

SHORT COMMUNICATION:

Chromosome analysis of benign expansive processes in the adrenal cortex

Luis Alberto Espinoza and Cacilda Casartelli

ABSTRACT

Chromosome analysis was performed on an adrenocortical hyperplasia and an adenoma. The most frequently observed chromosome aberrations were monosomy of chromosomes 14 (hyperplasia), 5 and 8 (adenoma). The findings were compared to those described in adrenocortical tumors.

INTRODUCTION

Hyperplasia of the adrenal cortex, the most frequent form of hyperadrenocorticism, can result either from primary overproduction of ACTH by the pituitary or by any of several common types of nonendocrine tumors (Wilson and Foster, 1985). The proliferative lesions of the adrenal cortex range from diffuse hyperplasia to benign adenoma and malignant tumor, and appear to be associated with steroidogenesis (Cotran *et al.*, 1989).

Only four studies of adrenocortical proliferation have been published so far. Limon *et al.* (1987a) described the involvement of chromosomes 3, 4, 5, 8, 9, 12, 14, 15, 18 and 20, both in numerical and in structural abnormalities, as well as hypotriploidy in a non-functional adrenocortical carcinoma. The karyotype 46,XX,t(4;11)(q35;p13) was found in all metaphases analyzed of a functional adrenocortical carcinoma (Limon *et al.*, 1987b). Marks *et al.* (1992) described an adrenocortical carcinoma with monosomy of chromosomes 5, 6, 12, 13, 15, 17, 18 and 22 and a clonal rearrangement t(1;11)(p13;q33). Della Rosa and

Vianna-Morgante (1994) found the breakpoints 8p23 and 16q12 in one adenoma.

We report here a cytogenetic study of an adrenocortical hyperplasia and an adenoma.

MATERIAL AND METHODS

Two white females, 23 and 26 years old, respectively, were diagnosed to have Cushing's syndrome and submitted to adrenal surgery. Samples were immediately minced, disaggregated mechanically, and transferred to culture flasks containing growth medium supplemented with 20% fetal bovine serum, l-glutamine and antibiotics. Primary cultures were exposed to colchicine at a final concentration of 0.01 µg/ml. The cells were then exposed to a hypotonic solution for 30 min and fixed in methanol/acetic acid (3:1). Slides were prepared and G-banded.

RESULTS

Cytogenetic analysis of the adrenocortical hyperplasia (case 1) revealed a modal chromosome

number of 46 (20.4% of the cells) in 113 cells (Table I). Chromosomes 5 and 8 were involved in clonal monosomy. Two markers were observed whose origins could not be determined.

No. of chromosomes	26	29	34	35	36	37	38	40	41	42	43
No. of cells	1	1	2	1	1	1	1	1	4	15	15
	44	45	46	47	48	49	69	76	88	89	92
	17	14	23	8	2	1	1	1	1	1	1

The chromosome study of the adrenocortical adenoma (case 2) included 48 mitotic cells. Although the modal chromosome number was 46 (15% of the cells), most of the cells were in the hypodiploid-haploid range (Table I).

No. of chromosomes	21	24	28	30	32	33	34	36	38	39	42		
No. of cels	1	1	1	1	1	2	1	2	3	2	4		
	43	44	45	46	47	48	49	62	78	81	84	89	92
	3	5	5	7	1	1	1	1	1	1	1	1	1

There was clonal monosomy fo chromosome 14 (Figure 1). Two marker chromosomes were observed. The origin of these markers could not be established. There were some almost tetraploid cells which were unsuitable for chromosome analysis.

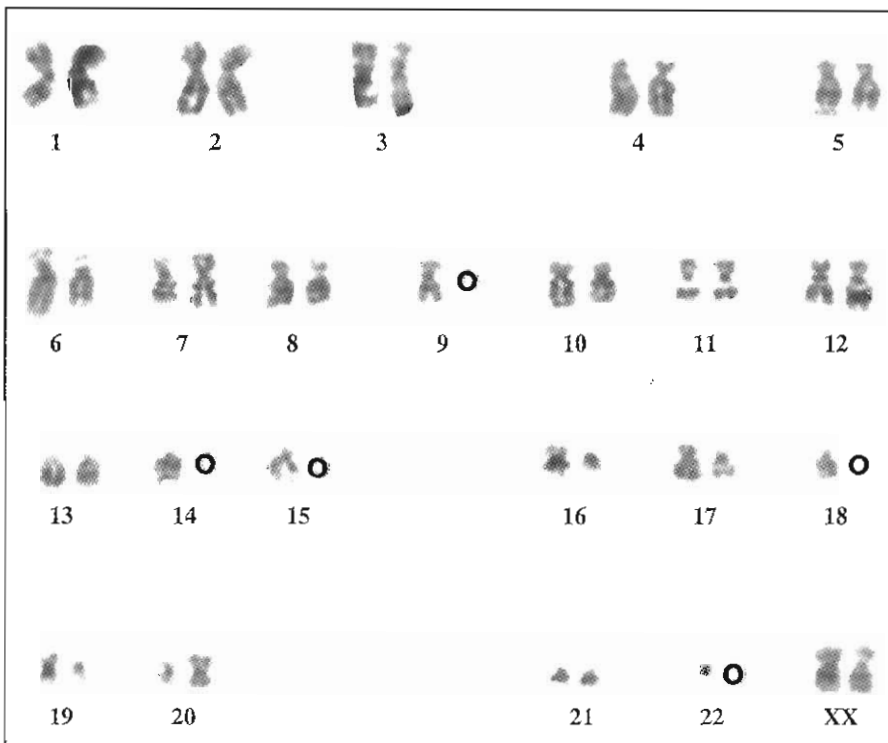


Figure 1 - Giemsa-banded karyotype of case 2, showing 41,XX, -9, -14, -15, -18, -22.

Table I - Cytogenetic distribution in two benign expansive processes of the adrenal cortex.

Cases	1	2
Variation	26-92	21-92
Haploidy (23-34)	3.5%	17%
Diploidy (35-57)	92%	71%
Triploidy (58-80)	1.8%	4%
Tetraploidy (81-103)	2.7%	8%
Modal number	46	46
Cells with modal number	20.4%	15%
Total number of cells counted	113	48

DISCUSSION

Diseases of the endocrine system may result from a vast array of pathogenetic mechanisms, leading to abnormalities in the biosynthesis and secretion of hormones, or in the interactions of hormones with specific receptors in target cells, or in postreceptor responses (Wilson and Foster, 1985). These abnormalities include the clinical appearance of a hypofunctional or hyperfunctional state. Hyperfunction can result from abnormalities of control mechanisms, with increased levels of tropic hormones or other factors leading to hyperplasia of the end organ. Thus, ACTH hypersecretion seems to play an important role in the pathogenesis of adrenal hyperplasia as well as in adrenal tumor formation (Cotran *et al.*, 1989).

Loss of chromosome 5 was described in one adrenocortical carcinoma (Marks *et al.*, 1992). In contrast to our data, chromosomes 5, 8 and 14 were involved in trisomies and marker chromosomes in two adrenocortical carcinomas (Limon *et al.*, 1987a; Marks *et al.*, 1992), and one adenoma (Della-Rosa and Vianna-Morgante, 1994). It is possible that these karyotypic findings involve genes related to cellular proliferation but not to malignant transformation. However, such anomalies may be associated with histopathologic progression, because loss or gain may represent important differences in the nature of the genic changes that play a role in the evolution of the neoplastic stemline (Nowell, 1989; Atkin and Baker, 1991). Furthermore, there is substantial evidence

for increased probability of cancerous proliferation in patients with congenital hyperplasia of the adrenal gland (Jaresch *et al.*, 1992).

Abnormalities in the cellular cycle are progressive in successive cell generations. Thus, one error tends to produce further aberrations, leading from excessive growth (hyperplasia) to malignant overgrowth, with enhanced ability to spread as well as to grow under conditions which would restrain the proliferation of unaltered cells (Studzinski, 1989). These errors are often produced by chromosome defects, particularly losses, deletions and translocations that affect cellular proto-oncogenes and are essential steps in the development and progression of neoplasms (Nowell, 1986; Bishop, 1987). It is possible that some tumor suppressor gene(s) are located in the chromosomes lost in our samples. Tumor suppressor genes contribute to oncogenicity through their loss rather than through their activation (Stanbridge, 1990; Weinberg, 1991). Thus, possible molecular events would be responsible for tumor formation and progression (Volpe, 1988; Nowell, 1989; Weinberg, 1991). Therefore, it would be of interest to compare the involvement of oncogenes and tumor suppressor genes in cascade signals for positive and negative cellular proliferation in adrenal tumors.

As few cytogenetic studies of adrenocortical tumors have been published to date, it is not possible to determine the specific chromosomal abnormalities that participate in tumorigenesis of the adrenal gland.

ACKNOWLEDGMENTS

This work was supported by CAPES, CNPq and FAPESP. We wish to thank Vanderci Massaro and Marcio R. Penha for technical assistance. We are also grateful to the Surgery Department of the Hospital das Clínicas at FMRP-USP for providing the biological material used in this work.

Publication supported by FAPESP.

RESUMO

A análise cromossômica foi realizada em uma hiperplasia e em um adenoma da supra-renal. A aberração cromossômica mais frequentemente observada foi a monossomia do cromossomo 14 (hiperplasia), 5 e 8 (adenoma). Esses achados cariotípicos foram comparados aos já descritos em tumores da supra-renal.

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(Received August 22, 1995)