ORIGINAL ARTICLE

Prevalence of hypothalamic-pituitary tumours – retrospective analysis of 20-year own material

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Abstract

OBJECTIVES: The prevalence of pituitary tumours has recently been identified to be higher than previously thought. The aim of our study was to assess the occurrence of hypothalamic-pituitary tumours in 20-year material of the Department of Endocrinology and Metabolic Diseases, Polish Mother`s Memorial Hospital – Research Institute, Lodz, Poland.

METHODS: We analyzed medical data of 845 patients, hospitalized from 1990 to 2009 due to presumptive diagnosis of hypothalamic-pituitary tumour. Among 340 cases with confirmed diagnosis, 278 tumours were classified as micro- or macroadenomas. Tumour type and size, as well as patient gender and age, were evaluated. In 252 tumours the exact volume was calculated, and 4 volume subgroups were assessed for each aforementioned parameter separately.

RESULTS: Prolactinomas and – at the next place – non-functioning adenomas were the most frequent, followed by pituitary tumors of non-epithelial origin, and – finally, the rarest – other secreting adenomas. Prolactinomas were found mostly in females (p=0.028), while non-functioning adenomas in males (p=0.045). Prolactinomas and non-functioning adenomas were found to be predominantly microadenomas (p<0.0001 and p=0.0003, respectively), while mixed-type adenomas were mostly macroadenomas (p=0.028). In females microadenomas were the most frequent (p<0.0001). Moreover, in persons under 50 years of age microadenomas predominated, whereas in older adults macroadenomas mostly occurred.

CONCLUSION: To conclude, our retrospective, single-centre study provides relevant estimates of prevalence of hypothalamic-pituitary tumours in the era of modern diagnostic tools and indicates that our data are comparable with results regarding other populations worldwide.

INTRODUCTION

Hypothalamic-pituitary tumours are diverse group of neoplasms, including adenomas and tumours of non-epithelial origin. Pituitary adenomas are relatively common and include various secreting (prolactinomas, corticotropic, somatotropic, thyrotropic, and gonadotropic adenomas) and non-secreting tumours. Apart from pituitary adenomas, a number of other neoplasms may arise from within the sella, and craniopharyngiomas are the most commonly diagnosed pituitary tumours of non-epithelial origin.

Recent epidemiological studies have revealed higher incidence of pituitary tumours than previously thought (Ezzat *et al.* 2004), as consequence of the wide use of neuroradiological imaging, resulting in an increased rate of visualized incidentalomas (Sanno *et al.* 2003; Vernooij *et al.* 2007). Clinically relevant pituitary tumours presenting with disturbances of hormonal secretion (e.g. Cushing's syndrome, acromegaly) or mass effect (e.g. hypopituitarism, optic nerve compression) are less common.

In Poland, the state of knowledge about the prevalence of pituitary tumours – both overall, and with respect to particular secreting type – is still insufficient. Thus, the aim of our study was to assess the prevalence of hypothalamic-pituitary tumours in our own 20-year material of the Department of Endocrinology and Metabolic Diseases, Polish Mother`s Memorial Hospital – Research Institute, Lodz, Poland.

MATERIAL AND METHODS

In our single-centre retrospective study, we analyzed demographic data, laboratory test results and pituitary magnetic resonance imaging (MRI) findings of 845 patients, mostly from Lodz macroregion, hospitalized in the Department of Endocrinology and Metabolic Diseases, Polish Mother`s Memorial Hospital – Research Institute from 1990 to 2009, with presumptive diagnosis of hypothalamic-pituitary tumour and/or pituitary dysfunction. Three hundred and forty patients (340) (i.e. 40.2% of all the cases) with confirmed diagnosis of pituitary tumour were enrolled into further analysis (Table 1), and 278 tumours were assigned as micro- or macroadenomas (<10 mm and ≥10 mm in diameter, respectively) (2-subgroup analysis). In patients with available MRI descriptive results (252 cases), tumour volume was calculated according to the formula: 0.5× width × length × height of the tumour (Lundin & Pedersen 1992) and 4 volume subgroups (volume ≤62.5, ≤500, ≤4 000, and over 4 000 mm^3, which corresponds to diameter of 5, 10, 20 and over 20 mm, respectively) were evaluated. Each volume subgroup was divided with respect to patient`s gender, tumour type and distinct age subgroups (defined as follows: children 0–10 years, adolescents 11–18, adults 19–50 and older adults 51–87). The correlations between tumor type and both gender and age were also assessed.

Data were statistically analysed, using Student's unpaired *t* test – for continuous variables [results are presented as means ± standard error of the mean (SEM)], or the ratio comparison test – for the frequency of events. The Pearson's chi-squared (χ^2) test of independence was used to determine frequency distribution of certain events. Statistical significance was determined at the level of $p<0.05$.

RESULTS

In our study group of 340 patients, prolactinomas and non-functioning adenomas were the most frequent (36.8% and 33.2%, respectively), followed by non-epithelial tumours (18.8%; including – among others – 25 craniopharyngiomas), somatotropic (4.7%), corticotropic (3.5%), mixed cell type (1.7%), symptomatic gonadotropic (0.8%) and thyrotropic adenomas (0.2%).

The statistical difference in age distribution between genders was found; among women with pituitary tumors, there was predominance of patients from 19 to 50 years of age (Table 2). Furthermore, prevalence of particular types of tumours varied between genders,

Tab. 1. Mean values (± SEM) of age (range values shown in the square brackets) in all patients, subgrouped according to the gender. Comparison between subgroups was performed by an unpaired Student's *t*-test. There were no statistically significant differences between these subgroups ($p=0.706$).

Age [years]	**All patients** (n=340)	31.66 ± 0.93 [1–87]
	Females (n=253)	31.45 ± 1.00 [1–81]
	Males (n=87)	32.26 ± 2.18 [3–87]

Tab. 2. The overall age- and gender-specific tumour incidences. Statistical evaluation for age distribution was performed by the Pearson's χ^2 test ($\chi^2 = 8.66$, $p=0.034$) and comparison between subgroups by the ratio comparison test (*p*-values are shown in the table). The values in brackets show the percentage of each age category in the total number of cases for the given gender and for the total number of patients.

Gender	Age categories [years]				Total
	≤ 10	11–18	19–50	51–87	
Female	25 (9.88%)	40 (15.81%)	151 (59.68%)*	37 (14.62%)	253
Male	9 (10.34%)	21 (24.14%)	37 (42.53%)	20 (22.99%)	87
***p*-value**	0.500	0.224	0.031	0.226	–
Total	34 (10.00%)	61 (17.94%)	188 (55.29%)	57 (16.76%)	340

with prolactinomas found mostly in females and non-functioning adenomas mostly in males (Table 3).

Both, in the 2-subgroup and 4-subgroup (n=278 and n=252, respectively) analyses, the tumour volume depended on the tumour type (Table 4 and Table 5, respectively); prolactinomas and non-functioning adenomas were found to be predominantly microadenomas whereas mixed type tumours were mostly macroadenomas (Table 4).

In the 2-subgroup analysis, the statistical difference in tumour volume distribution between genders was demonstrated. In the female group, microadenomas were the most frequent (Table 6). However, in the 4-subgroup analysis the relationship between tumour volume distribution and patient gender was not statistically significant (Table 7).

Tumour volume distribution varied depending on age in 2- and 4- subgroup analyses (Tables 8 and 9, respectively). In patients under 50 years of age, microadenomas were predominant, whereas in older adults macroadenomas mostly occurred (Table 8).

Additionally, the prevalence of specific tumour type differed, depending on age with predominance of non-functioning adenomas and non-epithelial tumours in children; non-functioning adenomas, prolactinomas and non-epithelial neoplasms in adolescents; prolactinomas and non-secreting adenomas in adults, and non-functioning adenomas among older adults (Table 10).

DISCUSSION

The existing data on prevalence of pituitary adenomas and of other hypothalamic tumours are scant, and MRI or autopsy based series are very often discordant (Ezzat *et al.* 2004). The present study is a comprehensive evaluation of the prevalence of pituitary adenomas in a selected Polish population, which indicates general – from epidemiological point of view – age and gender correlations of those tumours.

In our analysis, prolactinomas were the most frequent pituitary tumours with significantly higher prevalence in females. The obtained results are concordant with several previous epidemiological reports (Asa *et al.* 2009; Fernandez *et al.* 2010). In the representative groups of patients from Northern Finland and Switzerland (355 and 44 cases, respectively) with confirmed diagnosis of pituitary adenoma, prolactinomas were the most frequently found (Fontana & Gaillard 2009; Raappana *et al.* 2010). Fernandez and co-workers (2010), who studied a population of well-defined geographical area of the UK [Banbury, Oxfordshire], obtained results similar to our present data. The authors demonstrated that prolactinomas were the most common of all pitu-

Table 3. Frequency of tumours in female and male patients. Statistical evaluation was performed by the Pearson's χ^2 test ($\chi^2 = 20.98$, p=0.004) and by the ratio comparison test (p-values are shown in the table). The values in brackets show the percentage of each tumour type in the total number of cases for the given gender.

Tumour	Gender		*p*-value	Total
	Female	Male		
Prl-secreting adenoma	109 (43.08%)	16 (18.39%)	0.028	125
non-functioning adenoma	74 (29.25%)	39 (44.83%)	0.045	113
non-epithelial	41 (16.21%)	23 (26.44%)	0.167	64
GH-secreting adenoma	11 (4.35%)	5 (5.75%)	0.430	16
ACTH-secreting adenoma	9 (3.56%)	3 (3.45%)	0.469	12
mixed type adenomas	5 (1.98%)	1 (1.15%)	0.448	6
LH/FSH-secreting adenoma	3 (1.19%)	0 (0%)	0.431	3
TSH-secreting adenoma	1 (0.40%)	0 (0%)	0.326	1
Total	253	87	–	340

Table 4. Relationship between tumour type and volume (two groups). Statistical evaluation was performed by the Pearson's χ^2 test ($\chi^2 = 54.32$, p<0.00001) and by the ratio comparison test (p-values are shown in the table). The values in brackets show the percentage of tumours of given volume in the total number of particular type tumours.

Tumour	Volume of the tumour		*p*-value	Total
	≤500 mm³	>500 mm³		
Prl-secreting adenoma	107 (88.43%)	14 (11.57%)	<0.00001	121
non-functioning adenoma	70 (67.96%)	33 (32.04%)	0.0003	103
non-epithelial	9 (34.62%)	17 (65.38%)	0.072	26
GH-secreting adenoma	3 (27.27%)	8 (72.73%)	0.082	11
ACTH-secreting adenoma	7 (77.78%)	2 (22.22%)	0.071	9
mixed type adenoma	1 (25.00%)	3 (75.00%)	0.026	4
LH/FSH-secreting adenoma	1 (33.33%)	2 (66.67%)	0.179	3
TSH-secreting adenoma	0 (0.00%)	1 (100%)	0.500	1
Total	198	80	–	278

itary tumours, with the prevalence of 44.4 cases per 100,000 inhabitants (Fernandez *et al.* 2010).

Additionally, we proved that the majority of tumours in females are microadenomas, which can be – at least – partially explained by the fact that prolactinomas – being dominant tumours in women – are mainly found as microadenomas. However, it seems uncertain whether this difference is not related to some kind of gender-specific tumour behavior (Ciccarelli *et al.* 2005). Apart from gender, other factors like treatment strategies may also influence the size of prolactinomas. Nevertheless, studies have shown that patients with microprolactinomas who refused treatment, revealed a low risk for progression to macroprolactinomas, therefore, they may be considered as two separate disease entities (Saeger *et al.* 2007).

Non-secreting adenomas are the second most frequent type of pituitary tumours (Daly *et al.* 2006). In our study we have confirmed high prevalence of non-functioning adenomas, being 33.2% of all pituitary adenomas, which is comparable to other recent studies, for example to the study performed on English population – 28% of all pituitary adenomas (with the prevalence of 22.2 cases per 100,000 inhabitants) (Fernandez *et al.* 2010).

In the past, the majority of non-secreting adenomas came to medical attention mostly due to symptoms and signs related to mass effect. Nevertheless, for many years, it has been known from autopsy specimens that in general population pituitary adenomas are quite common findings. Nowadays, this observation has been confirmed, due to broad availability of radiological imaging, which has allowed for detection of pituitary tumours also in asymptomatic subjects (Daly *et al.* 2009). Incidentally found non-functioning adenomas are proved to be – in the majority of cases – microadenomas, which has been confirmed in our present material, as well. It is worth to note that these tumours were mostly diagnosed in children and adolescents who were investigated in our Department mainly for short stature, related to growth hormone (GH) deficiency. In some cases, clinically non-secreting adenomas are silent adenomas, characterized by insufficient secretion of active hormones into the circulation, despite their expression (Saeger *et al.* 2007).

Finally, likewise in previous studies (Greenman *et al.* 2009; Fernandez *et al.* 2010), male preponderance of patients with non-functioning adenomas was proved.

In our material, the distribution of particular pituitary adenomas is comparable to other authors' data (Fernandez *et al.* 2010), which confirms representativeness of the enrolled population of patients. Prevalence of corticotropic and thyrotropic adenomas in our study group remained comparable to prior analyses, however somatotropic adenomas were found in smaller proportion (Asa *et al.* 2009; Fernandez *et al.* 2010; Daly *et al.* 2006; Fontana & Gaillard 2009; Raappana *et al.* 2010). Due to symptomatic course (Cushing's syndrome)

Tab. 5. Relationship between tumour type and volume (four groups). Statistical evaluation was performed by the Pearson's χ^2 test ($\chi^2 = 75.86$, $p<0.00001$). The values in brackets show the percentage of tumours of given volume in the total number of particular type tumours.

Tumour	Volume of the tumour				Total
	≤62.5 mm³	≤500 mm³	≤4000 mm³	>4000 mm³	
PrI-secreting adenoma	63 (57.80%)	34 (31.19%)	10 (9.17%)	2 (1.83%)	109
non-functioning adenoma	44 (49.44%)	20 (22.47%)	13 (14.61%)	12 (13.48%)	89
non-epithelial	4 (15.38%)	5 (19.23%)	7 (26.92%)	10 (38.46%)	26
GH-secreting adenoma	1 (9.09%)	2 (18.18%)	6 (54.55%)	2 (18.18%)	11
ACTH-secreting adenoma	6 (66.67%)	1 (11.11%)	1 (11.11%)	1 (11.11%)	9
mixed type adenoma	0 (0.00%)	1 (25.00%)	1 (25.00%)	2 (50.00%)	4
LH/FSH-secreting adenoma	0 (0.00%)	1 (33.33%)	2 (66.67%)	0 (0.00%)	3
TSH-secreting adenoma	0 (0.00%)	0 (0.00%)	1 (100%)	0 (0.00%)	1
Total	118	64	41	29	252

Tab. 6. Relationship between tumour volume (two groups) and patient gender. Statistical evaluation was performed by the Pearson's χ^2 test ($\chi^2 = 10.38$, $p=0.001$) and by the ratio comparison test (p-values are shown in the table). The values in brackets show the percentage of tumours of given volume range in the total number of cases of particular gender.

Gender	Volume of the tumour		*p*-value	Total
	≤500 mm³	>500 mm³		
Female	162 (76.06%)	51 (23.94%)	<0.00001	213
Male	36 (55.38%)	29 (44.62%)	0.211	65
Total	190	80		278

Tab. 7. Relationship between tumour volume (four groups) and patient gender. Statistical evaluation was performed by the Pearson's χ^2 test ($\chi^2 = 5.76$, $p=0.124$). The values in brackets show the percentage of tumours of given volume range in the total number of cases of particular gender.

Gender	Volume of the tumour				Total
	≤62.5 mm³	≤500 mm³	≤4000 mm³	>4000 mm³	
Female	98 (50.00%)	50 (25.51%)	27 (13.78%)	21 (10.71)	196
Male	20 (35.71%)	14 (25.00%)	14 (25.00%)	8 (14.29%)	56
Total	118	65	40	29	252

Tab. 8. Relationship between tumour volume (two groups) and patient age. Statistical evaluation was performed by the Pearson's χ^2 test ($\chi^2 = 50.40$, $p<0.00001$) and by the ratio comparison test (p-values are shown in the table). The values in brackets show the percentage of tumours of given volume range in the total number of cases of particular age category.

Age categories [years]	Volume of the tumour		p-value	Total
	≤500 mm³	>500 mm³		
≤10	21 (87.50%)	3 (12.50%)	0.002	24
11–18	40 (81.63%)	9 (18.37%)	0.00001	49
19–50	125 (77.64%)	36 (22.36%)	<0.00001	161
51–87	12 (27.27%)	32 (72.73%)	0.003	44
Total	198	80		278

Tab. 9. Relationship between tumour volume (four groups) and patient age. Statistical evaluation was performed by the Pearson's χ^2 test ($\chi^2 = 43.98$, $p<0.00001$). The values in brackets show the percentage of tumours of given volume range in the total number of cases of particular age category.

Age categories [years]	Volume of the tumour				Total
	≤62.5 mm³	≤500 mm³	≤4000 mm³	>4000 mm³	
≤10	13 (61.90%)	5 (23.81%)	1 (4.76%)	2 (9.52%)	21
11–18	24 (57.14%)	10 (23.81%)	5 (11.90%)	3 (7.14%)	42
19–50	74 (49.33%)	44 (29.33%)	17 (11.33%)	15 (10.00%)	150
51–87	7 (17.95%)	5 (12.82%)	18 (46.15%)	9 (23.08%)	39
Total	118	64	41	29	252

ACTH-secreting pituitary neoplasms are usually found as microadenomas (Weiss *et al.* 2007). Gonadotropic and somatotropic adenomas tend to be more advanced in size and usually are found as macroadenomas (Chanson *et al.* 2005; Jaffe 2006), primarily as a result of insidious course and delayed diagnosis of acromegaly.

In our series of patients, the majority of diagnosed tumours in 0–10 year old subjects presented as non-epithelial tumours, including mostly craniopharyngiomas. Craniopharyngiomas, accounting from 2 to 5% of all primary intracranial neoplasms (Parisi & Mena 1993), are mostly characterized by bimodal age distribution, with peak incidence in children (5–14 years) and adults (50–74 years), and no gender prevalence (Bunin *et al.* 1998). Their asymptomatic course explains large size and mass effect at the time of diagnosis.

Tab. 10. Relationship between tumour type and patient age. Statistical evaluation was performed by Pearson's χ^2 test ($\chi^2 = 83.78$, $p<0.00001$).

Tumour	Age categories [years]				Total
	≤10	11–18	19–50	51–87	
Prl-secreting adenoma	2 (1.60%)	16 (12.80%)	101 (80.80%)	6 (4.80%)	125
non-functioning adenoma	18 (15.93%)	28 (24.78%)	41 (36.28%)	26 (23.01%)	113
non-epithelial	13 (20.31%)	14 (21.88%)	27 (42.19%)	10 (15.63)	64
GH-secreting adenoma	0 (0.00%)	1 (6.25%)	8 (50.00%)	7 (43.75%)	16
ACTH-secreting adenoma	1 (8.33%)	2 (16.67%)	5 (41.67%)	4 (33.33)	12
mixed type adenoma	0 (0.00%)	0 (0.00%)	4 (66.67%)	2 (33.33%)	6
LH/FSH-secreting adenoma	0 (0.00%)	0 (0.00%)	1 (33.33%)	2 (66.67%)	3
TSH-secreting adenoma	0 (0.00%)	0 (0.00%)	1 (100%)	0 (0.00%)	1
Total	34	61	188	57	340

Our study revealed the preponderance of microadenomas in younger patients, while in older adults macroadenomas were the most common. This observation may be explained by domination of prolactinomas – which are proved to be mostly microadenomas – in younger subjects (Mindermann & Wilson 1994), or – simply – by the fact that macroadenomas in older patients were diagnosed at the advanced stage of the disease, after long time period of slow progression from micro- to macrodenomas.

In conclusion, management of hypothalamic-pituitary tumours is an important issue for multidisciplinary team of specialists. Interestingly, the tumour size and clinical features may point to specific aspects in the pathogenesis of certain pituitary adenomas. Such classifications may improve the diagnosis and therapy even for rare types of pituitary adenomas. Our retrospective, single-centre study provides relevant estimates of prevalence of hypothalamic-pituitary tumours in the era of modern diagnostic tools and indicates that our data are comparable with results regarding other populations worldwide.

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