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Cytogenetic Analysis of Meningiomas

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Cytogenetic analysis of 4 cases of meningiomas from 3 male and 1 female patients is reported. One of male patients suffered from neurofibromatosis type 2. Histologically, the meningiomas were meningotheliomatous (1), transitional (2), and psammomatous (1). Chromosomal abonormalities were found in all cases with a karyotype 45,XY,-22, 45,XY,-16, 45,XX,-2, and 45,XY,t (15p;22q), respectively. Monosomy of chromosome 22 was detected only in the patient with neurofibromatosis type 2.

These cytogenetic analysis demonstrates that variable clonal karyotype aberrations exist in meningiomas.

Key Words: *Meningioma, chromosomal analysis, neurofibromatosis-2*

INTRODUCTION

Extensitive cytogenetic studies of in vitro cultured meningioma cells have shown that monosomy of chromosome 22 (Cogen PH et al., 1991; Fontaine B et al., 1991; Berra B et al., 1991; Wullich B et al., 1990; Dumanski P. et al., 1990; Westphal M et al., 1989; Casartelli C et al., 1989; Poulsgard L et al., 1989) was the most consistent chromosomal aberration. It was proposed that loss of genetic material on the long arm of chromosome 22 was associated with the tumorogenesis of meningioma and the development of central neurofibromatosis (NF-2) (Mayframk L et al., 1990). In addition, various chromosomal aberrations such as loss of the Y chromosome (Logan JA et al., 1990), trisomy 7 (Westphal M et al., 1989), trisomy 3 (Casartelli C et al., 1989), translocation between chromosome 4 and 7 (Westphal M et al., 1989) or 4 and 22 (Lekanne Deprez RH et al., 1991), and deletion of chromosome 1, 4, 6, 8, 9, 14 (Casartelli C et al., 1989) were also reported.

In this paper we present an analysis of chromosomal aberrations in 4 meningiomas including a case of neurofibromatosis-2.

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MATERIAL AND METHODS

The tumor tissue in DMEM was chopped aseptically with crossed scalpels to about 1 mm cubes. The pieces were transfered into a culture flask, removed most of the fluid, and added about 5 ml DMEM with 20% fetal bovine serum. After the cells grew confluently, subculture with trypsinization was done. (Freshney RI, 1987) For chromosome studies, in vitro cultured meningioma cells derived from after 3-4 generation were used. The cells were transfered to DMEM with colcemid (1μg/ml) media, incubated for 4-8 hours, and centrifuged (1500rpm, 2min). The supernatant was discarded and the pellet was collected. After that the cells were treated with hypotonic solution (0.075M KCl, 20min) and fixed with Carnoy's fixative solution (1 part acetic acid: 3 part methanol) 3 times. The chromosomes were analyzed with GTG banding technique (Seabright M, 1971) and karyotyping described according to the international system for Human Cytogenetic Nomenclature (1981). 30 metaphases were examined per sample. Over 90% among mitotic cells revealed chromosomal aberrations.

RESULTS

Chromosomal abnormalites were found in all meningiomas. The results with pertinent informations of the

patients are summarized in Table 1. Histologically the meningiomas were transitional (2), meningotheliomatous (1) and psammomatous (1). The tumor cells in culture of the meningotheliomatous (case 3) and transitional meningioms (case 1 and 2) had a polygonal shape and formed sheets. (Fig. 1, case 2). Whether it was a neurofibromatosis-2 or not, they showed closely similar morphology. However, a psammomatous meningioma was different in terms of a spindle shape with long cellular processes and pile-up growing over adjacent tumor cells. (Fig. 1, case 4) Actual chromosomes are shown in Figure 2-3. They included losses

Table 1. Summary of Patients Studied

Case	Age/Sex	Histopathology	Location	Chromosomal Aberrations (No. of ChA[a]/No. of M[b])	Associated Lesions
1.	23/M*	Transitional	Falx	45, XY,-22 (27/30)	Bilateral acoustic neuromas, multiple intraspinal tumors, optic nerve neuroma, no family history
2.	34/M	Transitional	Right Temporal	45,XY,-16, (28/30)	—
3.	31/F	Meningotheliomatous	Right Temporal	45,XY,-2, (29/30)	—
4.	16/M	Psammomatous	Lt. retroorbital	45,XY,t(15p;22q) (28/30)	—

* : A patient of neurofibromatosis-2, a: Number of chromosomal aberrations, b: Number of metaphases

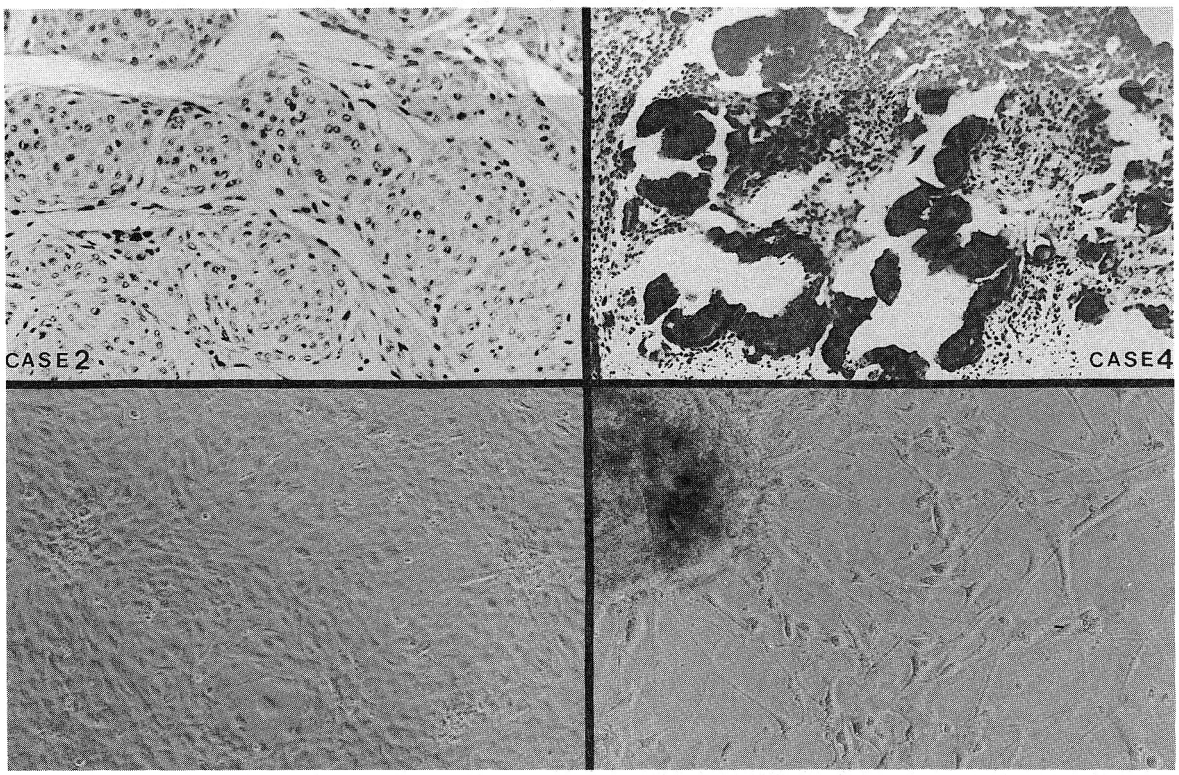

Fig. 1. Histopathologic findings and in vitro cultured tumor cells in case 2 (transitional meninigioma) and case 4 (psammomatous meningioma), respectively. (H&E X100, Inverted microscope X100)

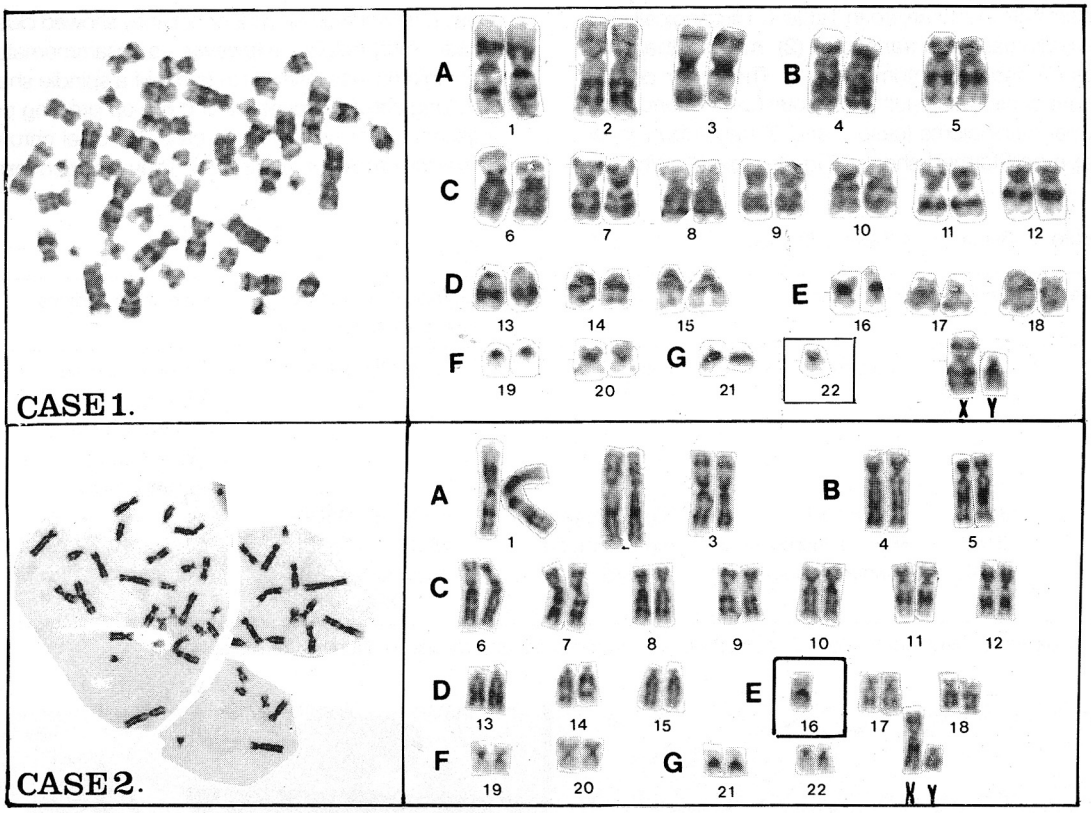

Fig. 2. G-banded karyotypes observed for case 1 of neurofibromatosis-2 and case 2. Chromosomal aberrations in square with 45, XY,-22 and 45,XY,-16, respectively.

of chromsome 22, 2, 16 and translocation between 15p and 22q. No significant difference among various histological types was found.

DISCUSSION

Greater cytogenetic variations were reported in extensive studies of meningiomas. (Cogen PH et al., 1991; Fontaine B et al., 1991; Berra B et al., 1991; Wullich B et al., 1990; Dumanski P. et al., 1990; Westphal M et al., 1989; Casartelli C et al., 1989; Poulsgard L et al., 1989). Most consistent chromosomal aberrations in chromosome 22 long arm may suggest tentative meningioma gene locus. The correlation between cytogenetic and histopathologic findings was also variable (Casalone R et al., 1990). However, meningiomas were generally hypodiploidy which appears to be correlated to a more aggressive biologic behavior. (Poulsgard L et al., 1989). As were described previously, we found several types of chromosomal aberrations, including monosomy 22, in all analyzed meningiomas, although all of our cases was benign with slow growing tendency. Interestingly, a psammomatous meningioma showd a translocation between chromosome 15 and 22 which has not described in the previous reports. We could not find any correlation between cytogenetic and histopathologic findings.

It was proposed that the pathogenesis of meningioma and neurofibromatosis-2 involved a gene located on chromosome 22 (Seizinger BR et al., 1987). Recently, it is suggested that two seperate genes are involved because neurofibromatosis-2 and meningioma have been linked with different loci in chromosome 22q; NF-2 with the centromeric and meningioma with the telomeric region (Dumanski JP et al., 1990). On one previous report (Poulsgard L et al., 1989), even most meningiomas without association of neurofibromatosis-2 revealed monosomy 22. On the other hand, our cases showed one monosomy 22 only in the patient with neurofibromatosis-2.

In conclusion, our four cases of meningiomas illustrated variable karyotypic aberrations.

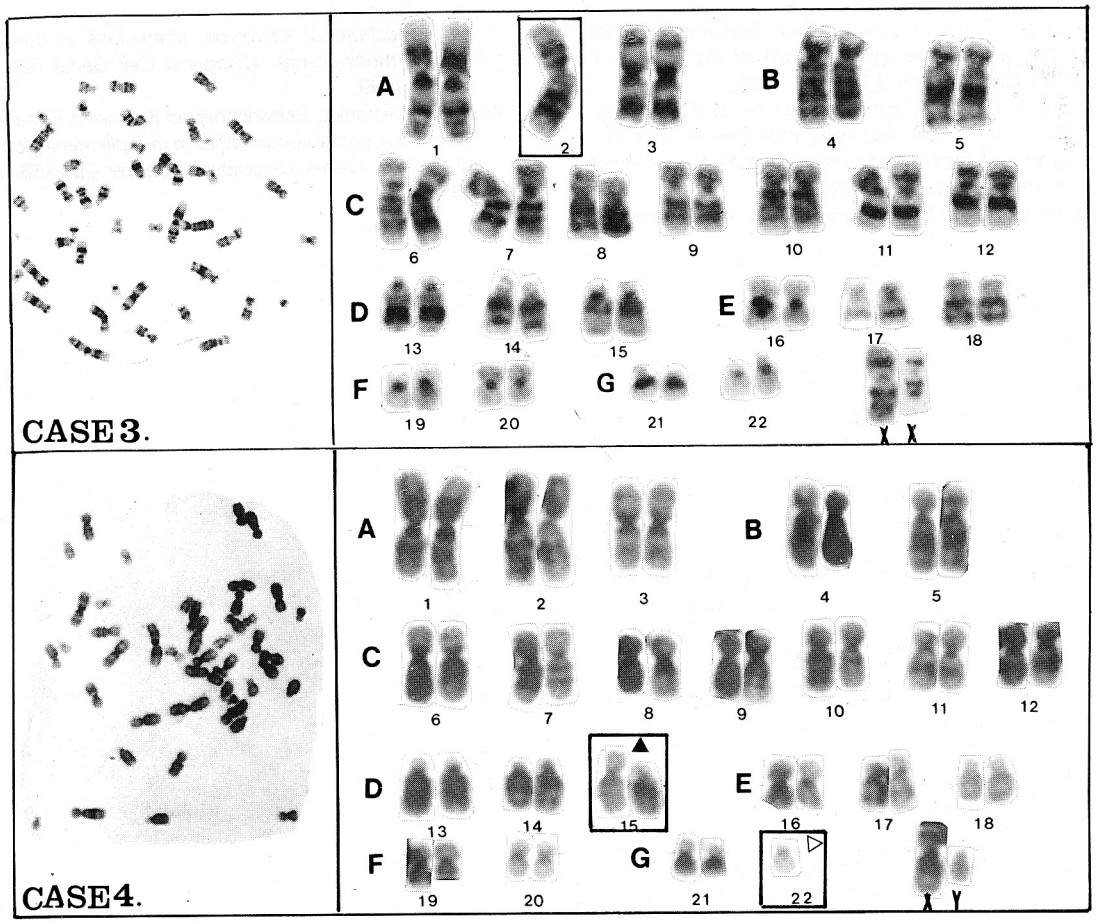

Fig. 3. G-banded karyotypes observed for case 3 and case 4. Chromosomal aberrations in square with 45,XX,-2 and 45,XY,t(15p;22q), respectively. (open arrow head: missing site of 22 chromosome, closed arrow head: translocated 22q to 15p)

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