

임상적 비기능성 뇌하수체 종양의 미세현미경적 가성피막의 제거

연세대학교 의과대학 신경외과학교실 김병우, 심유식, 장종희, 안정용, 김선호

Microsurgical Pseudocapsule Resection of Clinically Non-functioning Pituitary Tumors

Department of Neurosurgery, Brain Research Institute, Yonsei University College of Medicine, Seoul, Korea
Byeong Woo Kim, Yu Shik Shim, Jong Hee Chang, Jung Yong Ahn, Sun Ho Kim

교신저자 안정용

논문 접수일 : 2008년 5월 21일
심사 완료일 : 2008년 6월 23일
주소 : 135-720 서울시 강남구 도곡동 146-92
연세대학교 의과대학 영동세브란스병원
신경외과
전화 : 02-2019-3391
전송 : 02-3461-9229
E-mail : jyahn@yuhs.ac

Objective : The aim of this study was to investigate the precise histological characteristics of the boundary, using surgical specimens from patients who underwent intensive resection of “microsurgical pseudocapsule” of clinically non-functioning pituitary tumors (CNPTs). Furthermore, we compared the remission rate of CNPTs between subjects with (Group 1) and without (Group 2) intensive resection of microsurgical pseudocapsule in order to correlate the histological complete resection and endocrinological remission.

Patients and Methods : Between January 2000 and December 2007, 113 patients underwent intensive microsurgical dissection during the transsphenoidal surgery in one hospital (Group 1). In the other hand, 24 patients underwent conventional subcapsular resection without intentionally removing the microsurgical pseudocapsule in another hospital (Group 2).

Results : The overall surgical remission rate in Group 1 with intensive resection of microsurgical pseudocapsule were statistically higher than the rates in Group 2 (without intensive resection of microsurgical pseudocapsule) ($p=0.032$). However, there were no statistical differences in postoperative hormonal function change between Group 1 and 2.

Conclusions : Our results indicate that aggressive resection of psuedocapsules increases the cure rate without aggravating pituitary function.

Key Words Pituitary tumors, Pseudocapsule, Transsphenoidal surgery, Remission.

Introduction

Although the presence of a histological pseudocapsule around pituitary tumors was noted in the early 1900s,² how the pseudocapsule is formed and the histological characteristics of the pseudocapsule have not been clarified until now. In addition, terminology expressing the boundary of pituitary adenomas is unclear. Some researchers reported that pseudocapsule is originated from the condensation of the basement membranes of compressed peritumoral cell cord.³ On the other hand, some investigator reported that the boundary between the adenoma and the pituitary gland consisted of fibrous tissue originated from the normal pituitary gland, and regarded the boundary as a pseudocapsule.

To describe clearly the boundary zone, we define a “true pseudocapsule” as a definitive capsule-like structure identifiable histologically, and a “microsurgical pseudocapsule” as a peritumoral structure distinguishable intraoperatively under an operating microscope. In this study, we studied the precise histological characteristics of the boundary, using surgical specimens from patients who underwent intensive resection of “microsurgical pseudocapsule” of clinically non-functioning pituitary tumors (CNPTs). Furthermore, we compared the remission rate of CNPTs between subjects with (Group 1) and without (Group 2) intensive resection of microsurgical pseudocapsule in order to correlate the histological complete resection and endocrinological remission.

Patients and Methods

Between January 2000 and December 2007, 137 patients with CNPTs underwent transsphenoidal surgery at two different hospitals. In one hospital, 113 patients underwent intensive microsurgical dissection during the transsphenoidal surgery by one neurosurgeon. In the other hospital, 24 patients underwent conventional subcapsular resection without intentionally removing the microsurgical pseudocapsule by another one neurosurgeon. The demographic data of the patient population was listed in Table 1.

The evaluation involved a complete history, physical and neurological examination, and radiological assessment. Neuroradiological studies included plain X-rays and magnetic resonance imaging (MRI). The adenomas were classified according to the Hardy radiological classification scheme.⁷

Techniques in pituitary surgeries have advanced strikingly with development of surgical techniques, instruments, endoscopes, and intraoperative MRI. Total resection of pituitary tumors of Hardy grades 1 to 3 has been intended. However, it was impossible to evaluate the significance of intensive resection of microsurgical pseudocapsule in some cases, including those with extreme lateral extension into the cavernous sinus, due to difficulties in achieving complete resection. According to these criteria, 97 patients who had prominent cavernous sinus invasion (Hardy grade IV) were excluded from this study.

In all cases, MRI examination was performed annually to evaluate whether the tumor was removed completely or had

Table 1. Baseline characteristics of the patients and the tumors with and without intensive resection of microsurgical pseudocapsule in clinically non-functioning pituitary tumors.

	Intensive resection of microsurgical pseudocapsule	
	With (group 1; n=113)	Without (group 2; n=24)
Age (year)	45.7 (range, 23–74)	48.5 (range, 36–70)
Male/female	52/61	15/9
Hardy classification		
II	13	5
III	100	19

recurred. Remission for a CNPT was defined as a lack of evidence of tumor remnant or re-growth, as determined by MRI examination. A combined pituitary function test was carried out to evaluate pituitary function before surgery, one year after surgery, and at subsequent 1.5 year intervals from 2 to 13 years postoperatively.

Chi-square test for independence was used to determine the statistical significance of differences in tumor sizes, postoperative remission rate, and postoperative pituitary function between Group 1 and Group 2. A p value <0.05 was considered statistically significant.

■ Results

During the surgery, microsurgical pseudocapsules were found in 57 (50.4%) of 113 patients in Group 1. The pseudocapsule was visualized as a well-developed capsule entirely covering the tumor mass; a thin fibrous envelop; a yellowish, discolored, normal gland-like thin membrane; or thick fibrous tissue after removal of the main tumor mass. Some pseudocapsules exhibited dense fibrosis or calcifications. In smaller tumors, the microsurgical pseudocapsule tended to exist more prominently in and cover the entire mass of the tumor, and was more easily removed. On the other hand, in larger tumors, the microsurgical pseudocapsule tended to be discontinuous or disrupted, not cover the entire tumor, and was more difficult to manipulate surgically. In these situations, intraoperative frozen histological examination was necessary to achieve complete tumor resection.

The pseudocapsule was removed readily along with the main tumor mass in 31 (54.4%) patients. The remaining 26 (45.6%) patients underwent aggressive resection of the remnant pseudocapsule, including multiple intraoperative biopsies. Aggressive resection of the microsurgical pseudocapsule was more often required in larger tumor than in smaller ones. Among these 26 patients, tumor cells infiltration was identified in the microsurgical pseudocapsule of 12 (46.2%) patients.

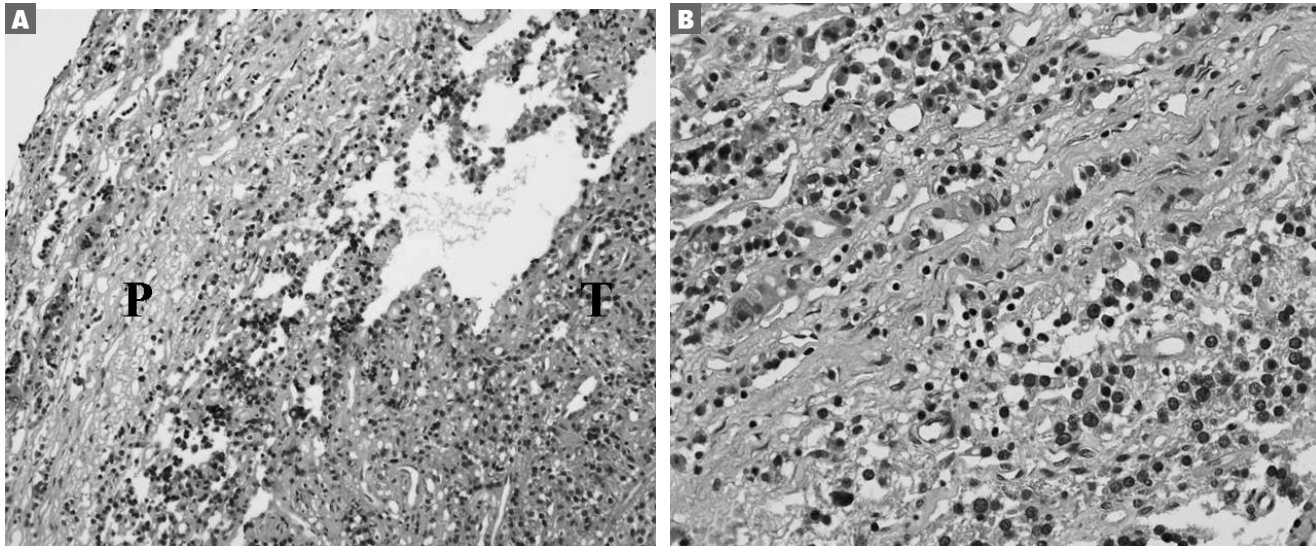
The overall surgical remission rate in Group 1 with intensive resection of microsurgical pseudocapsule were statistically higher than the rates in Group 2 (without intensive resection of microsurgical pseudocapsule) (p=0.032) (Table 2). However, there were no statistical differences in postoperative hormonal function change between Group 1 and 2 (Table 2).

■ Discussion

Some investigators advocated that surgical plane for pituitary adenomas should be included the pseudocapsule which is an accumulation of basement membrane, collagen, fibroblasts, pericytes, and compressed capillaries.¹⁾ On the other hand, other investigators reported that conventional conservative surgical methods are likely to leave tumor cells in the pituitary gland.⁸⁾ In our prospective study, we demonstrated the frequent infiltration of tumor cells within the microsurgical pseudocapsule, suggesting that tumor remnants in the microsurgical pseudocapsule could be a source of recurrence and an obstacle to achieving complete

Table 2. Postoperative remission rates and pituitary functions with and without intensive resection of microsurgical pseudocapsule in clinically non-functioning pituitary tumors.

	Intensive resection of microsurgical pseudocapsule	
	With (group 1; n=113)	Without (group 2; n=24)
Overall surgical remission rate	99.1%	83.3%
Postoperative pituitary function	52/61	15/9
Normal to normal	5 (4.4%)	0
Improved hypopituitarism	60 (53.1%)	12 (50.0%)
Persisted hypopituitarism	39 (34.5%)	9 (37.5%)
Aggravated hypopituitarism	9 (8.0%)	3 (12.5%)

Fig. 1

- A. Photomicrographs of the tumor specimen obtained in en bloc with distinct pseudocapsule during surgery, showing a relatively thick layer of connective tissue as a pseudocapsule (P) at the interface between the pituitary adenoma (T) (Hematoxylin & eosin stain, original magnification $\times 100$).
- B. With higher magnification, clusters of tumor cells are identified in the pseudocapsule (Hematoxylin & eosin stain, original magnification $\times 200$).

remission. These results indicate that intensive removal of the pseudocapsule could provide a higher remission rate without deteriorating pituitary function. The results of the present study correspond with the results of earlier studies, which have reported that intensive resection of the microsurgical pseudocapsule is essential to achieving histologically and surgically total resection of the pituitary adenoma.⁶⁾

From the surgical technical standpoint, identification of a microsurgical pseudocapsule is very important to achieve complete tumor removal. We also found frequent infiltration of tumor cells inside the microsurgical pseudocapsule. These infiltrates were difficult to remove from the normal gland surface with conventional tumor resection methods using curettage and were instead removed with fine instruments in a piece-by-piece fashion. From the author's experience, the microsurgical pseudocapsule was visualized in a variable fashion, such as a well-developed capsule entirely covering the entire tumor mass; a thin fibrous envelop; a yellowish, discolored, normal gland-like thin membrane; thick fibrous tissue; or a calcification. Careful inspection and

intraoperative tissue biopsy at the boundary of pituitary tumors was useful for complete resection of tumors.

The intensive resection of pituitary adenomas could be attributed to postoperative deterioration of pituitary function. However, Kawamata et al.⁵⁾ reported that intensive resection of pseudocapsules was advantageous in the treatment of GH-secreting pituitary adenomas and that it did not cause additional deterioration to pituitary function. Our results are consistent with the reported data, suggesting that aggressive resection of pseudocapsule does not affect pituitary function.

In conclusion, our results indicate that aggressive resection of pseudocapsules increases the cure rate without aggravating pituitary function.

References

1. Bergland R. Pathological considerations in pituitary tumors. *Prog Neurol Surg* 6:62-94, 1975
2. Costello RT. Subclinical adenoma of the pituitary gland. *Am J Pathol* 12:205-216, 1936
3. Farnoud M, Kujas M, Derome P, Racadot J, Peillon F, Li J. Interactions between normal and tumoral tissues at the boundary of human anterior pituitary adenomas. An immunohistochemical study. *Virchows Arch* 424:75-82, 1994
4. Hardy J. Transsphenoidal microsurgical removal of pituitary microadenoma. *Prog Neurol Surg* 6:200-216, 1975
5. Kawamata T, Kubo O, Hori T. Surgical removal of growth hormone-secreting pituitary adenomas with intensive microsurgical pseudocapsule resection results in complete remission of acromegaly. *Neurosurg Rev* 28:201-208, 2005
6. Teramoto A, Sano K, Osamura R, Watanabe K. Immunohistochemical observations of the pituitary adenomas with the use of enzyme-labelled antibody method-on the residual pituitary gland and "capsule" of the adenoma. *Neurol Med Chir (Tokyo)* 19:895-902, 1979
7. Wilson CB. A decade of pituitary microsurgery: The Herbert Olivercrona lecture. *J Neurosurg* 61:814-833, 1984
8. Wrightson P. Conservative removal of small pituitary tumors: is it justified by the pathological findings? *J Neurol Neurosurg Psychiatry* 41:283-289, 1978