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Review article

The clinical characteristics and microsurgical therapy of pituitary adenomas in elderly patients: A retrospective study of 130 cases

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ABSTRACT

Objective: To investigate the clinical characteristics and microsurgical therapy of pituitary adenomas in elderly patients.
Method: This article describes a retrospective study of 130 pituitary adenomas in elderly patients over 65 years of age who underwent a microsurgical operation using the transsphenoidal approach and were admitted to Peking Union Medical College Hospital (PUMCH) from January 2010 to December 2012.
Results: A total of 60 (46.2%) males and 70 females (53.8%) were included, and the mean age of the patients was 68.38 years. The main clinical manifestation was visual defects (35.4%), and the levels of growth hormone (GH), insulin-like growth factor-1 (IGF-1), adrenocorticotropic hormone (ACTH), and prolactin (PRL) were increased by 11.5%, 11.5%, 6.2%, and 7.7%, respectively. All patients underwent the transsphenoidal approach. The main comorbidity prior to surgery was hypertension (45.0%), and the average duration of follow-up was 39.6 ± 10.6 months. Tumor recurrence was observed in 19 patients, 17 of which received radiological therapy, and two patients underwent an additional operation at our hospital. The rate of loss to follow-up was 15.9%.
Conclusion: There was no significant difference in the surgical outcome, mortality in the perioperative period or complications between the elderly patients and the general population. However, the indications for pituitary adenomas in elderly patients still require further age-specific guidelines.

1. Introduction

Pituitary adenomas arising from adenohypophyseal cells have a prevalence of approximately 1/100,000, and they are one of the most frequently occurring intracranial tumors. Pituitary adenomas can be either endocrine or non-endocrine and are classified into functioning and non-functioning types. Most of the sellar region masses are benign, except for pituitary metastases. Many of the tumors are invasive or aggressive, multi-recurrent and resistant to therapies such as surgery and radiotherapy. Different types of tumors present not only with abnormal GH, PRL, ACTH, follicle-stimulating hormone (FSH)/luteinizing hormone (LH), thyroid-stimulating hormone (TSH), testosterone (T), estradiol 2 (E2), and progestational hormone (P) levels but also show multiple clinical manifestations, such as visual defects, anterior pituitary gland dysfunction, diabetes insipidus, postorbital pain, ophthalmoplegia, and others [1]. In this study, we detected the clinical characteristics, treatment methods, and prognosis of pituitary adenoma patients over 65 years old. The tumors were classified according to size (micro, macro and giant), type (PRL, GH, FSH/LH, ACTH, TSH, etc.) and grade (Knosp 1/2/3/4) through the use of pituitary magnetic resonance imaging (MRI) to diagnose cavernous or sphenoid sinus invasion and immunocytochemistry to conduct the pathology tests and measure cell cycle markers (Ki-67, mitosis) and p53 staining.

2. Methods

This study was a retrospective study of pituitary adenoma patients over 65 years old who were examined at PUMCH between January 2010 and December 2012 (due to the need to schedule follow-up for at least 36 months, we chose the patients examined

Abbreviations: GH, growth hormone; IGF-1, insulin-like growth factor-1; ACTH, adrenocorticotropic hormone; PRL, prolactin; PUMCH, Peking Union Medical College Hospital; TSS, transsphenoidal surgery; IHD, ischemic heart disease; COPD, chronic obstructive pulmonary disease; MRI, magnetic resonance imaging.

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during this period). A total of 130 patients underwent transsphenoidal surgery (TSS), and pituitary MRI and laboratory tests were conducted before and after the operation. The patients were seen for a follow-up visit 3 days, 1 month, 3 months, 6 months, 12 months, 24 months and 36 months after surgery, and the clinical manifestations, laboratory test results, radiology findings, and prognosis were recorded.

3. Results

3.1. General statement

In total, 60 males (46.2%) and 70 females (53.8%) were enrolled in the study; the average age of the males was 68.35 years, whereas that of the females was 68.41 years. In addition, there were no significant differences in the age or the number of participants between the males and females.

3.2. Clinical presentation

Of the 130 patients, 46 cases (35.4%) experienced visual defects, 42 cases (32.3%) experienced headache, 15 cases (11.5%) exhibited acromegaly, 11 cases (8.5%) exhibited vomiting and nausea, 8 cases (6.2%) exhibited Cushing disease, 3 cases (2.3%) exhibited polyuria and polydipsia, 2 cases (1.5%) exhibited central hypothyroidism, 1 case (0.8%) exhibited palpitations and irritability, 2 cases (1.5%) exhibited chills, and 23 cases (17.7%) experienced other manifestations such as anepithymia, sexual dysfunction, eyelid ptosis, absence of the pupillary light reflex, and eyeball movement disorder. There were 8 asymptomatic patients (6.1%) (Table 1). A total of 105 cases (80.9%) were clinically diagnosed with non-functioning pituitary adenomas, 15 cases (11.5%) were diagnosed with GH-secreting pituitary adenomas, 8 cases (6.1%) were diagnosed with ACTH-secreting pituitary adenomas, and 1 case (0.8%) was diagnosed with TSH-secreting pituitary adenomas.

3.3. Radiology

In total, 130 patients underwent MRI, and the average diameter of the tumors was 26.04 ± 10.72 mm, whereas the maximum diameter was 56 mm. In addition, 15 cases (11.5%) were microadenomas (maximum diameter < 10 mm), 85 cases (64.9%) were macroadenomas (10 mm ≤ maximum diameter < 30 mm), and 30 cases (23.1%) were giant adenomas (maximum diameter ≥ 30 mm). Furthermore, 58 cases (44.6%) had invaded the cavernous sinus, 13 cases (10.0%) had a compressed pituitary stalk, and 77 cases (59.2%) had a compressed optic chiasma. The cases were further divided into the 4 Knosp grades, and 18 cases (13.8%) were Grade 0, 18 cases (13.8%) were Grade 1, 46 cases (35.5%) were Grade 2, 12 cases (9.2%) were Grade 3, and 36 cases (27.7%) were Grade 4. Moreover, 48 cases (36.9%) were invasive adenomas (Table 2), and 18 cases (13.8%) were combined with pituitary apoplexy.

Table 1
Clinical manifestations of the 130 patients.

Manifestation	No. of cases (%)
Visual defects	46 (35.4%)
Headache	42 (32.3%)
Acromegaly	15 (11.5%)
Vomiting and nausea	11 (8.5%)
Palpitations and irritability	1 (0.8%)
Cushing disease	8 (6.2%)
Polyuria and polydipsia	3 (2.3%)
Central hypothyroidism	2 (1.5%)
Chills	2 (1.5%)
None	8 (6.2%)
Others	23 (17.7%)

3.4. Laboratory tests

The levels of free triiodothyronine (FT3), free tetraiodothyronine (FT4), triiodothyronine (T3), tetraiodothyronine (T4), TSH, PRL, GH, IGF-1, FSH, LH, E2, T, P, ACTH, and cortisol (F) were assessed in all of the patients before the operation. The results are shown in Tables 3 and 4.

3.5. Surgery

In this study, 130 patients underwent TSS. Of them, 87 cases (66.9%) underwent a total resection, 15 cases (11.6%) underwent a subtotal resection (resection of more than 90% of the tumor), and 28 cases (21.5%) underwent a partial resection (resection or more than 50% of the tumor). Nine patients (6.9%) had a leakage of cerebrospinal fluid during the operation that was immediately repaired. The average amount of bleeding among all of the operations was less than 100 mL.

3.6. Pathology

All patients underwent a pathology biopsy and immunohistochemical staining. A total of 105 cases (80.8%) were verified to be non-functioning pituitary adenomas, 15 cases (11.5%) were GH-secreting pituitary adenomas, 8 cases (6.2%) were ACTH-secreting pituitary adenomas, 1 case (0.8%) was a TSH-secreting pituitary adenoma, and 1 case (0.8%) was a multi-secreting pituitary adenoma (Table 5). The Ki-67 index was also detected. The results showed that the Ki-67 index was <1% in 30 cases (23.1%), ≥1% and <3% in 88 cases (67.6%), ≥3% and <5% in 11 cases (8.5%), and ≤5% in 1 case (0.8%) (Table 6). Furthermore, 6 cases (4.6%) were positive for p53.

3.7. Outcomes

The patients' clinical manifestations and laboratory test results were also observed after the operation. The visual defects improved in 33 cases (71.7%). A total of 15 patients had acromegaly before the operation; however, 3 days after the operation, GH testing showed that the level of growth hormone was less than 1.0 ng/mL in 9 cases. Furthermore, 8 patients were diagnosed with pituitary ACTH-secreting pituitary adenomas, and the levels of ACTH and F were reviewed 3 days after the operation. Of those patients, the levels of ACTH and F had decreased to normal in5 cases (62.5%), whereas the levels in 3 cases (37.5%) had decreased but not to within the normal range. Finally, 18 cases (13.8%) showed hypopituitarism before the operation, and 6 of these patients (33.3%) returned to normal immediately after surgery.

3.8. Comorbidities and complications

A total of 59 cases (45.4%) were also diagnosed with hypertension before the operation, 24 cases (18.5%) with ischemic heart dis-

Table 2
Knosp grade of the 130 patients.

Knosp grade	No. of cases (%)
Knosp 0	18 (13.8%)
Knosp 1	18 (13.8%)
Knosp 2	46 (35.5%)
Knosp 3	12 (9.2%)
Knosp 4	36 (27.7%)
Invasion	48 (36.9%)

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