Directional Regulation of Extrasellar Extension by Sellar Dura Integrity and Intrasphenoidal Septation In Pituitary Adenomas

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■ OBJECTIVE: **Pituitary macroadenomas extend into the extrasellar space, such as the sphenoid sinus, cavernous sinuses, and suprasellar region. However, factors that regulate the direction of their extensions into the surrounding anatomical structures remain unknown.**

■ METHODS: **This retrospective study included 162 patients who were treated for pituitary adenomas that had maximum diameters greater than 20 mm. According to the direction of adenoma extension, patients were divided into 4 groups: group A, inferior into the sphenoid sinus; group B, lateral into the cavernous sinus; group C, suprasellar region with enlarged sella turcica; and group D, supraellar region without enlarged sella turcica. Several anatomical structures surrounding the sella turcica were evaluated statistically, and multivariate logistic regression analysis was performed if the structures met the determining factors of adenomas extensions.**

■ RESULTS: **The maximum diameter of adenomas was significantly larger in groups A and D. The maximum diameter of the diaphragmatic foramen was largest in group C (19.3 mm) and was significantly narrower in groups B (12.7 mm) and D (12.5 mm). Intrasphenoid septation, attached on the midline of the sella turcica, was observed most frequently in group D (78.6%) and was not detectable in group A (0%). Extension into the cavernous sinus, classified as dural discontinuity, was highly prevalent in group B (80.0%) and was uncommon in group C (12.3%). Erosion of the posterior clinoid process was most apparent in group B (92.0%).**

■ CONCLUSIONS: **The integrity of the sella dura and the intrasphenoid septation can regulate adenoma extension by encouraging their growth towards paths of least resistance.**

INTRODUCTION

Pituitary adenomas can develop extrasellar extensions when they enlarge over the sella turcica. Macroadenomas, which are defined as having maximum diameters greater than 1 cm, grow on a path of least resistance.[1,2] Macroadenomas may extend into the surrounding structures around the sella turcica and may show inferior growth into the sphenoid sinus, lateral growth into the cavernous sinus, and superior growth into the suprasellar region.[3-6] It is reported that, among cases with pituitary macroadenomas, the most frequently detected growth was suprasellar extension, which occurred in nearly 80% of the cases.[3,7] Involvement of the cavernous sinus was found in 6%–10% of the cases diagnosed with pituitary adenomas.[5,8-10] However, it remains unknown how the extrasellar extension of pituitary adenomas is directed into the sphenoid sinus, cavernous sinus, or suprasellar region.[3]

In our previous study, the integrity of the sellar dura was thought to cause the manifestation of intratumoral hematoma symptoms in patients with pituitary adenomas. If there were less-resistant structures around the sella turcica, even rapid volume expansion by the hematoma would not cause an elevation of intrasellar pressure and the subsequent manifestation of several symptoms.[11,12] Therefore, our hypothesis is as follows: a wide

Key words
- Dura
- Extension
- Pituitary adenoma
- Regulation
- Sphenoid sinus

Abbreviations and Acronyms
CT: Computed tomography
FIESTA: Fast imaging employing steady-state acquisition
MRI: Magnetic resonance imaging
TSS: Transsphenoidal surgery
WI: Weighted image

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diaphragmatic foramen, a defect of the medial wall of the cavernous sinus, and not the intrasinus septum or ossification of the sphenoid sinus, would let pituitary adenomas chronically progress into the extrasellar space. In this study, we investigated the regulation of the sellar dura and its bony structures in the sphenoid sinus on the extrasellar extension of pituitary adenomas.

METHODS

Characteristics of Study Patients

This retrospective study included 162 patients who were treated for pituitary adenomas; adenomas featured a maximum diameter more than 20 mm. A total of 271 patients with pituitary adenomas underwent transsphenoidal surgery (TSS) at Kanazawa University Hospital between 2006 and 2016, and patients for this study were selected based on magnetic resonance imaging (MRI). Cases with pituitary adenomas, for which previous TSS was performed or whose diameters were less than 20 mm, were excluded in this study. Therefore, 109 cases were excluded during the study period.

Patients in this study were initially classified into the 3 groups according to the direction of tumor extension, such as inferior, lateral, and superior. Then, each group was divided according to the existence or absence of sellar enlargement, because we speculated that extrasellar extension, without sellar enlargement of macroadenomas, could be influenced by the integrity of the sellar dura. However, in the macroadenomas without sellar enlargement, inferior extension in only 1 patient and lateral extension was found in 2 patients. The 3 patients in these 2 subgroups were excluded from this study because appropriate statistical analysis was impossible with the small number of patients. Finally, 162 patients were enrolled in this study and divided into 4 groups, none of whom had cases of inferior and lateral extension without sellar enlargement.

Patient demographics, including age, sex, tumor histology, symptoms, presence or absence of intratumoral hemorrhage, and maximum diameters of the adenomas were obtained from clinical records. The diagnoses, according to tumor histology, were pituitary adenoma in all 162 patients (nonfunctioning in 145, prolactin-secreting in 15, and 1 case each of either growth hormone-secreting or thyroid stimulating hormone-secreting adenoma). As listed in Table 1, 108 patients (66.7%) reported disturbances in visual function, 26 patients (16.0%) reported headaches, 12 patients (7.4%) experienced diplopia, 10 patients (6.2%) had symptoms associated with hypopituitarism (e.g., general malaise), 3 patients (1.9%) encountered consciousness disturbance, and 12 patients (7.4%) had no symptoms associated with pituitary adenomas.

Neuroradiologic Evaluation

An MRI scanner, Signa HDx 3T (GE Medical Systems, Milwaukee, Wisconsin, USA), was used to obtain axial, coronal, and sagittal images before and after gadolinium administration. MRIs were captured for our study as described parameters in our previous report.[13] Radiologic characteristics of tumor extension, such as degrees and directions of extrasellar extensions, maximum diameter of tumors, diameter of the diaphragmatic foramen, cavernous sinus invasion (evaluated as discontinuity of the medial wall of the cavernous sinus), presence or absence of the posterior clinoid process erosion, intrasphenoidal septum (on-midline or off-midline), and ossification of the sphenoid sinus,

Table 1. Comparisons of Clinical Features Among the Groups of Patients with Pituitary Adenomas in This Study

		Patterns of Adenoma Extension (Groups)				
		A	B	C	D	*P* Value
Number	(%)	25 (15.4)	25 (15.4)	81 (50.0)	31 (19.1)	
Age	(yrs)	59.0 ± 16.1	58.4 ± 13.0	56.4 ± 13.5	60.0 ± 16.1	0.627
Sex	(men:women)	12:13	14:11	41:40	14:17	0.876
Tumor histology						
	NFA	20	23	73	29	0.376
	FA	5	2	8	2	
Symptoms						
	VD	10 (40.0)	5 (20.0)	64 (79.0)	29 (93.5)	<0.001*
	HA	3 (12.0)	8 (32.0)	13 (16.0)	2 (6.5)	0.067
	DP	1 (4.0)	10 (40.0)	1 (1.2)	0 (0)	<0.001*
	HP	3 (12.0)	2 (8.0)	4 (4.9)	1 (3.2)	0.521
	CD	0 (0)	1 (4.0)	2 (2.5)	0 (0)	Not evaluated
	Asymptomatic	8 (32.0)	1 (4.0)	3 (3.7)	0 (0)	<0.001*

NFA, nonfunctioning adenoma; FA, functioning adenoma; VD, visual function disturbance; HA, headache; DP, diplopia; HP, symptoms derived from hypopituitarism; CD, consciousness disturbance.
*$P < 0.01$.

were visualized via MRI and bone images of computed tomography (CT).[10]

The integrity of the dura mater at the pituitary fossa, including both the diaphragma sellae and the medial wall of the cavernous sinus, was evaluated using fast imaging employing steady-state acquisition (FIESTA).[14,15] The degree and direction of the extrasellar extensions were explored on T1-weighted image (WI) of MRI after contrast enhancement. Sphenoid sinus extension was defined as a downward extension of the tumor that was more than two-thirds of the height of the sphenoid sinus on the sagittal section of MRI.[14] Invasion into the cavernous sinus was defined as discontinuity of the medial wall of the cavernous sinus, depicted as linear hypointensity on the FIESTA images.[10] Suprasellar extension was defined as contact with or elevation of the optic chiasm.[14] The direction of the pituitary adenoma extension was determined by using the most dominant direction among 3 dimensions (inferior, lateral, and superior) on the enhanced T1-WI MRI and confirmed by consensus between at least 2 neurosurgeons (Y.H. and Y.S.) and a neuroradiologist (F.U.).

Basically, the most dominant direction was determined as the direction with the largest distance from the center of the sella turcica to the adenoma surface. In addition, patients included in this study were divided into 4 groups, according to the adenomas extension, and were classified as follows; group A, inferior extension into the sphenoidal sinus; group B, lateral extension into the cavernous sinus; group C, superior extension into the suprasellar region with enlarged sella turcica (ballooning); and group D, superior extension into the suprasellar region without enlarged sella turcica. Representative cases from each group that featured characteristic neuroradiologic findings on T1WI of MRI with contrast enhancement are shown (Figure 1A–D).

The diameter of each pituitary adenoma was measured in 3 dimensions (craniocaudal, transverse, and anteroposterior) on the T1WI of MRI with contrast enhancement. The largest value of the 3 measurements was considered to be the maximum diameter. The volume of the adenoma and hematoma was determined by multiplying their maximum height, width, and depth. The diaphragma sellae is depicted as a linear hypointensity on the FIESTA. The diameters of the diaphragmatic foramen, including the pituitary stalk, were measured on the coronal section.[14] In addition, the presence of adenoma invasion into the cavernous sinus over the medial wall was recognized as adenoma extension with discontinuity of the linear hypointensity on the FIESTA. Representative FIESTA images were shown in Figures 2 and 3. Finally, coronal, axial, and sagittal sections of the bone images in the CT scans were used to evaluate the intrasphenoidal septa attached to the sellar floor, erosion of the posterior clinoid process, and ossification of the sphenoid sinus, respectively. Representative cases from each characteristic finding on bone-image CT are shown.

Statistical Analysis

Post hoc analysis was used to compare ages of the patients at presentation, sex distribution, tumor histology, rates of occurrence for each symptom, maximum diameter of the adenomas, presence of intratumoral hematoma occupying more than 50% of the adenoma volume, diameter of diaphragma defects, number of intrasphenoidal septa attached to the sellar floor, presence of an intrasphenoidal septum on the midline of the sellar floor, frequencies of invasion into the cavernous sinus, presence of the posterior clinoid process erosion, and ossification of the sphenoid sinus among the 4 groups in this study. A forward stepwise method was used to construct a multivariate logistic regression model to determine how the anatomical factors surrounding the sella turcica related to directions of pituitary adenomas extension in the analysis of this study. These statistical analyses were performed using Microsoft Statview (ver. 5, SAS Institute Inc., Cary, North Carolina, USA). A P value of <0.05 was considered as statistically significant.

RESULTS

Comparisons of Clinical Features Among Groups of Patients with Pituitary Adenomas

All the 162 patients initially enrolled in this study were evaluated with the neuroradiologic items using MRI and CT before TSS, as described in the Methods section. This study consisted of 82 male and 80 female patients, with the age at diagnosis ranging from 20

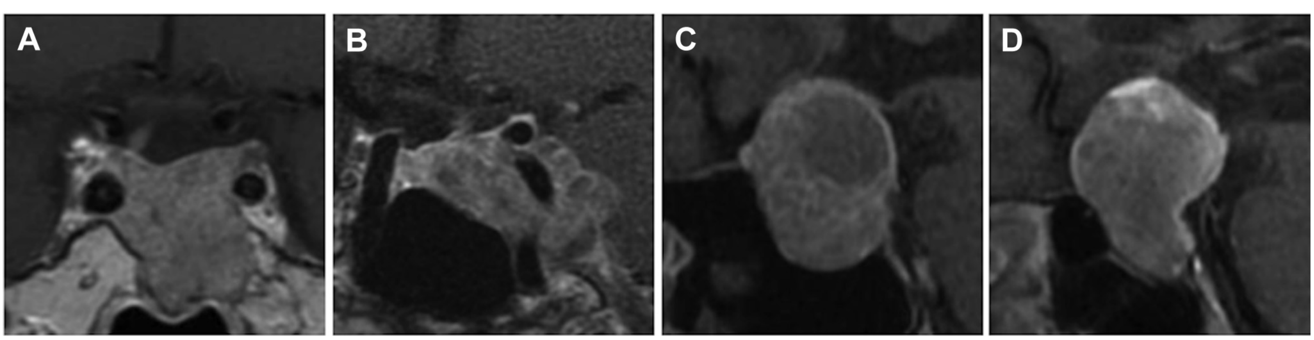

Figure 1. Representative cases of magnetic resonance imaging (MRI) in each group. Contrast enhancement (CE) of T1-weighted images (WI) of a coronal section shows a pituitary adenoma with extension into the sphenoid sinus (**A**) and into the cavernous sinus (**B**). Pituitary adenomas with suprasellar region were divided into 2 groups; T1WI with CE on a sagittal section revealed a pituitary adenoma with (**C**) or without (**D**) remarkable enlargement of the sella turcica.

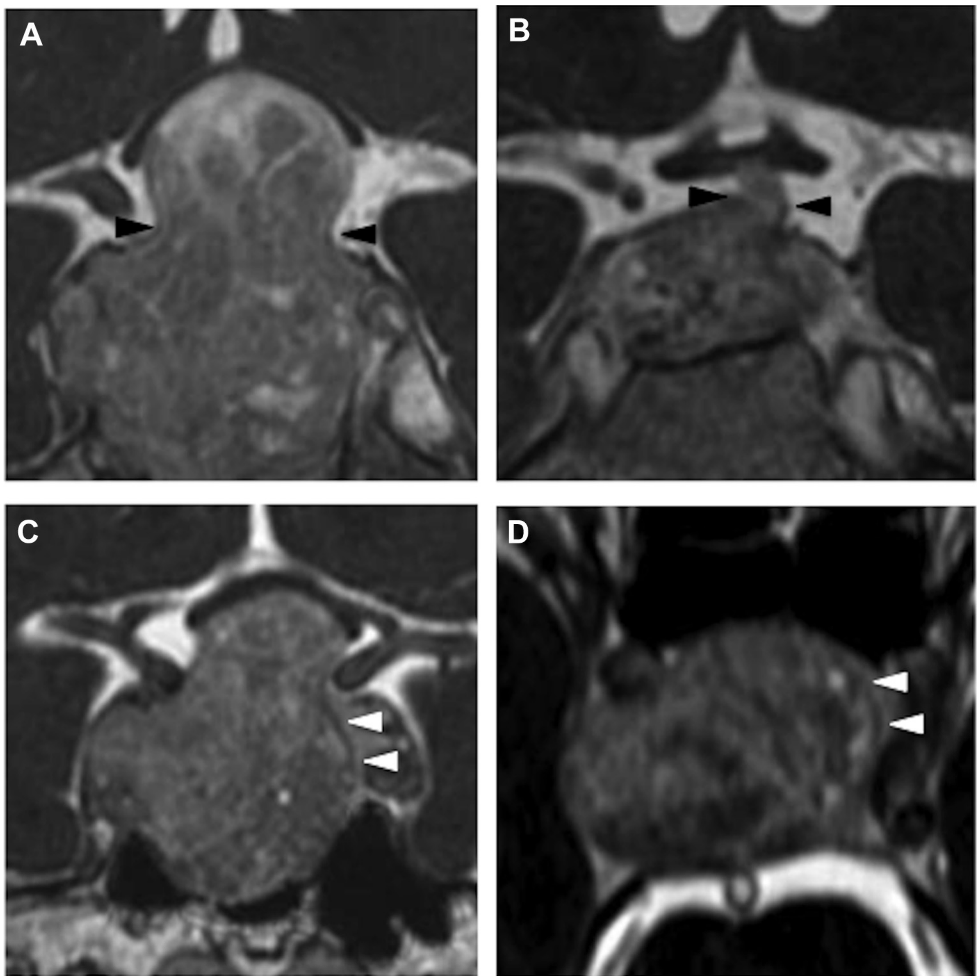

Figure 2. Representative cases of fast imaging employing steady-state acquisition (FIESTA) magnetic resonance images. FIESTA on a coronal section showed a pituitary adenoma with a wide opening (**A**) and a narrow opening (**B**) of the diaphragmatic foramen (*arrowheads*). (**C**–**D**) FIESTA with contrast enhancement showing the medial wall of the cavernous sinus was kept intact, as depicted by the continuous linear hypointensity (*white arrowheads*) on the right side. FIESTA images showing pituitary adenoma extension across the dural discontinuity at the medial wall of the cavernous sinus on the right side. (**C**) Coronal section; (**D**) axial section.

to 89 years old (mean age, 57.8 ± 14.3 years). There were 25 patients (15.4%) in group A, 25 patients (15.4%) in group B, 81 patients (50.0%) in group C, and 31 patients (19.2%) in group D. There was no significant statistical difference in age, sex distribution, and tumor histology among these 4 groups (Table 1). Although 12 patients (7.4%) in this study were asymptomatic, the remaining 150 patients (92.6%) manifested at least 1 symptom. Of the symptoms, visual function disturbance was significantly predominant in groups D (29 patients, 93.5%) and C (64, 79.0%) compared with group A (10, 40.0%) and group B (5, 20.0%, $P < 0.001$). In contrast, the occurrence of headache was not significantly different among the 4 groups ($P = 0.067$). A significant fraction of group B had diplopia (10, 40.0%), compared with groups A (1, 4.0%), C (1, 1.2%), and D (0, 0%, $P < 0.001$). Symptoms derived from hypopituitarism were not significantly different among the groups in this study ($P = 0.521$). Consciousness disturbance occurred in only 3 patients, 2 were in group C and 1 was in group B. Asymptomatic patients were more frequently observed in group A (8, 32.0%) than in groups B (1, 4.0%), C (3, 3.7%), and D (0, 0%).

Comparisons of Radiologic Features Among Groups of Patients with Pituitary Adenomas

Sizes of pituitary adenomas were compared based on the maximum diameter, as seen on preoperative MRI, among the 4 groups. The largest value among the 3-dimensional values derived from MRI with contrast-enhanced T1WI was considered to be the maximum diameter. The mean maximum diameter of the 4 groups was 33.9 ± 8.2 mm (group A), 27.4 ± 5.0 mm (group B), 29.1 ± 6.3 mm (group C), and 33.2 ± 9.7 mm (group D). The mean maximum diameters in

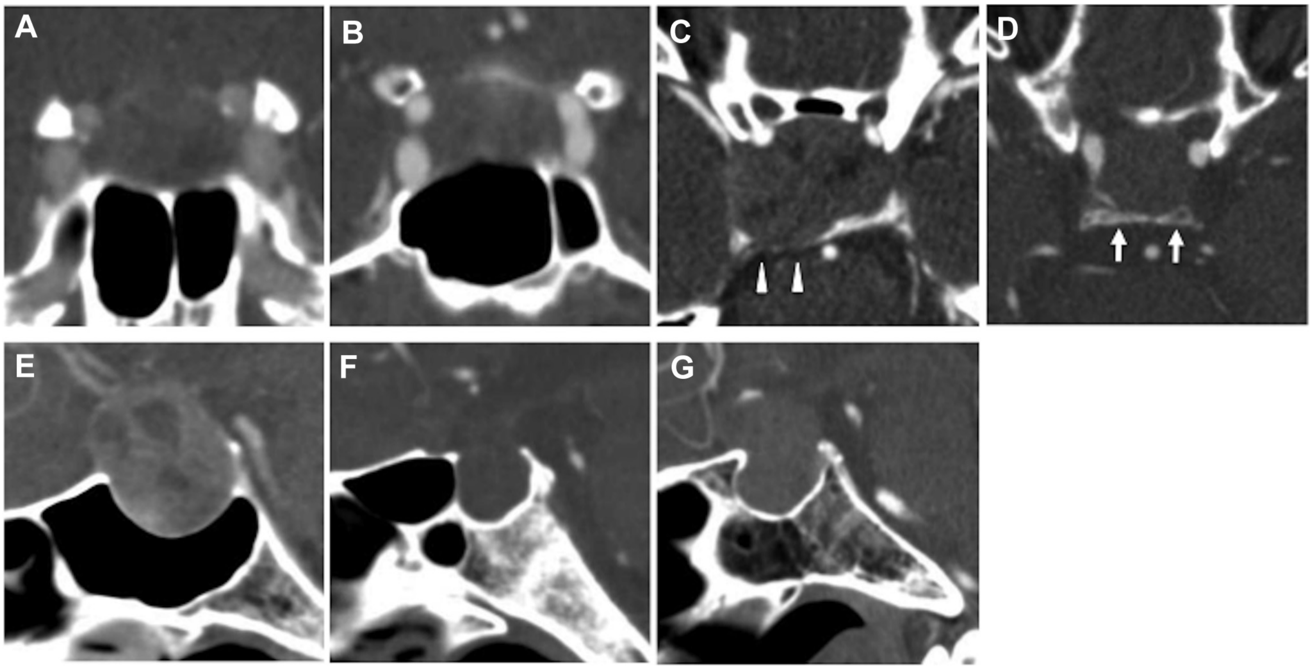

Figure 3. Representative cases of the bone-window computed tomography scan. Coronal section of the sella turcica with intrasphenoid septation attached to the sellar floor on the midline (**A**) and off the midline (**B**). (**C**) Erosion (*white arrowheads*) caused by pituitary adenoma with lateral-posterior extension was clearly detected. (**D**) The posterior clinoid process (*white arrows*) was kept intact without erosion. Sagittal sections showing ossification with varying extension into the sphenoid sinus and the sella turcica. (**E**) Sellar type; (**F**) pre-sellar type; (**G**) conchal type.

groups A and D were obviously larger than in groups B and C ($P = 0.008$, Table 2). Frequency of intratumoral hemorrhage greater than 50% of the volume of the pituitary adenoma was compared among the 4 groups. The frequency was 5 of 25 patients (20.0%) in group A, 12 of 25 patients (48.0%) in group B, 20 of 81 patients (24.7%) in group C, and 8 of 31 patients (25.8%) in group D. The frequency was not found to be statistically significant among these groups ($P = 0.099$, Table 2).

Table 2. Comparisons of Radiologic Features Among the Groups of Patients with Pituitary Adenomas in This Study

Group		Patterns of Adenoma Extension A	B	C	D	*P* Value
Number	(%)	25 (15.4)	25 (15.4)	81 (50.0)	31 (19.1)	
Size	(mm)	33.9 ± 8.2	27.4 ± 5.0	29.1 ± 6.3	33.2 ± 9.7	0.008*
Hematoma	(>50%)	5 (20)	12 (48.0)	20 (24.7)	8 (25.8)	0.099
Diaphragma defect	(mm)	14.5 ± 5.6	12.2 ± 5.7	19.3 ± 4.5	12.5 ± 1.8	<0.001*
Intrasphenoid septum	Number	0.25	0.91	0.97	1.11	<0.001*
	On midline	0 (0)	7 (35.0)	37 (56.9)	22 (78.6)	<0.001*
SS ossification	(%)	2 (8.0)	5 (20.0)	19 (23.5)	3 (9.7)	0.097
Cavernous sinus	(%)	10 (40.0)	20 (80.0)	10 (12.3)	4 (12.9)	<0.001*
PCP erosion	(%)	11 (44.0)	23 (92.0)	28 (34.6)	8 (25.8)	<0.001*

SS, sphenoid sinus; PCP, posterior clinoid process.
$^{*}P < 0.01$.

Diameters of the diaphragmatic foramen, including the pituitary stalk, were measured on the coronal section, and the mean diameters in the 4 groups were as follows; 14.5 ± 5.6 mm (group A), 12.7 ± 5.7 mm (group B), 19.3 ± 4.5 mm (group C), and 12.5 ± 1.8 mm (group D). The mean diameters were significantly larger in group C ($P < 0.001$), whereas there was no statistical difference among the rest of the 3 groups (Table 2). Our results indicated that wider diaphragmatic foramina could significantly facilitate suprasellar extension of pituitary adenomas.

Cavernous sinus invasion, assessed by discontinuity of the medial wall of the cavernous sinus, was compared among the 4 groups. This finding was detected in 10 patients (40.0%) in group A, 20 patients (80.0%) in group B, 10 patients (12.3%) in group C, and 4 patients (12.9%) in group D. Among the 4 groups the invasion was most frequently detected in group B ($P < 0.001$). In addition, the ones in groups C and D were significantly lower than the one in group A (Table 2). This result revealed that inferior extensions into the sphenoid sinus of pituitary adenomas were associated with extension into cavernous sinus to some extent, but the suprasellar extensions were not.

Next, erosion of the posterior clinoid process also was compared among the 4 groups. This phenomenon was found in 11 patients (44.0%) in group A, 23 patients (92.0%) in group B, 28 patients (34.6%) in group C, and 8 patients (25.8%) in group D. All cases of erosion of the posterior clinoid process were detected unilaterally. It was also obviously understandable that the greatest frequency was detected in group B ($P < 0.001$), but no statistical difference was found among the other three groups (Table 2). This result indicated that posterior extension with posterior clinoid process erosion was significantly associated with lateral extension of the pituitary adenoma into the cavernous sinus.

Numbers of intrasphenoid septation attached to the sellar floor were compared among the patients without ossification in the sphenoid sinus. The numbers of intrasphenoid septation were 0.25 ± 0.11 in group A, 0.90 ± 0.31 in group B, 0.97 ± 0.29 in group C, and 1.11 ± 0.36 in group D. The number of intrasphenoid septa was obviously smallest in group A ($P < 0.001$, Table 2). This result showed that inferior extension was obviously inhibited by intrasphenoid septation. In addition, frequency of intrasphenoid septum attached to the sellar floor on the midline also was evaluated, and the results were as follows; 0 of 26 patients (0%) in group A, 7 of 20 patients (35.0%) in group B, 37 of 65 patients (65.9%) in group C, and 22 of 28 patients (78.6%) in group D. The frequency was significantly greatest in group D, followed by in group C and group B, and lowest in group A ($P < 0.001$, Table 2). Therefore, this result suggested that suprasellar extension was well associated with the existence of the intrasphenoid septum attached on the midline of the sellar floor.

The ossification in the sphenoid sinus was assessed as either the pre-sellar type or the conchal type on bone-window CT scans, and was compared among the 4 groups. Ossification was detected in 2 of 25 cases (8.0%) in group A, in 5 of 25 cases (20.0%) in group B, in 19 of 81 cases (23.5%) in group C, and in 3 of 31 cases (9.7%) in group D. The frequency was not significantly different among the groups ($P = 0.097$, Table 2). This result showed no apparent relationship between ossification beneath the sellar floor, within the sphenoid sinus, and in the direction of pituitary adenoma extension.

Multivariate logistic regression analysis was performed to determine the relationship between the anatomical factors and the directions of pituitary adenomas extensions for each of the 4 groups (Table 3). In group A, there was a significant association of the inferior extension of the adenoma with the presence of large pituitary adenomas, fewer intrasphenoid septa attached to the sellar floor, and an absence of intraphenoidal septum on midline ($P = 0.005$, $P = 0.020$, $P = 0.003$, respectively). This result suggested that intrasphenoidal septa, especially septum on midline, were a resistant factor against inferior extension of the adenoma.

In group B, there was a significant association of lateral extension of the adenoma into the cavernous sinus with the presence of large pituitary adenomas, discontinuity of the medial wall of the cavernous sinus, and erosion of the posterior clinoid process ($P = 0.006$, $P < 0.001$, $P = 0.001$, respectively). This result suggested that destruction of the unilateral posterior clinoid process allowed lateral and posterior extension of the adenomas.

In group C, there was a significant association of superior extension of the adenoma into the suprasellar region with enlarged sella turcica and incidences of large pituitary adenomas, wider diameters of the diaphragm foramen, and continuity of the medial wall of the cavernous sinus ($P < 0.001$, $P < 0.001$, $P = 0.009$, respectively). This result suggested that less resistance to upward extension and a greater resistance to lateral extension facilitated the superior extension of the adenoma.

In group D, there was a significant association of superior extension into the suprasellar region without enlarged sella turcica and the occurrence of large pituitary adenomas, narrow diameters of the diaphragm foramen, and the presence of intrasphenoid septum on midline ($P < 0.001$, $P < 0.001$, $P = 0.002$, respectively). This result suggested that bony septation on the midline works as a strong resistant factor against the downward extension of the adenoma, and it can facilitate the superior extension of the adenoma, even if the diaphragmatic foramen is significantly narrower.

DISCUSSION

Basically, chronic enlargement of the pituitary adenoma volume is accompanied with expansion of the sella turcica and then extends into extrasellar space, such as inferior extension into the sphenoid sinus, lateral extension into the cavernous sinus, and superior extension into suprasellar region.[1-6] Extrasellar extensions might be caused by breakdown of the dural integrity and bony structures of the sella turcica.[1,2,16] In this study, association between patterns of extrasellar extension and a breakdown in integrity of the anatomical structures that surround the sella turcica was investigated.

The hypophyseal fossa is located in the sella turcica of the sphenoidal bone, laterally between the 2 cavernous sinuses, and contains the pituitary gland.[16] The diaphragma sellae is a small, circular, horizontal reflection of dura mater that forms a roofing over the sella turcica and covers the pituitary gland. The diaphragma sellae also had a small, central opening through which the infundibulum passes.[17] The lateral wall of the hypophyseal fossa is a linear, sagittal, dural wall that completely and medially separates the hypophyseal gland from the

Table 3. Comparisons of Radiologic Features in Each Group to Determine the Direction of Extrasellar Extension of Pituitary Adenomas in This Study

				95% CI	
		P Value	Regression Coefficient	Lower	Upper
Group A	Size	0.005*	−0.224	−0.018	−0.003
	Diaphragma defect	0.103	0.129	−0.002	0.018
	Intrasphenoid septum	0.020†	0.224	0.021	0.238
	Septum on midline	0.003*	0.294	0.072	0.339
	Cavernous sinus	0.513	−0.056	−0.196	0.098
	PCP erosion	0.076	0.151	−0.013	0.248
Group B	Size	0.006*	0.201	0.003	0.015
	Diaphragma defect	0.031†	0.155	0.001	0.018
	Intrasphenoid septum	0.131	−0.131	−0.162	0.021
	Septum on midline	0.735	0.029	−0.093	0.132
	Cavernous sinus	<0.001*	−0.421	−0.464	−0.217
	PCP erosion	0.001*	−0.251	−0.291	−0.072
Group C	Size	<0.001†	−0.288	−0.055	−0.018
	Diaphragma defect	<0.001†	0.513	0.062	0.112
	Intrasphenoid septum	0.988	−0.001	−0.271	0.267
	Septum on midline	0.179	0.123	−0.105	0.557
	Cavernous sinus	0.009*	−0.212	−0.849	−0.122
	PCP erosion	0.563	0.046	−0.228	0.416
Group D	Size	<0.001†	0.299	0.023	0.071
	Diaphragma defect	<0.001†	−0.349	−0.105	−0.041
	Intrasphenoid septum	0.913	−0.011	−0.381	0.339
	Septum on midline	0.002*	0.312	0.242	1.075
	Cavernous sinus	0.106	−0.138	−0.857	0.083
	PCP erosion	0.206	−0.107	−0.683	0.149

CI, confidence interval; PCP, posterior clinoid process.
*$P < 0.01$.
†$P < 0.05$.

cavernous sinuses.[18] The sphenoid sinus is well known to have variable degrees of pneumatization, and both the conchal and presellar sinus types develop ossification beneath the sellar floor.[19-21] In addition, a major intersinus septum is reported to be present in at least 70% of patients, and located along the midline in about 40% of patients.[14,22] These dural and bony structures may restrict the paths through which adenomas can extend outside the sella turcica.

In this study, we classified the extrasellar extension as having inferior, lateral, or superior directions. We focused on anatomical structures surrounding the sella turcica, that could function as barriers capable of resisting adenoma growth, including the diaphragma sellae, the medial wall of the cavernous sinus, the intrasphenoid septum, ossification in the sphenoid sinus, and the posterior clinoid process. First, the diaphragma sellae, has the potential to regulate adenoma extension into the suprasellar region.[7,23] However, the foramen of the diaphragm sellae, through which the pituitary stalk passes, becomes wider to allow suprasellar extension of pituitary adenomas, leading to compression of the optic chiasm and manifestation of visual function disturbance.[23,24] Therefore, in group C, pituitary adenomas have suprasellar extension and significantly wider foramens compared with the other groups. Conversely, the narrow diaphragmatic foramen inhibits suprasellar extension in groups A and B. Therefore, the extension of adenomas in groups A and B is promoted in the inferior and lateral directions.[23] In group D, although it may sound paradoxical, suprasellar extension of the adenomas was prominent despite of the presence of a narrow foramen. In this group, structures of the sella turcica inhibited inferior, lateral, and posterior extensions, and the adenomas grew on the path of least resistance into the narrow diaphragm foramen (Table 2). The narrow foramen of group D regulates the direction of adenoma extension compared to the group C, by restricting adenoma growth along the direction of the pituitary stalk and into the optic chiasm, and may lead to the highest rates of visual function disturbance among the groups in this study.

Subsequently, the intrasphenoidal septum, the bony structure in the sphenoid sinus, is considered to function as a buttress of the sellar floor and an anatomical barrier against the inferior extension of pituitary adenomas.[2,21] A high number of intrasphenoidal septa and septum attached to the midline of the sella turcica also may restrict downward growth of the adenoma into the sphenoid sinus, thereby directing pituitary adenoma growth into the suprasellar region.[2] Ramakrishnan et al.[2] proposed that the midline insertion of the intrasphenoidal septum redirected the compression and tension forces of an enlarging sellar mass by acting a structural buttress. They also revealed that intrasphenoid septum was thicker in pituitary adenomas with suprasellar extension than in those without suprasellar extension. In this study, the number of intrasphenoid septa was significantly lower solely in group A, as seen by the inferior extension of pituitary adenomas, compared to the other three groups (B, C, and D). In other words, the extensions into the directions other than inferior one took place because the intrasphenoid septum was attached to the midline of the sellar floor, and it encouraged suprasellar extension in groups C and D. Moreover, the highest rates of intrasphenoid septum on midline were found in group D, suggesting that the suprasellar extension in this group was the strongest redirecting force over the narrow diaphragmatic foramen (Table 2).

Our results showed that the frequency of lateral extension was most dominant in group B, and that there were significant differences between group A and groups C and D. This result suggests that the restriction of lateral extension may facilitate suprasellar extension, because the path though the diaphragmatic foramen provides less resistance than the medial wall of the cavernous sinus (Table 2). In contrast, Kursat et al.[1] reported in their anatomic study of cadavers that the thickness of the upper third of the medial wall of the cavernous sinus was significantly larger than that of the lower third (278.46 ± 162.79 μm vs. 161.53 ± 53.86 μm), leading to the speculation that the thickness of the lower third of the medial wall could be the major determinant of parasellar extension of the pituitary adenomas.

Moreover, lateral-posterior extensions of pituitary adenomas with the erosion of the unilateral posterior clinoid process were evaluated with the bone-window CT scan images. The frequency of erosion was greatest in group B, followed by occurrences in groups A, C, and D. This result was similar to the data obtained by the assessment of the cavernous sinus invasion described above. Although the posterior clinoid process erosion was most frequent in group A than in groups C and D, the statistical difference among these groups was not significant (Table 2). Pituitary adenomas may extend laterally into the parapeduncular space, invading through the roof of the cavernous sinus and into the oculomotor triangle,[25,26] and may also erode the unilateral posterior clinoid process.

Finally, the ossification in the sphenoid sinus, including presellar and conchal types, was suggested to be an anatomical barrier against inferior extension of pituitary adenomas into the sphenoid sinus.[27] In this study, however, existence of ossification was not statistically different among the groups, meaning that bony septum attached to the sellar floor had a greater influence on adenoma extension than ossification in the sphenoid sinus (Table 2).

In this study, we divided the extension patterns of pituitary adenomas into 4 groups as follows; inferior, lateral, and superior with or without enlarged sella (Table 3). First, pituitary adenomas with inferior extension (group A) were associated with significantly small numbers of intrasphenoid septa attached to the sellar floor and an absence of intrasphenoid septum on midline; however, the dural integrity at the sella turcica was maintained. Second, pituitary adenomas with lateral extension (group B) were associated with only dural discontinuity at the medial wall of the cavernous sinus, and a narrow diaphragmatic foramen was thought to inhibit extension in superior and inferior directions. However, lateral adenoma extension was accompanied with significant unilateral posterior extension and erosion of the posterior clinoid process. Third, pituitary adenomas with suprasellar extension with enlarged sella turcica (group C) were associated with wider diaphragmatic foramen, and the intact medial wall of the cavernous sinus thought to direct the extension of the adenomas by inhibiting adenoma extension in the lateral directions. Fourth, pituitary adenomas with suprasellar extension and without enlarged sella (group D) were associated with maintained dural integrity at the sella and intrasphenoid septa (especially septum on midline), and were thought to facilitate the superior extension of pituitary adenomas along the pituitary stalk and into the optic chiasm.

There are some limitations in our study. First, this study was retrospective in design. Second, the total number of patients (162 patients) was too small to provide significant statistical power for analysis among the subgroups. Third, although some pituitary adenomas harbored multidirectional extensions, which were shown in our previous study,[11] in this study, we defined the most prominent direction of pituitary adenoma extension, per case, of the 3 directions, inferior, lateral, superior, as described previously. Therefore, there may be some cases that may have influenced the significance calculated by statistical analysis. Fourth, extension of pituitary adenomas may not be defined only by the anatomically factors shown in our study, but many be affected by biological factors as well. Fifth, the surrounding anatomical variations might be the consequence of the tumor growth, not functioning as anatomical barrier, such as larger diaphragm foramen and discontinuity of the medial wall of the cavernous sinus.

CONCLUSIONS

It is clinically useful for pituitary neurosurgeons to consider the impact the anatomical structures surrounding the sellar turcica have on the extrasellar extension of pituitary adenomas on potential symptoms in patients. The integrity of the sella dura and the intrasphenoid septation can regulate adenoma extension by encouraging their growth towards paths of least resistance. Our present study clearly revealed that tumor size, the diameter of diaphragmatic foramen, intrasphenoid bony septation, septum on the midline, dural continuity at the medial wall of the cavernous sinus, and erosion of the posterior clinoid process were found to be significant anatomical factors that determine the patterns of extrasellar extension.

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