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PARENTAL ORIGIN OF CHROMOSOME 15 DELETION IN PRADER-WILLI SYNDROME

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Sir,—The Prader-Willi syndrome (PWS), generally sporadic in occurrence, is characterised by infantile hypotonia, early childhood obesity, mental deficiency, small hands and feet, short stature, and hypogonadism.[1–3] Recently, a deletion of chromosome 15 has been found in 50% of clinical diagnoses of PWS.[4]

In a clinical and cytogenetic survey of 37 PWS individuals, we have identified the interstitial deletion, based on blind studies of chromosome 15 (breakpoints q11 and q13) in 21 patients and normal chromosomes in the remaining individuals. Clinical differences between the deletion and non-deletion chromosome groups have been identified.[5,6] The mean ages at conception for 11 affected individuals in the deletion group were 30 years for the father and 27 years for the mother. The mean age of the PWS child at time of examination was 11 years.

Parental studies to determine the origin of the chromosome deletion in eleven families utilised variants affecting the satellite region of chromosome 15.[7] Short arm regions of acrocentric chromosomes are considered stable and a reasonable number of variants permits parental origin determination. These regions at or near the centromere are useful for linkage analysis because of their position and constitutive heterochromatin composition both of which preclude crossing over. The variants were identified at high resolution by sequential staining with G-banding and silver of the nucleolar organising region (NOR) or G and Q banding. In all eleven families, the chromosome 15 donated by the father was identified as the chromosome in which the deletion had occurred (table). Both sets of parents' chromosomes were normal; thus all chromosome deletions were de novo. The probability that the father would donate the chromosome resulting in the deletion in all cases in our sample by chance was less than 1 in 1000 $(½)^{11}$.

Why should the deletion affect only the chromosome donated by the father? The continued proliferation of male gametogenesis makes this stage more vulnerable to environmental insult than is female meiosis, which is arrested for a long period. If chromosome 15 is sensitive to a particular environmental agent, there may be a greater chance for chromosomal breakage to occur. One possible agent is human coronavirus. One or more loci for sensitivity to human coronavirus 229E have been identified on the long arm (qll→qter) of chromosome 15 by cell hybridisation.[8]

This finding of paternal origin of deletions in PWS suggests that other deletion syndromes be investigated to establish whether paternal origin of de novo deletions is more widespread.

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References

1. Prader A, Labhart A, Willi H. Ein Syndrom von Adipositas, Kleinwuch, Kryptorchismus and Oligophrenic nach Myatonieratigam Zustad in Neugeborcnenalter. Schweiz Med Wischr. 1956; 86:1260–61.
2. Zellweger H, Schneider HJ. Syndromes of hypotonia, hypornentia- hypogonadism – obesity (HHHO) or Prader-Willi syndrome. Am J Dis Child. 1968; 115:588–98. [PubMed: 5645106]
3. Hall BD, Smith DW. Prader-Willi syndrome. J Pediatr. 1972; 52:286–93.
4. Ledbetter DH, Riccardi VM, Airhart SD, Strobel RJ, Kennan BS, Crawford JD. Deletions of chromosome 15 as a cause of the Prader-Willi syndrome. N Engl J Med. 1981; 304:325–29. [PubMed: 7442771]
5. Butler MG, Meaney FJ, Kaler SG, Yu PL, Palmer CG. Clinical differences between chromosome 15q deletion and nondeletion Prader-Willi individuals. Am J Hum Genet. 1982; 34:119A.
6. Butler MG, Kaler SG, Yu PL, Meaney FJ. Metacarpophalangeal pattern profile analysis in Prader-Willi syndrome. Clin Genet. 1982; 22:315–20. [PubMed: 7160103]
7. Wachtler F, Musil R. On the structure and polymorphism of the human chromosome number 15. Hum Genet. 1980; 56:115–18. [PubMed: 6162775]
8. Berg K, Evans JH, Hamerton JL, Klinger H. Human Gene Mapping 6. Oslo Conference (1981); Sixth International Workshop on Human Gene Mapping. Birth Defects Orig Art Ser. 1982; 18:314.
9. Bergsma D. Paris Conference (1971): Supplement (1975): Standardization in human cytogenetics. Birth Defects Orig Art Ser. 1975; 11:6.

TABLE

PARENTAL ORIGIN OF CHROMOSOME 15 DELETION

	Age (yr)		Staining procedure									
			AgNOR			GTG			QFQ			
Proband sex	Pat	Mat	Pat	Mat	Child	Pat	Mat	Child	Pat	Mat	Child	Origin
F	27	27	-	-	-	mp/mp	sp/lp	mp*/lp	-	-	-	Pat
F	36	34	M/M	L/S	L/M*	mp/mp	lp/mp	lp/mp*	4/1	3/2	2/1*	Pat
M	22	23	M/−	S/S	M*/S	$-p^{+}$/sp	−p/−p	sp*/−p	-	-	-	Pat
M	26	26	-	-	-	sp^{-}/sp^{-}	mp/mp^{-}	sp^{-}*/mp	2/2	3/2	3/2*	Pat
M	39	30	M/M	L/S	M*/S	mp/mp	lp/mp	mp/mp*	-	-	-	Pat
M	23	21	M/M	M/−	M*/–	lp/mp	lp/−p	mp*/−p	3/3	2/1	3*/1	Pat
M	40	40	-	-	-	mp/mp	lp/sp	lp/mp*	l/1	3/1	3/1*	Pat
F	22	21	-	-	-	lp/lp	$-p^{+}$/mp	lp*/mp	4/2	1/1	4*/1	Pat
M	36	21	-	-	-	mp/sp	lp/lp	lp/sp*	3/1	5/2	5/1*	Pat
M	32	31	-	-	-	mp/mp	mp/mp	mp/mp*	2/2	4/4	4/2*	Pat
M	24	21	L/L	M/S	L*/S	lp/lp	sp/sp	lp*/sp	4/2	1/1	4*/l	Pat

The code for heteromorphisms described by AgNOR is: L = large, M = medium, S = small, − = inactive. GTG stained slides were scored for satellite stalk and short arm length (1 = long, m = medium, s = short, − = absent stalk, p^{+} = long, p = normal, p^{-} = absent p arm). QFQ stained slides were scored for satellite intensity after Paris nomenclature (1 = negative, 2 = pale, 3 = medium, 4 = intense, 5 = brilliant).

* The deleted chromosome in each case is identified by an asterisk.

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