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Hormonal Steroid Receptors in Intracranial Tumours and their Relevance in Hormone Therapy

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Abstract—*Determination of cytosolic estradiol and progesterone receptors was carried out in 30 intracranial tumors: 12 meningiomas, 13 metastases, two angioreticulomas, two gliomas and one sarcoma. The hormonal fraction found with the receptor and the dissociation constant (K_d) were determined by the Scatchard method. Values higher than 10 fmol/mg of protein were considered as positive. Ten of the 12 meningiomas (83%) showed progesterone receptors (RP), while estrogen receptors (RE) were not found in any of the cases; six of the 13 metastases showed the two types of receptors; the other tumors did not present detectable receptor levels. There was no correlation between the receptor level and patient age, sex or hormonal status. Thee results suggest the possible use of endocrine therapy for example in cases of high-risk patients or incomplete surgical resection.*

INTRODUCTION

THE DETERMINATION of estrogen and progesterone receptors (RE and RP) in mammary tumors plays an essential role in determining the treatment [1-5].

Moreover, the presence of sex steroid receptors in other neoplastic tissues [6, 7] in which the hormone dependence was not always detected such as kidney [8], pancreas [9] and more recently stomach [10] has been found.

A great number of authors [11-19] reported the presence of progesterone and(or) estradiol receptors in intracranial tumors. Even though the above-mentioned authors are in contradiction about the concentration, the presence of one or two types of receptors and their specificity [19], it was not excluded that sexual hormones could have an influence on the biological development of meningiomas and could explain, for example, the greater frequency in women than in men [20], their rapid growth during pregnancy [21, 22] and the observed association of breast cancer with meningiomas [23, 24].

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The aim of this paper is to determine the estrogen and progesterone receptor levels in 30 intracranial tumors.

MATERIALS AND METHODS

Tumor samples were taken in all cases during neurosurgical procedures, hence there was no doubt about their histopathology, and were immediately stored in liquid nitrogen.

The presence of cytosolic hormone receptors was determined by using the method recommended by the French Cancer Research Centers for human mammary tumors [25].

(1) The sample, still frozen in liquid nitrogen, was powdered in a tissue pulverizer (Thermovac) and the powder homogenized in a buffer system (10 mM Tris-HCl, 15 mM EDTA, 0.5 mM DTT, pH 7.4, room temperature).

(2) The homogenate was centrifuged at 105,000 *g* for 1 hr (Beckman L8-70); part of the supernatant was used to measure the cytosolic protein concentration by the method of Bradford [26].

(3) Aliquots of the other part were incubated overnight with increasing concentrations of tritiated estradiol (Amersham) for estrogen

receptor and promegestone (R 5020 New England Nuclear), and for progesterone receptor with and without an excess of the corresponding unlabeled hormone (to determine the non-specific binding level).

(4) After separation of the free form from the bound steroid by addition of dextran-coated charcoal and centrifugation, the supernatant was transferred into a scintillation vial containing Picofluor 15 scintillation mixture (Packard); the β activity was counted in a liquid scintillation spectrophotometer Packard Tricarb 360 CD.

(5) The data, fraction of steroid bound with the receptor and dissociation constant K_d, were analyzed according to the method of Scatchard [27]; in all cases, the linear regression was performed with six experimental points.

Values greater than 10 fmol/mg of protein were considered as positive.

RESULTS

Table 1 summarizes the clinical data (age, sex, hormonal status, nature of disease) and results obtained for the two types of receptors.

For the 12 meningiomas, in nine women and three men, all histopathologically identified, estrogen receptors were not found in any patients, while progesterone receptors were found in ten patients (83%).

For the 13 metastases (six of breast cancer, one of uterus neoplasia, two of lung carcinomas, one rectum tumor, one sarcoma and two unknown primaries), all the breast and uterus cancer metastases showed the two types of receptors; one of the two lung carcinoma metastases showed the two types at 14 fmol/mg for RE and 21 fmol/mg for RP; the last four metastases had no detectable receptors.

The two angiorecticulomas, the two gliomas and the sarcoma did not present detectable receptors.

DISCUSSION

In reference to mammary tumors which have been particularly studied [1-5], it is necessary to make some remarks upon the present results.

Meningiomas show only progesterone receptors in more than 83% of the cases, the level of cytosolic

Table 1. Clinical characteristics in relation to progesterone and estradiol receptor levels

No.	Sex	Age	Hormonal status	Nature of disease or primary tumor	Progesterone receptor Conc*	Progesterone receptor K_d†	Estrogen receptor Conc*	Estrogen receptor K_d‡
1	F	66	menopausal	meningioma	20	5.1	neg.	
2	F	61	menopausal	i.d.	neg.		neg.	
3	M	59		id.	17	4.2	neg.	
4	F	58	menopausal	id.	20	5.3	neg.	
5	F	69	menopausal	id.	15	4.7	neg.	
6	M	19		id.	neg.		neg.	
7	F	61	menopausal	id.	48	1.9	neg.	
8	F	62	menopausal	id.	38	3.6	neg.	
9	M	58		id.	17	5.0	neg.	
10	F	47	premenop.	id.	77	2.7	neg.	
11	F	63	menopausal	id.	72	1.5	neg.	
12	F	50	premenop.	id.	56	4.2	neg.	
13	F	52	premenop.	breast	24	0.2	49	0.5
14	F	61	menopausal	id.	21	1.9	14	1.7
15	F	35	ovariectom.	id.	neg.		neg.	
16	F	45	premenop.	id.	17	1.2	25	1.5
17	F	60	menopausal	id.	97	1.7	87	0.3
18	M	51		id.	17	0.9	20	0.1
19	F	52	menopausal	uterus	294	0.5	78	1.6
20	M	61		lung	21	1.9	14	1.7
21	M	52		id.	neg.		neg.	
22	F	26	premenop.	rectum	neg.		neg.	
23	M	51		sarcoma	neg.		neg.	
24	M	35		unknown	neg.		neg.	
25	M	52		id.	neg.		neg.	
26	M	70		angiorecticuloma	neg.		neg.	
27	M	62		id.	neg.		neg.	
28	M	57		glioma	neg.		neg.	
29	M	37		id.	neg.		neg.	
30	M	51		sarcoma	neg.		neg.	

*fmol/mg cytosolic proteins.
†10^{-9}M (dissociation constant), $r = -0.98$; ‡10^{-10}M, id. $r = -0.98$.

estradiol receptors being inferior to the limit of positivity in all cases; however, for the mammary tumors the case RE^- and RP^+ is only found in less than 10% of the cases (6% of the 1000 tumors treated in the Claudius Regaud Center from 1982). Since the hormone sensitivity of these types of tumors is thought to be due to the presence of RE, it seems logical to think that if meningiomas are hormone dependent, the mechanism of action is probably different.

From a quantitative point of view, the level of RP observed is never too high; its limits are between 15 and 77 fmol/mg of protein; in mammary tumors the limits are more extended. From a more fundamental aspect, the dissociation constants K_d determined by the Scatchard plot [27] were higher than 10^{-9} M for meningiomas while for mammary tumors were about 10^{-9} M; these results indicate a lower affinity of progesterone for its specific receptor in the first case. In none of the cases investigated was the presence of higher affinity receptors detected, as reported by Poisson *et al.* [12] and Chaudhury *et al.* [28].

The results of references [11-18] can be classified into four principal types: Donnell *et al.* [11] observed only RE, Poisson *et al.* [12] observed the two types of receptors in 59% of the cases, RP alone in 41% of the cases but RP in all cases. Here the presence of RE could be explained by the fact that the previous authors determined cytosolic and nuclear receptors. Schnegg *et al.* [13] did not observe RE and only RP in 40% of the patients and Vaquero *et al.* [18] observed RP in 87.7% of the patients while RE was never found to have values higher than 10 fmol/mg; our results are comparable to those of the last author.

The 13 metastases investigated only presented the two types of receptors in the cases where the primary tumor was a breast or uterus cancer and in one of the two cases where it was a lung tumor; the presence of the two types of receptors is normal in the first cases since the hormone sensitivity of mammary and uterus tumors is currently accepted [1-5].

For the other metastases, we have no reports about the presence of receptors in the primary tumors and therefore no elements to allow identification, in the metastases, of particular modifications of the receptor levels with regard to the primary neoplasia.

However, our present understanding is not sufficient to be able to state that hormonal therapy can be associated with pre- or post-neurosurgery in the strategy of meningioma treatment.

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