



Combined supra-infrasellar approach to pituitary macroadenoma with oculomotor cistern extension: surgical strategy and experience

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Abstract

Background Oculomotor cistern extension (OMCE) of pituitary adenoma through the oculomotor triangle may be one of the major characteristics of multi-lobulated adenoma. The OMCE may be hard to remove only through the endonasal approach.

Method We applied the simultaneous combined supra-infrasellar approach to remove pituitary adenoma with relatively large OMCE. Four (7.3%) of 55 consecutive patients with initially operated pituitary macroadenoma (> 10 mm) had OMCE. The combined supra-infrasellar approach was adopted in two cases with relatively large OMCE.

Results The simultaneous combined supra-infrasellar approach was performed with the transcranial microscopic transsylvian anterior temporal approach and the nasal endoscopic approach. The medial main mass was removed through the nasal side. The lateral OMCE was also removed through the nasal side by pushing the tumor in the sellar direction from the transcranial side. The oculomotor nerve was confirmed with electrical nerve stimulation. The main medial mass and the OMCE were mostly removed in both cases. Remnant tumor in the cavernous sinus was treated by gamma knife radiosurgery. Endoscopic transsphenoidal removal was performed in the other two cases with relatively small OMCE.

Conclusions Pituitary macroadenomas with OMCE are a newly recognized form of progression with important implications for surgical strategy. The combined supra-infrasellar approach performed with the transcranial microscopic transsylvian anterior temporal approach using electrical nerve stimulation and the nasal endoscopic approach may be useful for this type of multi-lobulated pituitary adenoma.

Keywords Pituitary adenoma · Oculomotor cistern extension · Combined supra-infrasellar approach · Anterior temporal approach

Abbreviations

EOG electrooculography
MR magnetic resonance
OMCE oculomotor cistern extension

Introduction

Oculomotor cistern extension (OMCE) is a recently proposed pattern of tumor progression in pituitary macroadenoma

occurring through the oculomotor triangle, which is a weak point of the cavernous sinus [3, 6, 19]. OMCE may be involved in oculomotor nerve palsy associated with pituitary adenoma [6, 7] and may be one of the major reasons for the multilobulated character of pituitary adenoma. However, OMCE of adenoma is hard to remove through the endoscopic endonasal approach [6]. We have adopted the simultaneous combined supra-infrasellar approach to treat multilobulated pituitary adenoma with relatively large OMCE [10, 14].

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Patients and methods

Four (7.3%) of 55 consecutive patients with initially operated pituitary macroadenoma (> 10 mm) had OMCE, including three cases of clinically non-functioning pituitary adenoma and one case of follicle-stimulating hormone-secreting adenoma. No patient had clinical pituitary apoplexy. The combined

supra-infrasellar approach was adopted in two of four cases. The institutional research board of Gunma University Hospital approved the study and written informed consent for the study was obtained from all patients.

Operative procedure for combined supra-infrasellar approach

Anesthesia was induced with bolus injection of propofol and remifentanyl, then maintained with inhalation general anesthesia. Electrooculographic (EOG) monitoring was performed with surface electrodes placed on the skin around the eyeball [4]. A navigation system (StealthStation; Medtronic Sofamor Danek, Memphis, TN) was used for image-guided surgery. A 4-mm rigid high definition endoscope was used with a 0°, 30°, or 70° angled lens and a fixation system (Endoarm; Olympus Corporation, Tokyo, Japan). The head was rotated 30 degrees to the left in the supine position. The operating microscope (OME9000; Olympus Corporation) and navigation system (StealthStation) were positioned in the operation room. First, the endonasal procedure was performed. The sellar floor was widely opened as previously described [20]. Subsequently, the endoscopic surgery was paused, and craniotomy was performed. The transsylvian anterior temporal approach was performed using the operating microscope, as previously described [5, 18]. The superficial sylvian veins were separated from the temporal lobe and moved to the frontal lobe. The anterior temporal artery was completely separated from the medial surface of the temporal lobe. The temporal lobe was retracted posteriorly [5, 18]. The pituitary adenoma displacing the optic chiasm was visualized in the prechiasmatic cistern or optico-carotid space and subsequently identified posterolateral to the right internal carotid artery. Simultaneous manipulations at both the cranial and nasal sides were then started. Removal of the medial main mass was performed at first. Intracapsular removal was performed from the nasal side. Shrinkage of the main mass during suctioning from the nasal side could be observed from the cranial side. Adhesion of the surrounding arachnoid and protection of the optic nerve and perforating artery from traction due to the mass shrinkage were performed from the cranial side, and the medial tumor was pushed from the craniotomy side in the sellar direction to support endonasal resection of the tumor. Subsequently, the lateral mass of the OMCE was targeted. A white cord could be observed passing along the capsule of the OMCE part of the tumor from the cranial side, which was confirmed as the thinned oculomotor nerve by nerve stimulation with a monopolar electrode. Retroangular pulses of 0.2 msec duration were applied with a repetition rate of 1 Hz. The intensity of stimulation for the oculomotor nerve was increased gradually up to 2 mA. We think that this capsule may have consisted of the outer thickened arachnoid and the inner pseudocapsule

of the pituitary adenoma in our two cases [12]. The endoscopic surgeon could detect the light of the operating microscope as the connecting point between the sellar and OMCE parts of the tumor. Simultaneously with the microscopic surgeon pushing the tumor in the suprasellar direction, the endoscopic surgeon could suction and remove the OMCE part of the tumor from the infrasellar direction through this connecting route (porus oculomotorius). Both cases had cavernous sinus invasion of Knosp grade 4. We did not remove the most remote cavernous sinus part of the tumor (gamma knife radiosurgery was planned). Cerebrospinal fluid leakage was not observed. Abdominal fat and/or fascia were grafted to the sellar space.

Results

The clinical and histological characteristics and results of these four cases are shown in Table 1 [16]. The combined supra-infrasellar approach was applied in two cases with relatively large OMCE and endoscopic transsphenoidal removal in the other two cases with relatively small OMCE.

Case presentations

Case 1

A 66-year-old woman presented with blurred vision. Magnetic resonance (MR) imaging performed for mild symptoms demonstrated a pituitary adenoma. Two years later, she suffered from general fatigue and cold intolerance, and hyponatremia and hypopituitarism were identified. MR imaging showed tumor growth with the right OMCE through the oculomotor triangle (Fig. 1a–c). The tumor volume was estimated as 10.3 cm³, including the OMCE volume of 1.9 cm³. The right cavernous invasion was Knosp grade 4. Best corrected visual acuity was right 0.9 and left 1.2. Visual field perimetry revealed upper right superior quadrantanopia in the right eye. Supraduction and abduction limitation of the right eye movement and mild dilation of the right pupil indicated right oculomotor palsy. No other neurological symptoms were found. She was accepted to undergo supra-infrasellar removal of the pituitary tumor at age 71 years. The operative time flow is illustrated in Fig. 2. The thinned oculomotor nerve was directly observed in the front capsule of the OMCE tumor from the craniotomy side (anterolateral side of the OMCE tumor) and confirmed by nerve stimulation with a monopolar electrode. The oculomotor nerve was not dissected from the tumor capsule. The OMCE part of the tumor was suctioned from the nasal side supported by pushing from the craniotomy side. Postoperative MR imaging

Table 1 Clinical characteristics and surgical results in patients with pituitary macroadenomas

Case no.	Age, sex	Symptoms on presentation	Tumor volume (cm ³)	Volume of OMCE (cm ³)	Knosp grade	Strategies	Extent of resection (%)	Postoperative symptoms	Histopathology ^a	Adjuvant therapy
1	71, f	Diplopia, Rt. partial ONP, APD, headache	10.3	1.9	4	Combined approach	95	Rt. partial ONP, APD	Silent ACTH producing adenoma	Gamma knife
2	60, f	Diplopia, Rt. partial ONP, bitemporal hemianopia, APD	18.8	1.8	4	Combined approach	90	Rt. partial ONP, APD	Null cell adenoma	Gamma knife
3	38, f	Diplopia, headache	4.5	0.31	3	ETSS	93	No symptoms	Null cell adenoma	Gamma knife
4	74, f	Incidentally detected adenoma, chronological tumor growth on imaging	7.4	0.057	4	ETSS	93	No symptoms	Gonadotropin producing adenoma	None

OMCE oculomotor cistern extension, ONP oculomotor nerve palsy, APD anterior pituitary dysfunction, ETSS endoscopic transsphenoidal surgery, ACTH adrenocorticotropic hormone

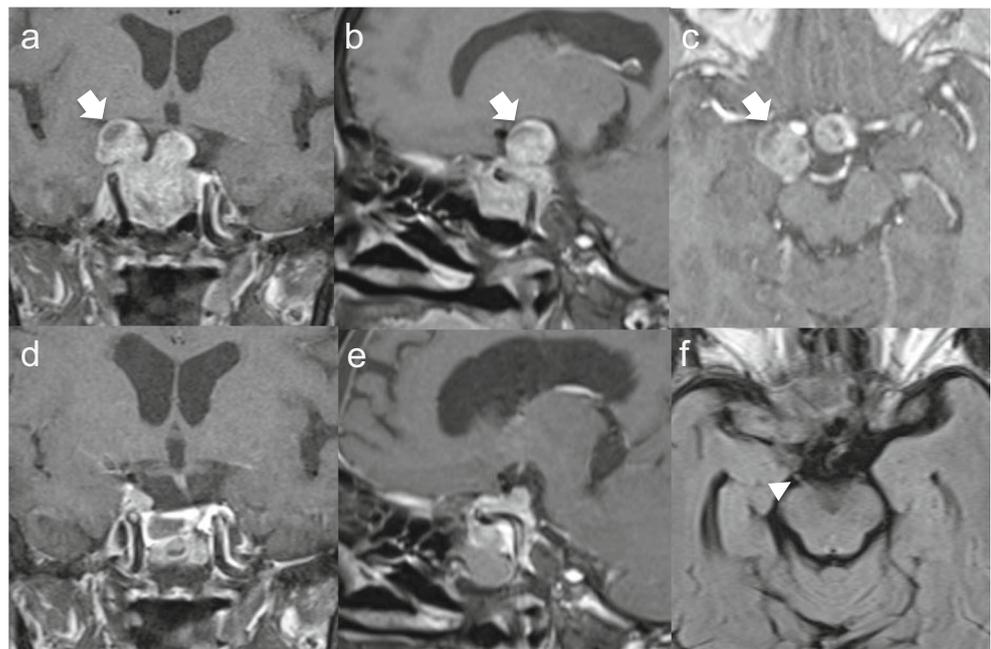
^a according to World Health Organization classification of pituitary adenoma, 2004 [16]

indicated subtotal removal of the tumor (Fig. 1d–f). The postoperative fluid-attenuated inversion recovery (FLAIR) image demonstrated the right oculomotor nerve on the lateral side of the OMCE small tumor remnant (Fig. 1f). Visual field perimetry revealed no limitation of the visual field. She did not feel diplopia in daily life after surgery. However, supraduction and abduction limitation of the right eye movement and mild dilation of the right pupil were the same as before surgery. Best corrected visual acuity was right 1.0 and left 1.2. The remnant tumor in the cavernous sinus was treated by gamma knife radiosurgery (maximum dose 32 Gy, marginal dose 16 Gy). MR imaging revealed no regrowth after 3 years.

Case 2

A 58-year-old woman recognized blurred vision while driving. Right oculomotor palsy was pointed out, and MR imaging demonstrated a pituitary tumor, with mild compression of the optic nerve. The patient was observed because of the mild symptoms. However, she presented with bitemporal hemianopia 3 years later. MR imaging showed tumor growth with right OMCE through the oculomotor triangle (Fig. 3a–c). The tumor volume was estimated as 18.8 cm³, including the OMCE volume of 1.8 cm³. The right cavernous invasion was Knosp grade 4. The best corrected visual acuity was right 0.5 and left

Fig. 1 Case 1. Preoperative coronal (a), sagittal (b), and axial (c) T1-weighted MR images after injection of gadolinium showing the oculomotor cistern extension (OMCE) of the adenoma (arrow). Postoperative coronal (d) and sagittal (e) T1-weighted MR images after injection of gadolinium and axial fluid-attenuated inversion recovery (FLAIR) image (f), indicating subtotal removal of the tumor and removal of the OMCE. The postoperative axial FLAIR MR image (f) demonstrates the right oculomotor nerve on the lateral side of the OMCE small tumor remnant (white arrowhead)



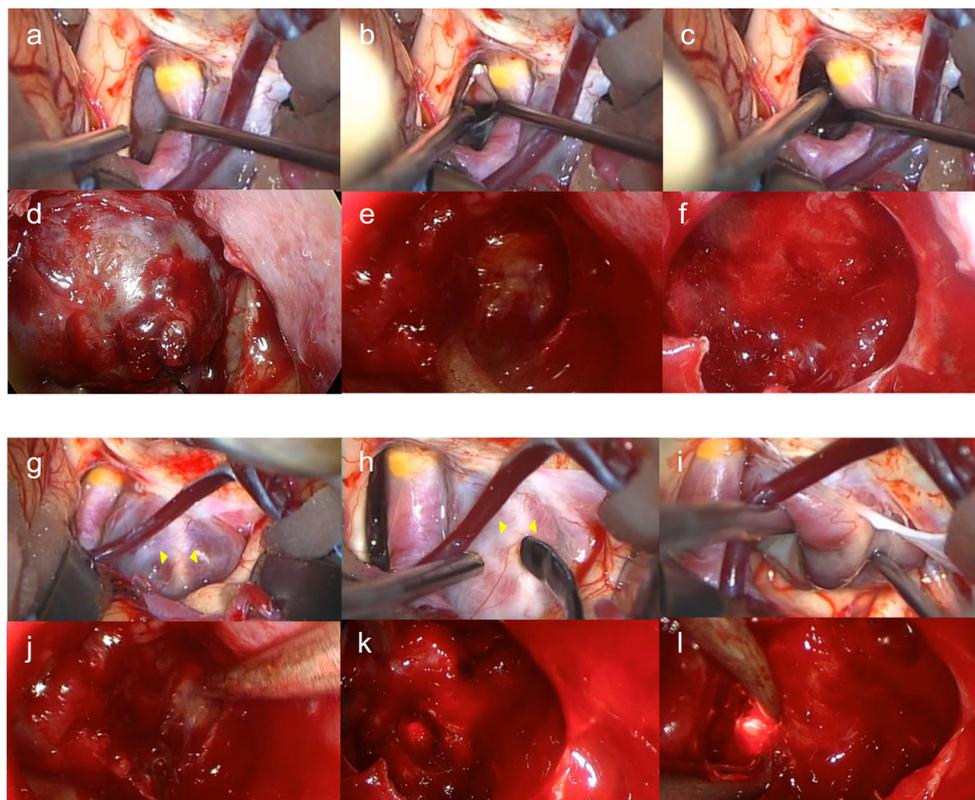


Fig. 2 Intraoperative photographs of the transcranial microscopic view (**a–c**, **g–i**) and endonasal endoscopic view (**d–f**, **j–l**) in case 1. Removal of the medial main mass is shown in (**a–f**), and removal of the OMCE in (**g–l**). The time flow of removal passes from left to right in each line (**a–c**, **d–f**, **g–i**, **j–l**). The medial main mass was revealed transcranially between the optic nerve and internal carotid artery (**a**). The sella was opened (**d**). The tumor capsule was pushed with forceps from the cranial side (**b**, **c**), and removed from the nasal side (**e**, **f**). The lateral OMCE was revealed

transcranially posterolateral to the internal carotid artery. The oculomotor nerve was observed in the capsule as a white cord (yellow arrowheads) in front of the transcranial microscopic view (**g**) and confirmed with nerve stimulation and electrooculographic monitoring (**h**). The tumor capsule was pushed by forceps from the cranial side (**i**) and removed from the endonasal side, referring to the transparent microscopic light as the site of the porus oculomotorius (**k**, **l**)

0.5. Visual field perimetry revealed bitemporal hemianopsia. Supraduction limitation of the right eye movement and mild dilation of the right pupil indicated right oculomotor palsy. She was accepted to undergo combined supra-infrasellar removal of the pituitary tumor. Preoperative endocrinological examination revealed anterior pituitary dysfunctions. The operative time flow is illustrated in Fig. 4. The oculomotor nerve was detected visually as attached to the tumor capsule at the anteromedial site of the OMCE mass. Simultaneous push and suction technique of the combined supra-infrasellar approach was performed for removal of the pituitary tumor. Subtotal removal was achieved (Fig. 3d–f). The bitemporal hemianopia was resolved after the operation. The blurred vision was not felt in daily life after the surgery. However, supraduction limitation of the right eye movement and mild dilation of the right pupil was almost the same as before surgery. The remnant tumor in the cavernous sinus was treated by gamma knife radiosurgery (maximum dose 32 Gy, marginal dose 16 Gy). MR imaging revealed no regrowth after 3 years.

Discussion

Removal of complex pituitary adenomas from only the infrasellar side is sometimes both difficult and hazardous, particularly as the tumor is frequently tightly attached to surrounding structures such as the arteries, perforators, optic apparatus, and cranial nerves. However, large remnant adenoma may cause postoperative bleeding, increased mass effect, and neurological deterioration [8, 13, 14]. Pituitary macroadenoma with OMCE was first described in a series of seven cases resected only through the transsphenoidal route [6]. Exposure of the cisternal segment of oculomotor nerve was extremely difficult via the endonasal approach, because of the hidden tumor location in the superior part of the cavernous sinus, forming a posteroinferior border with the anterior clinoid process anterolateral to the posterior clinoid process [1]. However, complete removal of the intrasellar part and the OMCE part of the tumor was reported in five of six cases through only endoscopic endonasal surgery [19]. The volumes of the OMCE part of the tumor were smaller in these cases (0.011–0.919 cm³) than in our case 1 (1.9 cm³) and case

Fig. 3 Case 2. Preoperative coronal (a), sagittal (b), and axial (c) T1-weighted MR images after injection of gadolinium showing the OMCE of the adenoma (white arrows). Postoperative coronal (d), sagittal (e), and axial (f) MR images indicate subtotal removal of the tumor and removal of the OMCE. The right oculomotor nerve is indicated by the white arrowhead

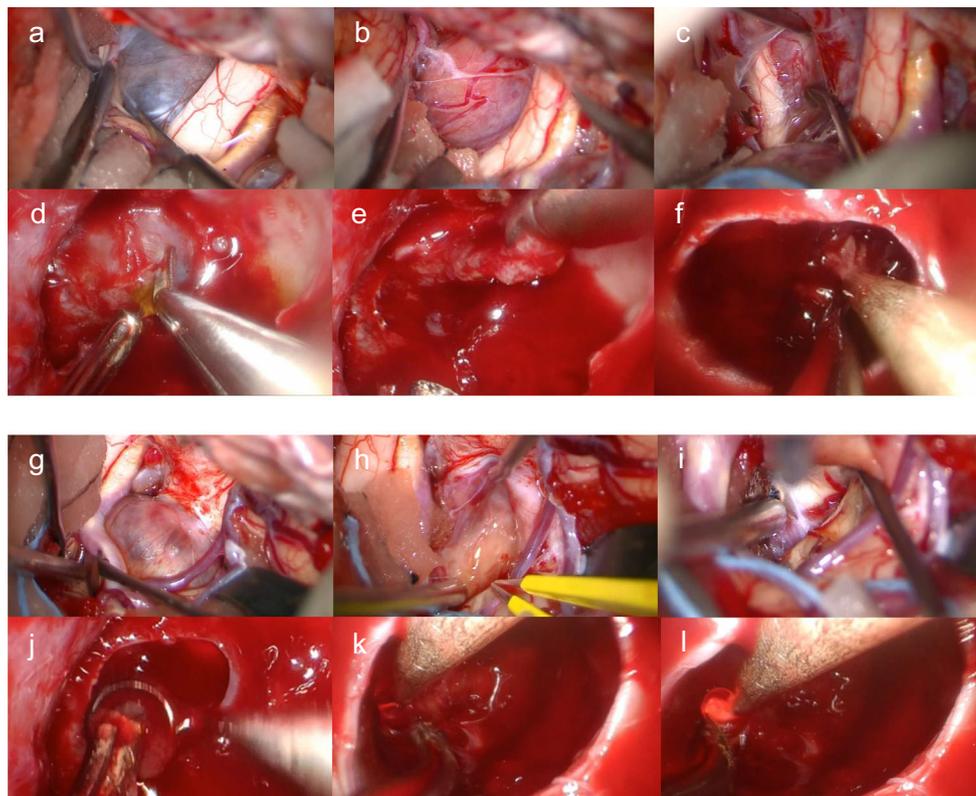
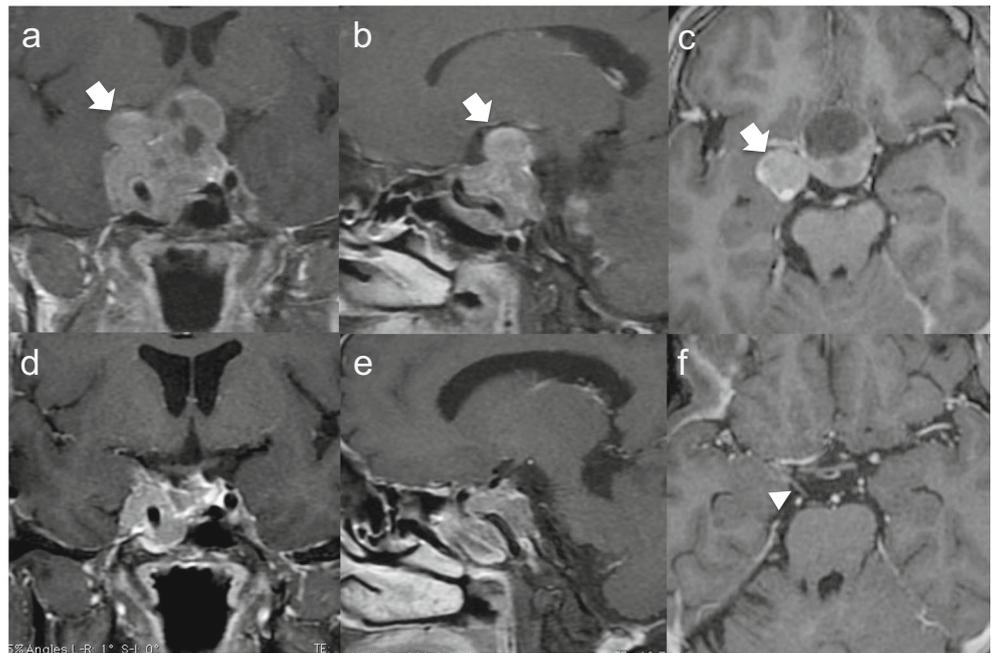


Fig. 4 Intraoperative photographs of the transcranial microscopic view (a–c, g–i) and endonasal endoscopic view (d–f, j–l) in case 2. Removal of the medial main mass is shown in (a–f), and removal of the OMCE is shown in (g–l). The time flow of removal passes from left to right in each line (a–c, d–f, g–i, j–l). The medial main mass was revealed anterior to the left optic nerve (a). The dura of the sella was opened (d). The tumor capsule was shrunk after endonasal removal of the main mass (b, e). Endonasal removal was supported by pushing the tumor capsule with

transcranial forceps (c, f). The lateral OMCE was revealed transcranially posterolateral to the internal carotid artery (g). The tumor capsule was shrunk with endonasal removal of the OMCE (h). The oculomotor nerve was observed medial to the OMCE mass (i). The tumor capsule was pushed by forceps from the cranial side (j) and removed from the nasal side, referring to the transparent microscopic light as the site of the porus oculomotorius (k, l)

2 (1.8 cm³) [19]. More recently, the endoscopic endonasal transoculomotor triangle approach was tried through the endonasal route [3]. Identification of the oculomotor nerve and posterior communicating artery were important to avoid injury to these structures. On the other hand, several cases of giant adenomas treated through the combined supra- and infrasellar approaches were suspected to include OMCE although not specified as such [2, 9, 11, 14, 15]. We consider that the combined supra-infrasellar approach with the transcranial transsylvian anterior temporal approach may be safer than only the endonasal approach to remove macroadenoma with relatively large OMCE, although not giant adenoma, as the nerve and arteries can be easily confirmed.

The cisternal portion of the third cranial nerve is considered to be an endoscopic endonasal “blind spot” [1]. The transcranial transsylvian anterior temporal approach provides a wide operative field in the retro-carotid space and excellent access to the oculomotor cistern tumor [5, 18]. This approach may be especially useful as a transcranial approach in combined supra-infrasellar approaches to multilobulated pituitary macroadenoma with OMCE. The oculomotor nerve was displaced superomedially in all four cases of pituitary adenoma with OMCE [3]. We confirmed the oculomotor nerve at the medial side of the tumor in our case 2. However, we found that the third cranial nerve was located anterolateral to the OMCE part of the tumor capsule in front of the intraoperative microscopic view, as identified by electrophysiological oculomotor nerve stimulation in our case 1. This capsule was suspected to consist of the outer thickened arachnoid and the inner pseudocapsule of the pituitary adenoma in our two cases [12]. The arachnoid forming the oculomotor cistern is continuous in the distal direction along the oculomotor nerve. The thickened arachnoid may capture the oculomotor nerve. The lateral part of the OMCE mass may include the oculomotor nerve. If removal of the OMCE is intended, confirmation of the oculomotor nerve by EOG monitoring may be required to preserve the nerve. Therefore, we did not dissect the third cranial nerve to avoid injury, instead, pushing the mass in the sellar direction and suctioning the tumor from the nasal side. This push and suction technique has sometimes been reported in various different supra- and infrasellar combined approaches for giant pituitary adenoma [2, 11, 14, 15]. We emphasize the usefulness of this technique for the removal of multilobulated adenoma with OMCE.

If the OMCE of the tumor is relatively small and not immediately adjacent to the optic apparatus, stereotactic radiation therapy after surgery without definite resection of the OMCE part may be a possible strategy [6, 17]. In fact, postoperative irradiation of the cavernous sinus part of the tumor with the gamma knife was necessary in three of our four cases. Transsphenoidal removal of the medial main mass followed by radiosurgery for the cavernous sinus part and OMCE part of the tumor is also an important alternative strategy [17].

MR imaging findings of giant pituitary adenoma with OMCE are rarely reported but not characterized as such. Clinical features and the prognosis of pituitary adenoma with OMCE have not been discussed. Pituitary adenoma with OMCE may be typically characterized by oculomotor nerve paresis. Our patients presented with oculomotor nerve paresis, including blurred vision and diplopia. Such eye movement complaints and double vision were improved after surgery, but objective partial oculomotor nerve paresis and anisocoria persisted. Assessment of pre- and postoperative neuropathy, and consideration of the surgical indication should consider both visual functions caused by optic chiasm compression and oculomotor neuropathy associated with the OMCE part of the tumor.

Conclusion

Multilobulated pituitary adenoma with OMCE requires special consideration of strategy and operative technique. Combined supra- and infrasellar approaches may be one of the important candidate strategies for this type of tumor. The transsylvian anterior temporal approach provides good visualization of the OMCE tumor and cisternal oculomotor nerve. The push and suction method with the combined supra-infrasellar approach is effective to decrease the OMCE volume avoiding injury of the surrounding structures. EOG monitoring may be required for the preservation of oculomotor nerve function.

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Compliance with ethical standards

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

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committees of the country of each participating member and with the 1964 Helsinki declaration and its later amendments or comparable standards.

Informed consent Informed consent was obtained from all participants included in the study.

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