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Original Article

Causes and treatment of acute visual dysfunction after trans-sphenoidal resection of a pituitary adenoma

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Abstract: Objective: Acute visual dysfunction after trans-sphenoidal resection of a pituitary adenoma is a severe post-operative complication. We determined the causes and treatment of early secondary acute visual dysfunction after trans-sphenoidal resection of a pituitary adenoma. Methods: The clinical data of 12 patients with early acute visual dysfunction after trans-sphenoidal resection of a pituitary adenoma were analyzed retrospectively. All patients were treated at the Peking Union Medical College Hospital between January 1991 and May 2014. Results: Among the 12 patients, there were 8 with intrasellar bleeding, 2 with suprasellar bleeding, and 2 with vasospasm. After treatment, 10 patients achieved good recovery of visual function, 1 had poor recovery due to the rupture of an intracranial aneurysm, and 1 died due to suprasellar bleeding. Conclusion: Long-term compression of the optic nerve and chiasma by a pituitary adenoma leads to a poor blood supply. A combination of factors, such as secondary intrasellar bleeding, direct surgical injury, acute ischemia of the optic nerve, and excessively tight intrasellar packing, led to early secondary acute visual dysfunction after trans-sphenoidal resection of pituitary adenomas. Indeed, the timely discovery and confirmation of the causes of acute visual dysfunction and early treatment can effectively save a patient's visual acuity.

Keywords: Pituitary adenoma, trans-sphenoidal approach, post-operative complications, visual dysfunction

Introduction

Pituitary adenomas are common benign tumors in the sellar area which account for approximately 10% of intracranial tumors. With the development of medical imaging modalities in recent years, the detection of pituitary tumors has significantly increased, and is now reported to be 15%-20%. With the development of microsurgical techniques, the trans-sphenoidal resection of pituitary adenomas is on the rise. Currently, the single nostril trans-sphenoidal approach is the preferred treatment for the majority of pituitary adenomas. The single nostril trans-sphenoidal approach is used not only for removing intrasellar tumors, but also for removing suprasellar tumors. Although the single nostril trans-sphenoidal approach for pituitary adenomas has been utilized for nearly a decade, complications do occur, of which post-operative acute visual dysfunction is one of the most serious. This paper retrospectively summarized the data of 12 patients with acute visual dysfunction after trans-sphenoidal resection of pituitary adenomas at Beijing Union Medical College Hospital between January 1991 and May 2014, and determined the causes and preventive measures of decreased visual acuity after trans-sphenoidal resection of pituitary adenomas.

Subjects and methods

Study subjects

The data of > 7000 patients who underwent trans-sphenoidal resection of pituitary adenomas at Beijing Union Medical College Hospital between January 1991 and May 2014 were statistically analyzed. Twelve patients had acute visual dysfunction (incidence = 12/7000 [0.17%]), including 8 males and 4 females. The patients ranged in age from 27-69 years, with an average of 52.5 years. The course of the dis-

Table 1. Visual acuity status among 12 patients before and after surgery

Time	Normal visual acuity	Visual acuity index 4.0-4.8	Counting figures	Monocular blindness	Binocular blindness
Pre-operatively	4	5	1	2	0
Early period post-operatively	0	0	5	4	3
3 months post-operatively	6	3	0	2	0

Note: 1 patient died post-operatively.

Table 2. Visual field status in 12 patients pre- and post-operatively

Time	Normal visual field	Unitemporal hemianopsia	Bitemporal hemianopsia	Tubular visual field	Monocular blindness
Pre-operatively	4	2	2	2	2
3 months post-operatively	6	2	1	0	2

Note: The visual field was not examined in the early period post-operatively, and 1 patient died post-operatively.

ease ranged from 1 week to 15 years, with an average of 5 years. The clinical manifestations of pituitary adenomas in the study population included the following: (1) Based on an endocrine examination, the pituitary adenomas were non-functioning in 9 patients, growth hormone type in 2 patients, and thyroid-stimulating hormone type in 1 patient. There were 4 patients with pre-operative normal visual acuity, 8 patients with decreased visual acuity (1 patient with monocular blindness, 1 patient with counting figures, 5 patients with visual acuity indices between 4.0 and 4.85, and 8 patients with different degrees of visual field defects; **Table 1**). Five patients had headaches, one patient had amenorrhea, one patient underwent gamma knife surgery, two patients had hypopituitarism, and two patients had acromegaly. (2) All patients underwent MRI + C examinations pre-operatively, which showed that the tumors were located in the intra- and supra-sellar areas. There were 3 patients with large adenomas (tumor diameter = 1-3 cm), and 8 patients with giant adenomas (tumor diameter = 3.1-7.5 cm).

Surgical mthods

Twelve patients were treated using a single nostril trans-sphenoidal approach. Intra-operatively, it was noted that there were 7 patients with soft texture tumors, 5 patients with tough texture tumors, 9 patients with rich blood supplies, and 5 patients with cavernous sinus invasion. Seven patients underwent total resections under microscopy, 5 patients underwent subtotal resections, and 1 patient was noted to have a cerebrospinal fluid leakage intra-operatively (the leakage opening was repaired immediately).

Results

All 12 patients in this group had secondary acute visual dysfunction between 2 hours and 3 days post-operatively. Craniocerebral CT re-examinations were performed immediately after the decreased visual acuities were detected, which showed that 10 patients had post-operative bleeding, including 8 patients with intrasellar bleeding and 2 patients with suprasellar bleeding. There were 2 patients with no obvious hematomas; the decreased visual acuity was thought to reflect vasospasm in the optic nerves of these patients. All 10 patients with post-operative bleeding underwent evacuation of the hematomas upon diagnosis. Eight patients with intrasellar bleeding underwent repeat trans-sphenoidal surgery to remove the hematomas, and visual function was restored that was better than at baseline. Of the two patients with suprasellar bleeding, 1 underwent a craniotomy for hematoma removal, and the other patient underwent external ventricular drainage and a repeat VP shunt due to concurrent post-operative hydrocephalus (he died 10 days post-operatively). One patient with a subarachnoid hemorrhage caused by a ruptured intracranial aneurysm was treated conservatively; he also had concurrent hydrocephalus and underwent external ventricular drainage and placement of a VP shunt (the patient regained consciousness 1 month post-operatively, but had persistent aphasia and was bedridden; thus, the patient was trans-

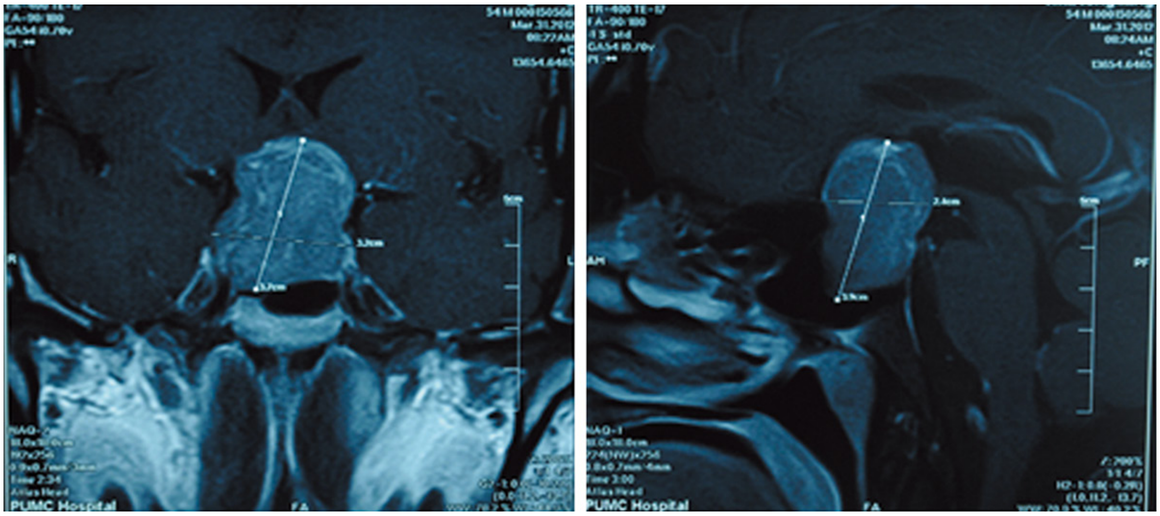

Figure 1. A 54-year-old male patient with a non-functioning giant pituitary adenoma complained of decreased binocular visual acuity over 5 years. The eye examination showed right optic nerve atrophy. Visual acuity was as follows: left eye, 4.0; right eye with counting fingers vision; left temporal hemianopia; and right total blindness. Pre-operative MRI (enhanced): giant pituitary adenoma with a height of approximately 3.2 cm. No optic chiasm was observed.

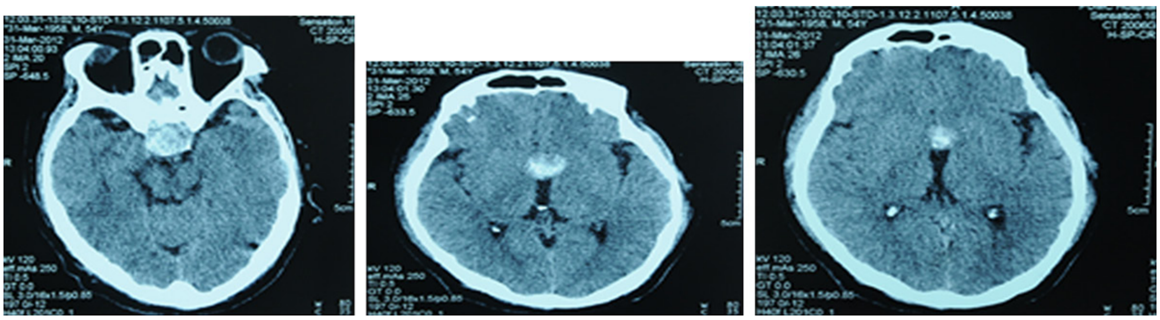

Figure 2. Two hours after trans-sphenoidal resection of pituitary adenomas, the patient complained that both eyes had no light sensation. Emergency cranial CT was performed. Abnormally high-density lesions were observed in the original tumor area of the sellar area, and the possibility of a hematoma was significant.

ferred to another hospital for rehabilitation and hyperbaric oxygen treatment). Two patients with optic nerve ischemia caused by vasospasm in the optic nerve were treated symptomatically, including blood vessel dilation, improving the circulation, and nourishing the nerves; the visual function recovered to some extent compared with baseline (**Tables 1** and **2**). Representative patient cases are shown in **Figures 1** and **2**.

Discussion

The incidence of acute visual dysfunction after trans-sphenoidal surgery has been reported to be 0-10% [1-3], the incidence of acute visual dysfunction after trans-sphenoidal surgery is 0.6%-1.6% and 0.4%, respectively. Zervas [4] retrospectively analyzed 2677 patients with large adenomas in an international multi-center study; 39 patients (1.5%) had a post-operative deterioration in visual function. Among 2606 patients with microadenomas, there were 3 with permanent visual damage (0.1%). Atkinson [5] retrospectively analyzed 2312 patients undergoing trans-sphenoidal surgery at the Mayo Clinic between 1987 and 2007, of whom 3 had post-operative re-bleeding (0.13%) and developed progressive visual dysfunction. The incidence of visual dysfunction after trans-sphenoidal surgery in our hospital was 0.17% (12/7000). Combining the experiences reported in the literature and the current study, the causes, prevention, and treatment of decreased visual acuity after trans-sphenoidal resection of pituitary adenomas are summarized and discussed as follows:

Post-operative bleeding is the main cause for acute visual dysfunction after trans-sphenoidal resection of pituitary adenomas. Among 12 patients with visual impairment in this group, the visual impairment in 10 patients was caused by post-operative bleeding, which could be divided into intra- and supra-sellar bleeding. Intrasellar bleeding is more common than suprasellar bleeding in situations, such as residual tumor stroke, tumor bed bleeding (especially in the huge dumbbell-shaped pituitary adenoma), intercavernous sinus bleeding, intra-operative incomplete hemostasis, and coagulation disorders. It is necessary to carry out adequate hemostasis after tumor resection, pack the hemostatic materials appropriately, elevate the blood pressure to the pre-operative level, and observe for at least 5 min. If there is continued intra-operative bleeding, a soft silicone tube of 3-mm diameter can be placed into the sella turcica for local drainage to prevent secondary hematomas, while sellar reconstruction can be performed by padding an appropriate amount of autologous fat and biomedical fibrin glue into the sella turcica and sellar floor. The autologous fat and biomedical fibrin glue have characteristics, such as good hemostasis, easy to shape, no water absorption and swelling, good compliance, reliable sealing, and easily distinguished from the tumor tissues and hematoma by post-operative imaging. The patients discontinue oral anticoagulants at least 1 week before surgery. In addition to standard laboratory testing, such as bleeding and clotting times and the platelet count, thrombelastography (TEG) should be performed to help elucidate platelet function and blood coagulation factor levels pre-operatively. The diaphragma sellae will collapse rapidly after resection of giant pituitary adenomas. The residual tumor is easily left in the area inside the reverse folds of the diaphragma sellae, thus leading to post-operative bleeding. Based on our experience, when the tumor is being removed, the tumor tissues on both sides and posteriorly should be removed first, then the suprasellar tumor should be removed to protect the tumor in the posterior area from premature collapse of the diaphragma sellae. The intra-sellar area should be carefully explored after tumor resection, especially the area inside the reverse folds caused by the collapse of the diaphragma sellae. The collapsed diaphragma sellae is slowly elevated with gauze. The reverse folds are carefully explored to confirm tumor is not missed, thus leading to post-operative hemorrhage in residual tumor and tumor recurrence. In recent years, along with the application of new hemostatic materials, such as fluid gelatin sponge, the incidence of post-operative intrasellar bleeding has been significantly reduced. (2) Although the pituitary adenoma will break through the diaphragma sellae and grow into the suprasellar area, instruments rarely enter the suprasellar area directly during surgery, therefore the probability of direct damage to suprasellar blood vessels is small. The giant pituitary adenoma grows slowly and expansively in the sella turcica, will elevate the diaphragma sellae, and make contact with suprasellar structures, such as the optic nerve and optic chiasm, and invade through the arachnoid membrane to form fibrous adhesions, which are rich in small blood vessels. The diaphragma sellae will be pulled down during tumor resection so that the more brittle small blood vessels get ruptured and bleed. In addition, the diaphragma sellae is quickly collapsed after tumor resection, and the small artery branches attached to the diaphragma sellae are also stretched and broken, thus causing suprasellar hematomas or subarachnoid bleeding [6]. We believe that the integrity of the arachnoid membrane above the tumor should be maintained as much as possible to prevent cerebrospinal fluid leakage. If cerebrospinal fluid leakage has occurred, the leakage opening should be sealed with gauze to avoid the outflow of cerebrospinal fluid and a sudden change in intracranial pressure. When a giant pituitary adenoma, which grows towards the suprasellar area, is being removed, the suprasellar area can be padded with gauze and pressed slightly, while the tumor is gradually removed, thus avoiding rapid collapse of the diaphragma sellae due to tumor total resection. The residual cavity will be packed with hemostatic materials, such as fluid gelatin sponge, so that the residual cavity has adequate support. If the residual cavity is too large, inflating the balloon of a Foley urethral catheter can be adopted to achieve a compressive effect and the sellar floor is not sealed. The Foley urethral catheter, which can play the role of hemostasis and drainage, will be removed 24 hours later. Mannitol, hyperventilation, and restricted ventilation are used intra-operatively to adjust the intracranial pressure and to prevent the tumor and diaphragma sellae from being squeezed excessively into the sella turcica due to excessive intracranial pressure; the suprasellar tumor and diaphragma sellae cannot be adequately collapsed into the sella turcica due to low intracranial pressure. Two patients in this group had suprasellar bleeding; one case was related to bleeding from the blood vessels of the skull base or the post-operative blood pressure fluctuation, which was a reflection of the drop in intracranial pressure and the intra-operative leakage of cerebrospinal fluid, and the other case with bleeding from a ruptured intracranial aneurysm was very rare. In summary, the post-operative bleeding was generally shown by the appearance of headaches with a sharp decline in visual acuity, and symptoms of hypothalamic dysfunction, such as loss of consciousness, fever, and diabetes insipidus within a few hours of surgery. When the patient with decreased visual acuity was examined post-operatively, the patient was immediately re-examined by CT if intra-or supra-sellar bleeding was observed. It is advisable to perform trans-sphenoidal surgery or a craniotomy to remove a hematoma, which can often improve the visual acuity of the patient quickly and be life-saving.

Direct damage can occur to the optic nerve or optic chiasma during surgery. Deviation in the direction of use of the nasal retractor or when chiseling the sellar floor may injure the slender lower wall within the optic nerve canal in the superior wall of the sphenoid sinus with good gasification. In individual cases, due to anatomic variations, there is a congenital absence of bone in the lower wall within the optic nerve canal so that the sphenoid sinus mucosa directly contacts the optic nerve within the optic nerve canal. This side of the optic nerve may be injured when the sphenoid sinus mucosa is removed. The rough surgical procedure may also cause a basilar skull fracture involving the optic canal and the surrounding bones. As the tumor is removed, the diaphragma sellae, optic nerve, and chiasma, which are originally compressed and elevated, the optic nerve may be directly damaged if the surgeon attempts to scrape upwards to remove the tumor blindly through the foramen of Pacchioni. Therefore, when trans-sphenoidal surgery is performed, the midline approach should be strictly followed. The sellar floor window is not too high, and the intrasellar tumor should be removed gradually in proper sequence after the intrasellar area is fully empty. The suprasellar tumor will slowly descend down into the intrasellar area, and the tumor resection is continuously performed again. In patients with huge dumbbell-shaped tumors, the diaphragma sellae is tight and narrow, thus the descent of the suprasellar tumor is unsatisfactory. The anesthetist can be asked to perform maneuvers to increase intracranial pressure, such as suspend breathing and the Queckensted test, to promote descent of the diaphragma sellae and the suprasellar tumor into the intrasellar area, and the tumor resection is performed again. Scraping upwards to remove the suprasellar tumor blindly should be avoided in situations, such as a tight and narrow diaphragma sellae, additional bleeding, and an obscure surgical field [7]. According to the pre-operative images, attention should focus on the clear judgment on the positional relationship between the diaphragma sellae and the suprasellar tumor. After these technical improvements, no further cases of intra-operative direct damage to the optic nerve occurred at Beijing Union Medical College Hospital in nearly 20 years.

Intrasellar overpacking of hemostatic materials, such as fat, muscle, and gelatin sponges, may compress the optic nerve and chiasma, thus causing deterioration of visual function. There is often a rapid decline in visual acuity. The hemostatic materials packed in the intrasellar area begins to swell excessively after absorbing the blood, which can also result in decreased visual acuity due to optic nerve compression. The patient has a headache, which is often not severe, is also shown as a high density on CT scan, but is heterogeneous and a mixed high density compared with a hematoma. When the above situation occurs, the dehydrating agents and large doses of adrenocortical hormone should be used for symptomatic treatment. If no symptom improvement is achieved, the surgery should be performed immediately again. A good effect can be achieved if the intrasellar packing materials are removed during surgery. Sometimes, no overpacking is found or only small blood clots and

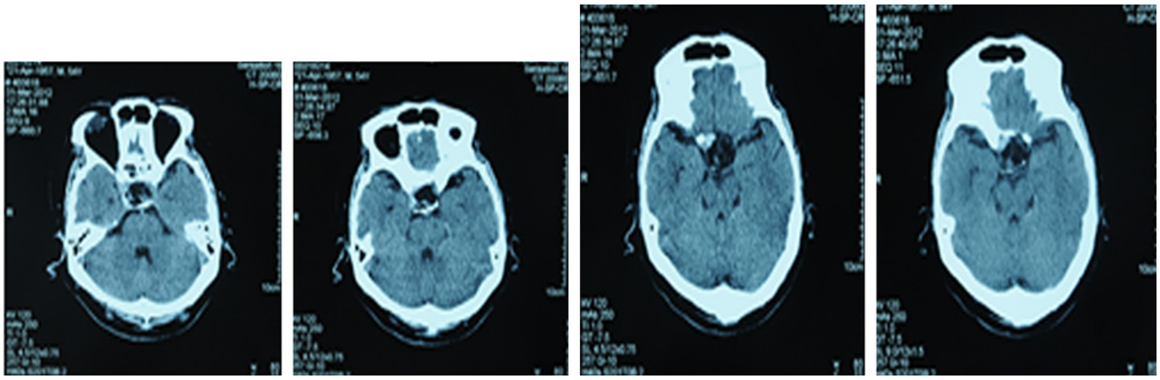

Figure 3. Three hours post-operatively, the secondary trans-sphenoidal removal of hematoma was performed in emergency treatment, and the patient claimed that vision acuity improved significantly. The head CT was re-examined immediately post-operatively and it was empty in the original hematoma area and the efficacy of hematoma removal was satisfied.

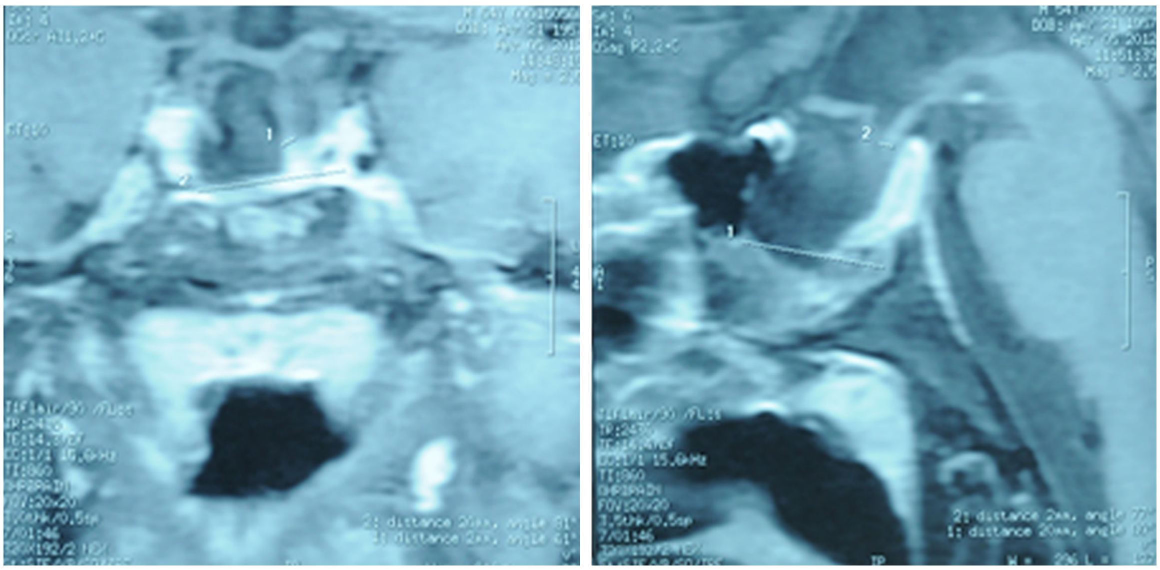

Figure 4. The visual acuity of the patient 5 days post-operatively. Left eye, 5.0; right eye, 4.0. Re-examination of nuclear magnetic resonance (enhanced): the efficacy of tumor resection was satisfied, and the optic chiasm was clearly visible.

sponges are observed during surgery, and there is no space-occupying effect, but the re-operation can rapidly improve visual acuity. According to our experience, attention should focus on the direction when packing hemostatic materials during surgery, and the hemostatic materials should be packed into the periphery of the intrasellar area instead of the suprasellar area. If the hemostatic materials are packed into the suprasellar area blindly, the collapsed diaphragma sellae will be lifted up to the suprasellar area. A hemostatic effect would not be achieved, and the optic nerve may be compressed. Currently, we pay attention to appropriate intrasellar packing during surgery so that a similar situation does not recur. In addition, the use of new hemostatic materials, such as fluid gelatin sponge material, can also significantly improve the hemostatic effect.

Guinto [8] believes that there may be adhesions between large adenomas that develop in the suprasellar area, the optic nerve, and chiasm if the diaphragma sellae descends too fast and too low during surgery. If the optic nerve and chiasm, which are already fragile, are pulled down mechanically, deterioration of visual function is more likely. According to our experience, if the site where the diaphragma sellae descends during surgery is too low, exceeding the normal level of the sellar floor, autologous fat or absorbable hemostatic materials to properly fill the intrasellar area should be considered. Autologous fat or absorbable hemostatic material has a supporting role; specifically, the diaphragma sellae can ascend back up to the normal position of the sellar floor to prevent descent and excessive angulation of the optic nerve and chiasm, which affect the blood supply and prevent a post-operative acute empty sella turcica.

Acute ischemia of the optic nerve is caused by vasospasm in the optic nerve. The anterior superior hypophyseal artery originates from the inner sidewall of the supraclinoid segment of the internal carotid artery, and feeds the inner- and under-sides of the optic nerve in the anterior horn of the optic chiasma and the neighboring areas of the optic chiasm. The end branch anastomoses with the contralateral anterior superior hypophyseal artery in the middle part of the optic chiasm and the front of the base of the pituitary stem then gives off several sub-branches, which are distributed in the soft membrane in the middle of the underside of the optic chiasma and the pituitary stem. The anterior superior hypophyseal artery is compressed to lead to visual pathway ischemia, and this is one of the main reasons that patients with pituitary adenomas usually have decreased visual acuity and bilateral temporal visual field defects. Trans-sphenoidal surgery is no less likely to damage the blood vessels directly, but in all situations, such as the use of the heat conduction effect of bipolar coagulation intra-operatively, the vasospasm due to the blood vessels is pulled after the collapse of the diaphragma sellae. The long-term tumor compression of the blood vessels and the ischemia reperfusion caused by vascular recanalization after decompression can lead to optic nerve ischemia. Two patients in this group had decreased visual acuity, but had no significant headaches. The CT re-examination showed no demonstration of intrasellar bleeding. Therefore, the decreased visual acuity was thought to be optic nerve ischemia post-operatively. The patients received symptomatic treatment with vasodilator drugs and hormones, thus improving the microcirculation and the neurotrophic drugs. The binocular visual acuities recovered more significantly compared with baseline (**Figures 3** and **4**).

Hydrocephalus leads to intracranial hypertension and the pulsatile impact of the lower part of the third ventricle towards the undersurface, and the optic nerve and chiasm may be involved. Two patients in this group had post-operative intrasellar bleeding. The patients had concurrent hydrocephalus after surgical removal of the hematoma, then underwent external ventricular drainage and placement of a VP shunt. The visual function in one patient was restored to some extent in the early stage, but the patient ultimately died at an advanced age with a secondary intracranial infection and multiple organ failure. Another patient had secondary aneurysmal rupture, and the duration of coma was longer post-operatively.

One patient in this group underwent pre-operative gamma knife treatment. The visual acuity and visual field were deteriorating. The optic nerve had been compressed for a long time and was very fragile. The impact of surgery and hematoma compression led to further deterioration of the visual acuity and visual field. Therefore, for patients with giant adenomas and evident compression of the optic nerve, caution must be exercised to carry out gamma knife treatment; however, surgical treatment is preferred over gamma knife treatment.

Disclosure of conflict of interest

None.

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