Lesions of the oculomotor nerve as the first sign of pituitary adenoma are rare. The cause of such lesions without other clinical symptoms is discussed in this study. A small cohort of 4 patients (3.1%) with oculomotor nerve palsy (third nerve palsy) as the only neurologic deficit, from 129 patients who got operated upon for pituitary adenomas, is presented. In this group (mean age: 55 years, range: 36–65 years), all patients (two women and two men) underwent surgery. In two cases, there was arrested pneumatization and thickened bone. In the remaining two cases, a macroscopically visible, very solid opaque diaphragm was present, after the removal of the tumor and thickened bone. Complete adjustment was observed in all patients within 1 week after the surgery. Two factors that seem to increase the high risk for the development of oculomotor nerve palsy are that the cavernous sinus may be the only weak structure surrounding the sella turcica when the diaphragm and bone are thickened; and the rapid development of increased pressure in this region. The increased pressure on the cavernous sinus during the anatomical variations is the primary cause for lesions on the oculomotor nerve. However, this conjecture cannot be statistically demonstrated because of the small number of cases. Future research should be conducted on larger samples to increase statistical inference and generalizability.

**Keywords**
- pituitary apoplexy
- oculomotor nerve
- anatomical variations
- sella turcica

**Introduction**

Pituitary apoplexy is caused by an acute ischemic stroke, with secondary bleeding after the stroke, or it could be due to a primary bleeding event in pituitary adenomas. Some evidence indicates that pituitary apoplexy is associated with the sudden onset of neurological and/or hormonal disorder. One possible neurologic symptom is paresis/plegia of the third cranial nerve. Lesions of the third cranial nerve are rare. However, the possible cause of a lesion of the oculomotor nerves passing through the cavernous sinus as well as the trochlear and abducens nerves and visual acuity deficits may be an acute onset of pressure on the cavernous sinus. However, the most common nerve lesion is the oculomotor nerve with varying degrees of paresis. The nerve lesion of the oculomotor nerve is very rare (14.28% from all pituitary apoplexy), though the incidence in the patient group is relatively high and the formation of this nerve lesion has always been associated with pituitary tumor apoplexy (100%). Possible causes of the nerve lesion and anatomical variations are discussed by the authors.

**Materials and Methods**

From April 2011 to August 2012, 129 patients underwent surgery for pituitary adenoma at the Department of Neurosurgery, First Medical Faculty and Central Military Hospital, Military Faculty Hospital, Prague. The group of patients comprised 62 women and 67 men, with a mean age of 52.5 years (range: 9–81 years). In the patient group, there were 51 hormonally active tumors and 78 were hormonally inactive (requiring surgery for visual disorder or for compression of the surrounding structure). Four patients (3.1%) presented lesions of the oculomotorius nerve—complete oculomotor...
nerve palsy (ptosis, diplopia, and mydriasis). In this group of four patients (mean age: 55 years, range: 36–65 years), all patients (two women and two men) underwent surgery. Early clinical symptoms appeared anywhere from 1 to 3 weeks before the surgery. The appearance of lesions of the oculomotor nerve was sudden in all cases. One patient suffered from panhypopituitarism preoperatively. The tumor size varied from 18 to 23 mm (diameter 20 mm). In one case, a tumor penetration into the cavernous sinus was demonstrated based on preoperative magnetic resonance imaging (MRI). Disintegrating portion of tumor and marks of bleeding were typically presented on the MRIs. In two patients, the arrested pneumatization and thickened bone were observed on MRI. In the remaining two patients, a thickened diaphragm was more easily noted after the removal of the tumor in the control MRI scan the next day.

Since November 2006, our team has used the binos tril endoscopic endonasal approach with the aid of a Storz 0 degree endoscope (Karl Storz Endoscope). The binostril technique (four-hand technique) is the standard surgical technique in our department. This procedure does not require septum lateralization. We resect only a small area (0.5 × 0.5 cm) in the posterior part of the nasal septum. The use of both nostrils offers several advantages, including greater working space and a large range of instrument movement. At a certain point during the surgical procedure, two instruments have to be used simultaneously, namely, a drain cannula and an endoscope (hence, the four-hand technique). Our operations take place in a multifunction room, where data are transmitted from an intraoperative 3.0-TMR system (General Electric) and subsequently updated in a surgical navigation system (Brainlab).

Results
In two cases, there was the absence of the sphenoid cavity, as well as evidence of thickened bone. In these two cases, it was necessary to grind the bone (width from 6 mm to 1 cm) (Fig. 1). A very solid opaque diaphragm was macroscopically visible after the removal of the tumor and thickened bone in the remaining two cases (Fig. 2). The diaphragm was white, smooth, and strong in appearance. There was no typical decline of the diaphragm in these two cases after the removal of the tumor. A tougher, but fragile, bruising tumor with initial high pressure was found in all cases after cutting the dura mater. After cutting the dura mater, there was always a massive sharp leakage of old blood as a part of the sellar expansion. All patients showed a very fast recovery. Partial recovery generally occurred during the first 24 hours. Complete adjustment was observed in all patients within 1 week after the surgery. MR radical resection (3 months postoperatively) and hormonal radical resection (for hormonal active tumors) were achieved in 73% of the cases with the help of intraoperative MRI (129 operations for pituitary adenomas in all patients). Magnetic resonance (MR) radical resection of a subgroup of patients (the subgroup consisted of adenomas with lesions of the oculomotor nerve) was achieved in three adenomas, 75%. On postoperative MRI, we observed the remains of the left side of the adenomas in the lateral compartment of the cavernous sinus. We did not encounter any postoperative complications in the cases with lesions of the oculomotor nerve. Pituitary hypofunction remained in patients with substituted hypofunctional hypophysis before surgery. Postoperative substitution has been necessary in two patients, 5 years after the surgery. Histologically, bruising was seen in all of the adenomas.

Discussion
Pituitary apoplexy is caused by acute ischemic injury or spontaneous hemorrhage of the pituitary tumors. The frequency of stroke ranges from 2 to 7%. However, it is important to determine whether it is a clean bleeding, which is shown on MR, or clinically developed clinical symptoms (sudden malfunction of the pituitary gland, visual disturbances, or disorders of the ocular nerves). The increased fragility of tumor vessels has been suggested as a cause of pituitary apoplexy. The embolism in atherosclerotic disease
has been also suggested as a cause of pituitary apoplexy.\textsuperscript{4} Predisposing factors of pituitary apoplexy include high blood pressure, head injury, pituitary irradiation in the past, anticoagulant therapy, treatment with dopamine agonists and pregnancy, diabetes mellitus, high altitude, dengue hemorrhagic fever, dynamic endocrine tests, and spinal anesthesia.\textsuperscript{5,6} The latter factor can also support the hypothesis that the rapid enlargement of pituitary adenoma may lead to the oppression of veins, which are a part of the portal system in the pituitary stalk through diaphragm. This condition can lead to congestion and hemorrhage;\textsuperscript{7} however, small tumors can also develop apoplexy events.\textsuperscript{8} Intratumoral vasculopathy rendering the vessels more susceptible to hemorrhage has been proposed as an option.\textsuperscript{2} Furthermore, a significant correlation between the intratumoral expression of vascular endothelial growth factor and tumor necrosis factor-\alpha and the presence of tumor hemorrhage has been found, suggesting a possible causal relationship, although other group did not confirm this finding.\textsuperscript{9}

Lesions of the oculomotor nerve that result from pituitary apoplexy can have several causes. The notion of direct pressure on a nerve by a large pituitary adenoma is apparently the most logical cause.\textsuperscript{10} Pituitary apoplexy is an acute condition in which the wall of the cavernous sinus is not primarily infiltrated yet is enhanced pressure inside the sinus. The conjecture pertaining to vascular lesions of the oculomotor nerve, which is based on a reflex spasm of vessels from the pressure of the tumor that encases the internal carotid artery, is much more intriguing.\textsuperscript{10} This belief explains the emergence of acute lesions, but cannot explain why it would be limited only to the disability of the oculomotor nerve and not to the trochlear and abducens nerves.\textsuperscript{11} Presently, the theory that is best is still being debated. The basic premise is that the oculomotor nerve, which passes through the lateral wall of the cavernous sinus, is much more vulnerable than the other nerves. It has been suggested that the abducens nerve is more vulnerable than the oculomotor nerve. The cause of the sixth cranial nerve lesion is beyond the cavernous sinus and this lesion is described more often in relation to either an inflammation or to a skull base tumor.\textsuperscript{12} The highest position of the third cranial nerve (the oculomotor nerve) in cavernous sinus is another explanation as to why the nerve is affected. The anterior part of the cavernous sinus is relatively the most mobile part.\textsuperscript{13}

We believe that the most likely cause of the disability of the oculomotor nerve is the anatomy of the sella turcica and its surroundings. The frontal, caudal, and dorsal surfaces are made up of bone. The cranial saddle surfaces are covered with the diaphragm. The lateral surface forms the inner walls of the cavernous sinus. The pressure is transmitted to the wall of the cavernous sinus if the diaphragm is very rigid, or if the base of the saddle is rigid. The cavernous sinus is not an open tube resembling an enlarged vein, but rather it is a patchwork of lagoons (sometimes described as spicules, which form a dense network). This structure resembles a sponge, with high blood flow.\textsuperscript{14} Congestion in the sella turcica leads to high pressure inside the cavernous sinus. The oculomotor nerve is located uppermost, above the trochlear nerve in the lateral wall of the cavernous sinus at the transition to the upper surface. These conditions explain why the highest pressure is at this particular point. The conditions also explain why the site of the pressure is at the lesion of the oculomotor nerve.

This hypothesis is confirmed by our results. All operations were performed by the four-hand endoscopic technique through two nostrils (standard procedure at our institution).\textsuperscript{15} In all patients, perioperative MRI was applied at the same time. The maximum radicality of tumor removal is guaranteed by this technique at this time.\textsuperscript{16} No complications were seen in any of our patients. All patients were transmitted by car to the Department of Endocrinology at the Charles University Hospital in Prague.

As our subgroup consisted of only four patients, no statistical analyses could be done. Nevertheless, we found some evidence to support our hypothesis. The most important finding concerns the underdevelopment of the sphenoid sinus with a solid saddle base that was seen in two patients (conchal type of sphenoid sinus). In the remaining two patients, we observed a very strong diaphragm that became visible through MRI after tumor removal and thickened bone (presellar type of sphenoid sinus). We found anatomical variety in all patients with lesions of the third cranial nerve. This observation is a new concept which was found. These findings suggest that the primary pressure is at the lateral wall of the cavernous sinus. The incidence of presellar type was reported to be 5.5 to 27% in the literature and conchal type is reported to be none to 3%.\textsuperscript{17-19}

In the whole group of 129 patients (including hormonally active microadenomas), the average tumor size was 21 mm; in the subgroup (lesions of the oculomotorius nerve), tumor size ranged from 18 to 23 mm (diameter 20 mm). These findings suggest that lesion formation is not determined by the size of the tumor, but rather by the speed of the pressure buildup in the event that anatomical variations are present where the pressure is directed toward the cavernous sinus.

The hypothesis that pressure is the cause of the oculomotor nerve lesion was confirmed by the rapid speed of adjustment, that is, all patients demonstrated partial modification in the first 24 hours after the surgery. Moreover, all patients were able to lift their eyelids on the first postoperative day.

**Conclusion**

Early tumor resection is the treatment of choice for lesions of the oculomotor nerve, which are caused by pituitary apoplexy. The hypothesis that sudden pressure causes oculomotor nerve lesions is highly plausible in the event that anatomical variations are present, but this could not be demonstrated statistically in the present report because of the small number of cases.

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Conflicts of Interest
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