29	146	44	0	2	19	15	15	5
		<1.0	3	0	0	9	6	16	66
		<1.0	10	0	4	5	10	5	66
Brother (G. M.)	31	0							
Normal values		20-200	73.0	2.7	8.6	6.1	8.6	1.0	<0.5

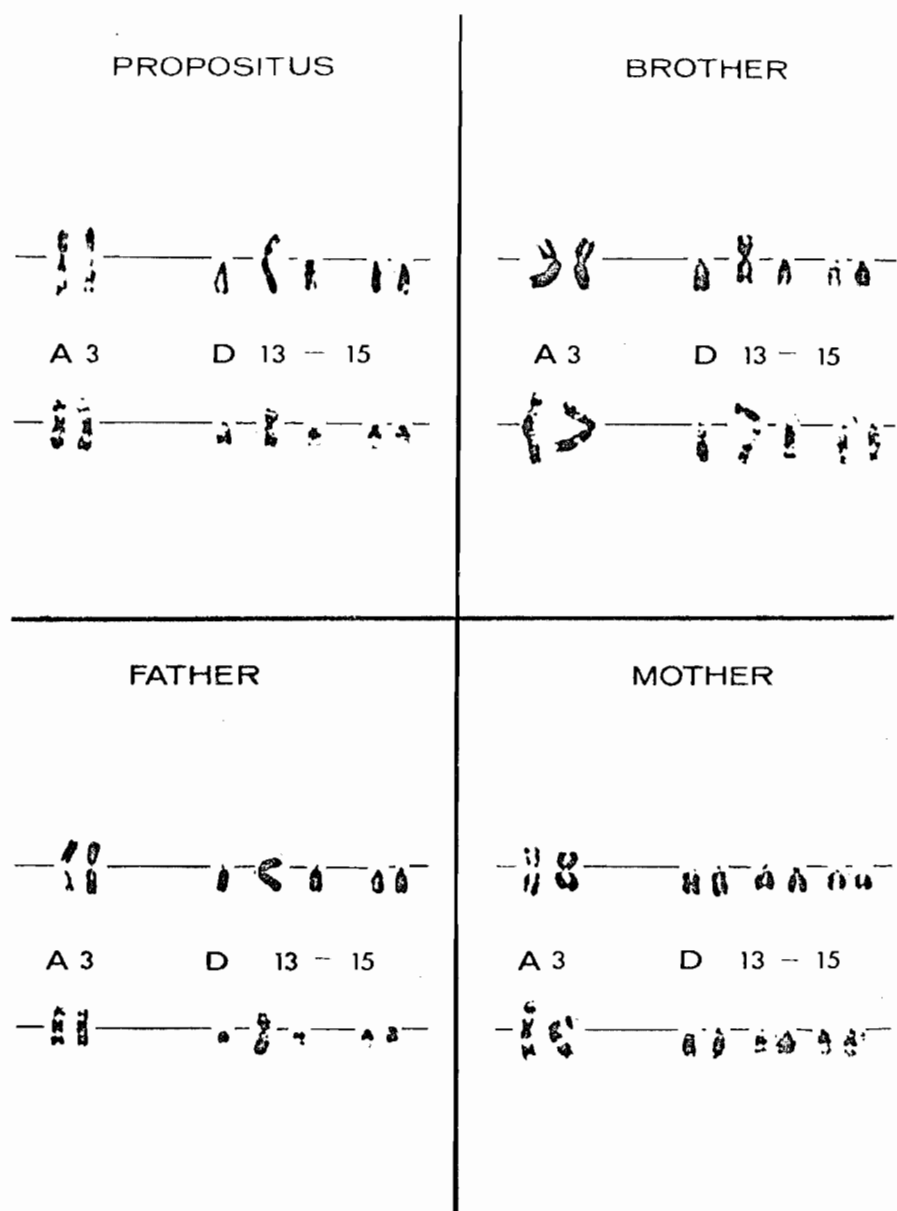


FIG. 2. Partial karyotypes with Giemsa banding in patients with a 13/14 translocation and the normal mother. An A-group chromosome is included for comparison with the translocated D-group chromosome.

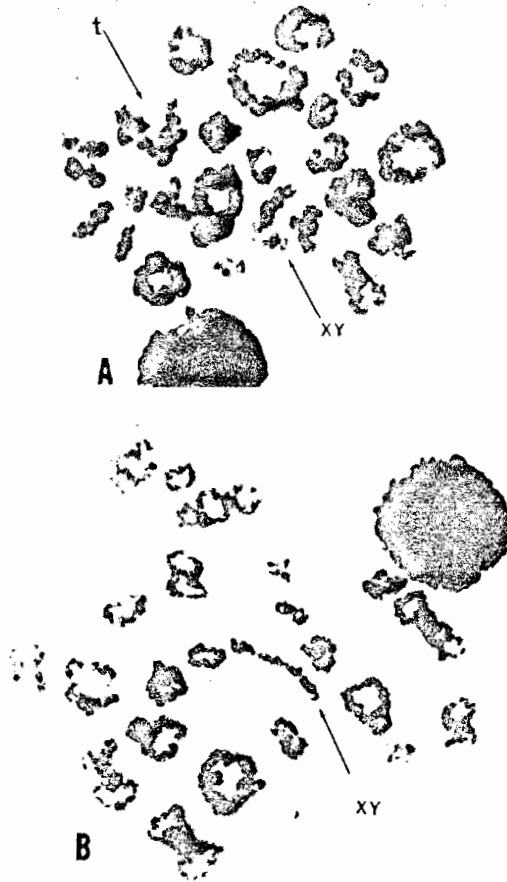


FIG. 3. A, Diakenesis from testicular culture of S. M., demonstrating the trivalent arrangement of the translocated chromosome. B, Normal diakenesis.

fect that was recognized only with detailed studies of semen morphology.

In most of the patients reported with D/D translocations, the specific chromosomes involved have not been identified because of the technical limitations of the standard metaphase examination. With the newer chromosome banding methods, specific identification of each chromosome pair is possible and the various translocations can be more precisely described. In the present study, the translocation in the family was specifically identified as $45,XY,-13,-14,+t(13q14q)$. The more specific methods of chromosome identifi-

cation allow more accurate correlation of clinical syndromes and chromosomal defects. In this way, it may be found that certain translocations within the D-group are associated with spermatogenic defects or recurrent abortion, while others lack such an association.^{17, 18}

The final proof of an association between D-group translocations and defective spermatogenesis awaits a large, prospective study of families ascertained by population surveys to carry the translocation. The males in such families should be studied carefully with regard to testicular function, including at a minimum, a physical examination; measurement of luteinizing hormone, follicle-stimulating hormone, and testosterone levels; and careful analyses of several seminal fluid specimens, including sperm counts, motilities, and morphologies. Chromosome banding studies will also be necessary in the subjects carrying the translocation, to identify the specific chromosomes involved.

SUMMARY

D-group chromosome translocations have been associated in isolated cases with infertility in males. In this study, we demonstrated the effect of a translocated D-group chromosome on spermatogenesis as it had segregated among three male members of one family. Although the father, who carried the translocation, was obviously fertile, the effects of the translocations on his sperm were noted in the morphologic examination. This study demonstrates the need for more careful evaluation of patients with chromosomal abnormalities for effects on spermatogenesis. Furthermore, it shows the possibility of autosomal chromosomal influences on testicular function.

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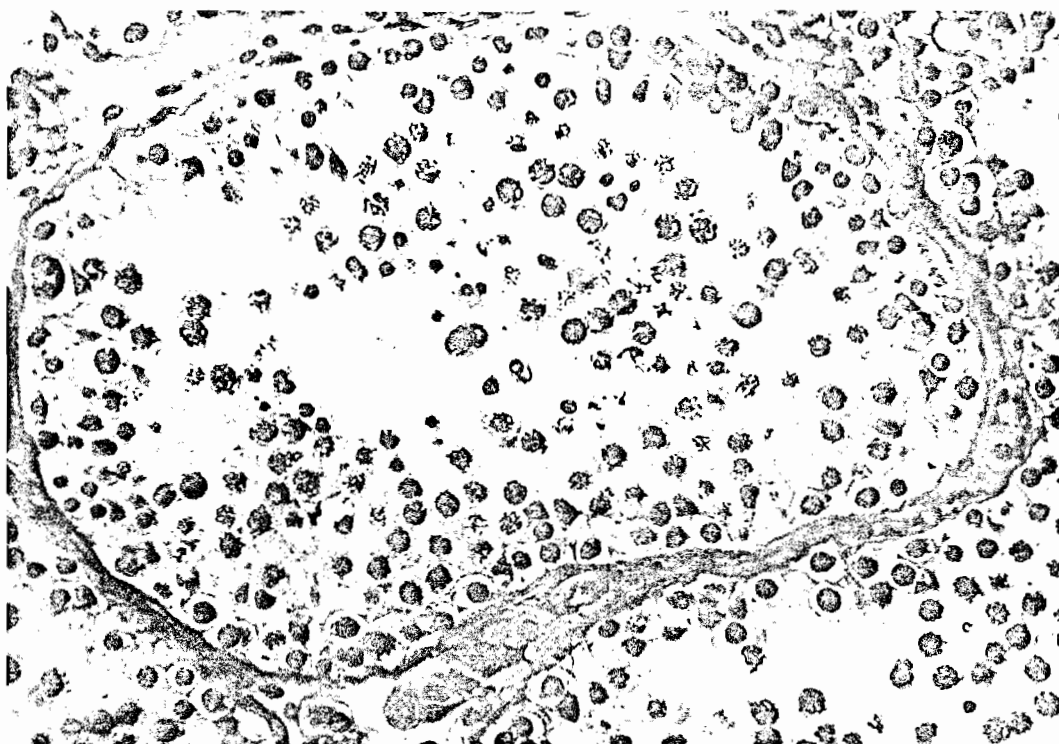


FIG. 4. Testicular biopsy of S. M., demonstrating impaired spermatogenesis.

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