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Pituitary incidentalomas: analysis of a neuroradiological cohort

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Abstract
Purpose Most pituitary lesions are detected during the investigation of symptoms associated with hormonal dysfunction and vision abnormalities. When the lesion is identified in an image performed for reasons not related to the tumor, the term incidentaloma applies. Our aim was to describe the diagnosis behind pituitary incidentalomas, patient characteristics and their follow up.
Methods We searched for the terms «pituitary», «hypophysis» and «incidentaloma» in the requisitions and reports of all CTs and MRIs performed between 1st September 2008 and 30th October 2013. We retrieved demographic data as well as information regarding presentation and follow-up.
Results We detected 71 pituitary incidentalomas, 3 in children/adolescents. In adult patients, mean age was 51.6 ± 18.46 years and 42 were female (61.8 %). The most frequent reason for imaging was headache (33.8 %). The image that first detected the incidentaloma was CT scan in 63.2 and 17.6 % patients presented symptoms that could have led to earlier diagnosis. Pituitary adenoma is the most prevalent lesion (*n* 48; 70.6 %), followed by Rathke's cleft cyst (*n* 9; 13.2 %). Hormonal evaluation revealed hypopituitarism in 14 patients and hypersecretion in 6: 5 prolactinomas and 1 somatotroph adenoma. Twenty-one (28.8 %) patients underwent surgery and there was no malignancy.
Conclusions In concordance with available literature, adenomas are the most frequent incidentally found pituitary lesions. Hormonal dysfunction is quite prevalent, including symptomatic presentations, which suggests that there seems to be a low sensitivity for the diagnosis of pituitary disease.

Keywords Pituitary · Incidentaloma · Adenoma · Hormonal dysfunction · Headache

Introduction

An incidentaloma is a mass lesion, serendipitously noted during radiological evaluation performed for other reasons than the detection of that mass. Incidentalomas of various endocrine glands are a relatively recent health issue and its increasing prevalence in clinical practice is in association with the development of imaging techniques, such as CT scanning and MRI [1]. Notwithstanding, the prevalence of pituitary incidentalomas in large autopsy series was approximately 20 % in unselected patients both in 1936 and 1995 [2, 3], ranging from 1.5 to 27.0 % if all major series are included [4]. The Endocrine Society guidelines [5] defines pituitary incidentaloma as a previously unsuspected pituitary lesion discovered on an imaging study performed for an unrelated reason, thereby excluding patients under investigation due to visual loss attributable to the tumor and/or manifestations of hormone deficit or excess. More than 90 % of pituitary incidentalomas are reported to be

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adenomas, although the prevalence depends on criteria of inclusion [5–7]. According to Sanno et al. [8] 13.3 % of incidentalomas increased in size during a mean follow of 45.5 months, of which a third were microadenomas, while Donovan [9] reported that only patients with macroincidentalomas, defined as lesions more than 10 mm, have any risk of enlargement. More recently, growth of incidentalomas was estimated to occur in 10 % of microadenomas and 24 % of macroadenomas [10]. Hypopituitarism is present in 41.3 % of patients [7] and, according to the same authors, immunohistochemical analysis revealed plurihormonal non-secreting adenomas in 40 % and null cell adenomas in 30 %.

The aim of this study was to describe, in daily clinical practice, the reasons that led to the detection of incidentalomas in our hospital, characterize the patients regarding demographic and clinical variables, describe the follow up period, and histologic findings if surgery was performed.

Methods

This was a retrospective, observational study. We searched the Neuroradiology Unit database for the terms «hypophysis», «pituitary» and «incidentaloma», in every imaging requisition and report over the period comprised between 1st September 2008 and 30th October 2013. We considered incidentaloma as every pituitary lesion discovered while investigating nonrelated ailments, as proposed by the Endocrine Society Guidelines [5]. The incidental pituitary findings in our study were all diagnosed on the basis of imaging, but the imaging characteristics of all lesions were typical and considered diagnostic. We excluded empty sella turcica and imaging abnormalities unconfirmed in subsequent exams and patients whose reason that led to MRI/CT was not clear in the medical records. We collected demographic, clinical, presentation and follow up data from clinical records. Hormonal dysfunction was determined by analysis of laboratory results and/or statement of dysfunction in the patient records. Patients under follow up by Endocrinologists in our institution usually undergo basal hormone measurements: prolactin, ACTH, morning cortisol, urinary free cortisol, IGF-1, FSH, LH, total testosterone/estradiol, TSH and free T4 levels. If it is unclear whether they have hormonal dysfunction, they may also undertake dynamic testing with insulin tolerance and TRH/LHRH tests. Pathological confirmation of presumed pituitary adenomas was obtained when surgery was performed. Variation in size in subsequent imaging was considered as a reduction or increase in 1 mm in any axis. All images were reviewed by the same Neuroradiologist. Statistical analysis was made with IBM SPSS Statistics 20.0© and we used Chi-square and Mann–Whitney tests when applicable. Statistical significance was considered for a p value <0.05. Data is presented as frequencies and mean ± SD (minimum–maximum).

Results

During the study period 1232 patients from all hospital departments underwent imaging in accordance with the specified criteria. We detected 71 pituitary incidentalomas, which accounts for a prevalence of 5.8 %. Twenty-eight (39.4 %) patients were male and 43 (60.6 %) female. Three patients were children, with mean age 7.7 ± 6.81 years (0.0–13.0), diagnosed with Rathke's cleft cyst (n 2) and craniopharyngioma (n 1).

The remaining analysis refers solely to adults. Among these, mean age was 51.6 ± 18.46 years (18.0–86.0 years) and 42 (61.8 %) were female. The mean follow-up time was 3.2 ± 1.34 years. The reasons that led to the requisition of the first CT/MRI are described in Table 1—with headache being the most prevalent (33.8 %).

The imaging technique that first documented the presence of a pituitary incidentaloma was CT scan in 63.2 % of the patients and 15.1 % of them had no documented imaging reevaluation.

Pituitary adenoma is the most prevalent diagnosis in our series, accounting for 70.6 % of cases—Table 2. Among pituitary adenomas, 18 (37.5 %) were microadenomas and 30 (62.5 %) were macroadenomas. Mean size of incidentalomas was 14.2 ± 10.49 (1.5–49.5) mm. Men had larger lesions than women (19.9 ± 12.95 vs 10.9 ± 7.12 mm; $p = 0.011$), a higher likelihood of being diagnosed with adenomas (88.5 vs 59.5 %; $p = 0.010$) and, among these, presented more often with macroadenoma (78.3 vs 48.0 %; $p = 0.030$). Four patients presented with imagiological signs of hemorrhage.

Table 1 Reasons which led to the requisition of MRI or CT

	n (%)
Headache	23 (33.8)
Neurological signs	14 (20.6)
Trauma	7 (10.3)
Vertigo/tinnitus/hypoacusis	6 (8.8)
Dementia/behavioural disturbance	3 (4.4)
Visual disturbance not related to the tumor	2 (3.0)
Unrelated galactorrhea	1 (1.5)
Vertebral column symptoms	1 (1.5)
Other diseases of the CNS	2 (2.9)
Other reasons	9 (13.2)
Total	68 (100.0)

Table 2 Diagnosis of pituitary incidentalomas

Diagnosis	*n* (%)
Adenoma	48 (70.6)
Microadenoma	18 (37.5)
Macroadenoma	30 (62.5)
Rathke's cleft cyst	9 (13.2)
Pituitary hyperplasia	5 (7.3)
Meningioma	2 (3.0)
Astrocytoma	1 (1.5)
Undetermined cystic lesion	3 (4.4)
Total	68 (100.0)

Table 3 Histology and immunohistochemistry results

	n (%)
Adenoma—FSH and/or LH	9 (45.0)
Null cell adenoma	5 (25.0)
Adenoma—FSH, prolactin and TSH	1 (5.0)
Adenoma—prolactin	1 (5.0)
Adenoma—somatotroph	1 (5.0)
Papillary meningioma	1 (5.0)
Pilocytic astrocytoma	1 (5.0)
Normal pituitary gland	1 (5.0)
Total	20 (100.0)

Six patients had absolutely no record of pituitary function evaluation and five had only thyroid function requested for other reasons during follow-up, although among these patients 4 had confirmed macroincidentalomas. Endocrinological evaluation revealed hormonal hypersecretion in six patients (8.8 %): five prolactinomas (three women and two men) and one somatotroph adenoma. Hypopituitarism was present in 14/56 patients (25.0 %), but, as stated, not all patients were submitted to testing. Ten patients in 54 had hypogonadism (18.5 %), 9 in 53 had hypocortisolism (16.7 %), 8 in 62 had hypothyroidism (12.9 %) and 7 in 50 had growth hormone deficiency (14.0 %). The diagnosis of macroadenoma was associated with a higher prevalence of hypopituitarism than microadenomas (45.2 vs 0.0 %; $p = 0.000$).

Twelve patients presented with symptoms that could have led to an early diagnosis: erectile dysfunction (*n* 9), asthenia (*n* 7), weight loss (*n* 5) and galactorrhea/oligomenorrhea (*n* 3). Twenty-nine patients had no reference to symptoms in the records.

Regarding visual impairment, among 21 patients with macroadenoma that had formal visual field testing, 4 patients presented abnormalities.

Five patients, all of them with prolactinoma, had medical treatment with dopamine agonists: 3 with bromocriptine and 2 with cabergoline. Another 11 patients were being treated with hormone replacement for hypopituitarism. Twenty-one patients (30.9 %) underwent surgery and 3 (4.4 %) were treated with adjuvant radiation therapy. Histology and immunohistochemical results are described in Table 3, excluding one case of cystic fluid aspiration. There were no cases of malignancy. Among individuals with pre-operative hypopituitarism (*n* 9/19) one had resolution of hormonal dysfunction, and among individuals with no pre-operative hypopituitarism one had de novo hormonal dysfunction. Among individuals with pituitary adenoma, men were more likely to undergo surgical management (57.1 vs 25.0 %; $p = 0.029$). Symptomatic patients also had a higher likelihood of surgical or medical therapy (53.8 vs 18.5 %; $p = 0.004$) although there was not a significant association between headache and surgery when analyzed separately ($p = 0.415$). Twenty (76.9 %) incidentalomas managed conservatively with available imaging reevaluation (*n* 26) had no variation in size during follow up and only 1 (3.8 %) increased in size. Among macroincidentalomas in this group (*n* 12) eight had no change and three had a reduction in size. One macroincidentaloma had an increase in size, corresponding to a meningioma. Among microincidentalomas (*n* 14) 2 had a reduction in size.

Discussion

The prevalence of pituitary incidentalomas in our series was 5.8 %, somewhat lower than described by Famini et al. [12]—10.8 %. This slight difference might relate to the methodology used, i.e., all images (MRI or CT) that had included a reference to the pituitary gland in the requisition and/or report versus pituitary MRIs. On the other hand, the macroadenoma prevalence in our series is 2.4 %, similar to the prevalence reported by Famini [12] (3.4 %) but significantly higher than stated by Vernooij et al. [17], who involved a population-based cohort and found macroadenomas in 0.3 %. These data suggest that the prevalence of macroadenomas is considerably higher in the healthcare setting than in population based studies.

As previously described, headache is the most frequent reason for requisition of cerebral imaging. In light of recent data on the causes of headaches in these patients [11] it might be reasonable to argue against including headache in pituitary incidentaloma series, as there may be a causal relation with this symptom, as suggested by a high prevalence of improvement after surgery and the larger size of incidentalomas in series based in clinical practice comparing with autopsy series [4]. Contrary to previously

thought, the mechanism through which pituitary lesions may be related to headache is not necessarily associated with mechanical aspects, but also with hormonal hypersecretion and local inflammation [11]. In spite of this, in our series, the presence of symptoms in adenoma patients is associated with the need for surgical/medical therapy but not when headache was analyzed separately, suggesting a low likelihood of causal association of the latter with pituitary disease.

The considerable prevalence of hormonal dysfunction associated symptoms at presentation suggests a low index of suspicion for pituitary disease by health professionals or a low importance attributed to those symptoms by patients, which might be particularly prevalent for erectile dysfunction.

The prevalence of adenomas in our series was 70.6 %, lower than usually described [5, 6] although higher than described by Famini et al. [12], that found 154 adenomas among 282 incidentalomas (prevalence 54.6 %), but included non-neoplastic lesions.

Hypopituitarism had a considerable prevalence, although a substantial number of patients was not hormonally evaluated. Many of these patients had a pituitary incidentaloma that was overlooked by physicians from specialties other than Endocrinology or Neurosurgery. Notwithstanding, the prevalence of hypopituitarism in our series is within that previously reported: 13–46 % [7, 13–15].

Prolactin is the most frequent hormone in hypersecretory dysfunction, similarly to previous reports [7, 12], and there was also one case of growth hormone secretion, highlighting the importance of biochemical testing in incidental adenomas, as stated in the Endocrine Society guideline [5]. One should note that a significant number of patients had no imaging reevaluation, as these findings are frequently neglected by physicians, particularly from other specialties. However, we could not exclude functional or imaging studies in other health care units, in patients that were lost to follow up.

Men had a higher likelihood of undergoing surgery, in relation with a higher prevalence of non-functioning macroadenomas. Gender differences regarding incidentaloma size aren't usually mentioned in most series, although Fainstein et al. [7] mentioned similar findings. Such difference may also explain the increased prevalence of hypopituitarism among men and might be related to a greater time lag to diagnosis due to less frequent reference to headache than women [16] or overlooking of erectile dysfunction as a clinically relevant sign in our society.

Increase in size of incidentalomas seemed to be a rare event in our series compared to previous data [4], but a short follow up duration was an important limitation of our study regarding tumor growth.

Conclusions

In general, pituitary incidentalomas have a benign course but there is a high prevalence of clinically significant lesions. Beyond hypersecreting adenomas, whose treatment might prevent future comorbidities, most cases of hypopituitarism must be corrected, particularly the ones involving adrenal and thyroid axis deficiency, and visual field defects must be promptly resolved. The prevalence of pituitary incidentalomas seems to be high in the healthcare setting. A significant number of pituitary incidentalomas wasn't formally evaluated as such, revealing lack of awareness for this clinical problem among physicians. Increased physician training on pituitary disease is paramount.

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Soule SG, Jacobs HS (1996) The evaluation and management of subclinical pituitary disease. Postgrad Med J 72:258–262
2. Costello RT (1936) Subclinical adenoma of the pituitary gland. Am J Pathol 12(2):205–216
3. Teramoto A, Hirakawa K, Sanno N, Osamura Y (1994) Incidental pituitary lesions in 1000 unselected autopsy specimens. Radiology 193:161–164
4. Molitch ME (2009) Pituitary incidentalomas. Best Pract Res Clin Endocrinol Metab 23:667–675
5. Freda PU, Beckers AM, Katznelson L et al (2011) Pituitary incidentaloma: an Endocrine Society Clinical practice guideline. J Clin Endocrinol Metab 96:894–904
6. Scangas GA, Laws ER (2014) Pituitary incidentalomas. Pituitary 17(5):486–491
7. Fainstein Day P, Guitelman M, Artese R et al (2004) Retrospective multicentric study of pituitary incidentalomas. Pituitary 7(3):145–153
8. Sanno N, Oyama K, Tahara S, Teramoto A, Kato Y (2003) A survey of pituitary incidentaloma in Japan. Eur J Endocrinol 149:123–127
9. Donovan LE, Corenblum B (1995) The natural history of the pituitary incidentaloma. Arch Intern Med 155(2):181–184
10. Daly AF, Burlacu MC, Livadariu E, Beckers A (2007) The epidemiology and management of pituitary incidentalomas. Horm Res 68(suppl 5):195–203
11. Kreitschmann-Andermahr I, Siegel S, Weber Carneiro R et al (2013) Headache and pituitary disease: a systematic review. Clin Endocrinol 79:760–769
12. Famini P, Maya MM, Melmed S (2011) Pituitary magnetic resonance imaging for sellar and parasellar masses. Ten-year experience in 2598 Patients. J Clin Endocrinol Metab 96(6):163–1641
13. Igarashi T, Saeki N, Yamaura A (1999) 1999 Long-term magnetic resonance imaging follow-up of asymptomatic sellar tumors—their natural history and surgical indications. Neurol Med Chir (Tokyo) 39:592–598
14. Dekkers OM, Hammer S, de Keizer RJ et al (2007) The natural course of nonfunctioning pituitary macroadenomas. Eur J Endocrinol 156:217–224

15. Karavitaki N, Collison K, Halliday J et al (2007) What is the natural history of nonoperated nonfunctioning pituitary adenomas? Clin Endocrinol (Oxf) 67:938–943
16. Steiner TJ, Stovner LJ, Katsarava Z et al (2014) The impact of headache in Europe: principal results of the Eurolight project. J Headache Pain 15(1):31
17. Vernooij MW, Ikram A, Tanghe HL et al (2007) Incidental findings on brain MRI in the general population. N Engl J Med 357:1821–1828