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Case Report

A Rare Complication of Pituitary Adenoma Surgery in a Patient with Multiple Endocrine Neoplasia 1 Syndrome with Two Novel Genetic Mutations

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Abstract

Pituitary adenoma surgeries are common in neurosurgical setup. Majority are tackled by a transsphenoidal route either by endoscopic or microscopic aid. Complications such as cerebrospinal fluid (CSF) leak, meningitis, diabetes insipidus, hematoma, and loss of vision are known, but midbrain infarct is rarely reported. We report and discuss the possible mechanism of this rare and unusual complication in transsphenoidal surgery. A 36-year-old nulliparous female with no comorbidities suffering from primary infertility presented with intermittent headache for 9 months with bitemporal vision disturbances for 3 months, pigmentation around the neck and nape, oligomenorrhea with an established diagnosis of plurihormonal secreting pituitary tumor (predominantly adrenocorticotropic hormone and prolactin), hyperparathyroidism, and diabetes. The whole symptom fitted into the diagnosis of multiple endocrine neoplasia 1 (MEN-1) syndrome. Molecular genetic testing was done with full gene sequencing analysis of MEN-1 gene using polymerase chain reaction. Furthermore, Sanger DNA sequencing was done, and two novel variations, namely *IVS 9c.1364 + 99C>G* and *EXON 10 c.1813 C>T (p. L605 L),* were detected. Radiology detected a microadenoma in the right lobe of the pituitary with mild deviation of the pituitary stalk on dynamic contrast-enhancing magnetic resonance imaging. Gross total excision of the tumor was done through transsphenoidal approach. The surgery was uneventful other than some blood-mixed CSF leak. Post excision, fat and tissue glue was packed. The patient did not wake up from anesthesia and had bilateral dilated pupil with no oculocephalic reflex. Investigations revealed bilateral thalamic and midbrain infarct. The patient subsequently expired. This case is reported in view of its unusual complication and to create awareness for such a fatal complication following transsphenoidal surgery for pituitary microadenoma and the importance of diligent approach to transsphenoidal surgery and to report novel genetic mutation of MEN-I gene.

Keywords: *Adenoma, hemorrhage, infarction, multiple endocrine neoplasia 1, pituitary, subarachnoid, thalamic, transsphenoidal*

Introduction

Transsphenoidal surgery for pituitary tumor is a common procedure performed in neurosurgery. Initial attempts at transcranial surgery for pituitary removal were associated with significant mortality and morbidity. Schloffer first suggested the use of a transsphenoidal route as a safer, alternative approach to sella turcica.[1] He first reported the first successful removal of a pituitary tumor through the transsphenoidal approach in 1906. A. E. Halstead modified the procedure in 1910 to a sublabial gingival incision for the initial stage of exposure. Although postoperative complications associated with transsphenoidal approach are low as compared to that of transcranial approach, there are a few significant ones such as cerebrospinal fluid (CSF) leak, meningitis, diabetes insipidus, dyselectrolytemia, visual disturbances, intracranial bleeding/hematoma, and hydrocephalus, which are well documented.[5]

In this article, we present a rare case of bilateral thalamic and rostral midbrain infarct following an uneventful transsphenoidal surgery for resection of pituitary microadenoma and describe the possible mechanism of such an unusual complication.

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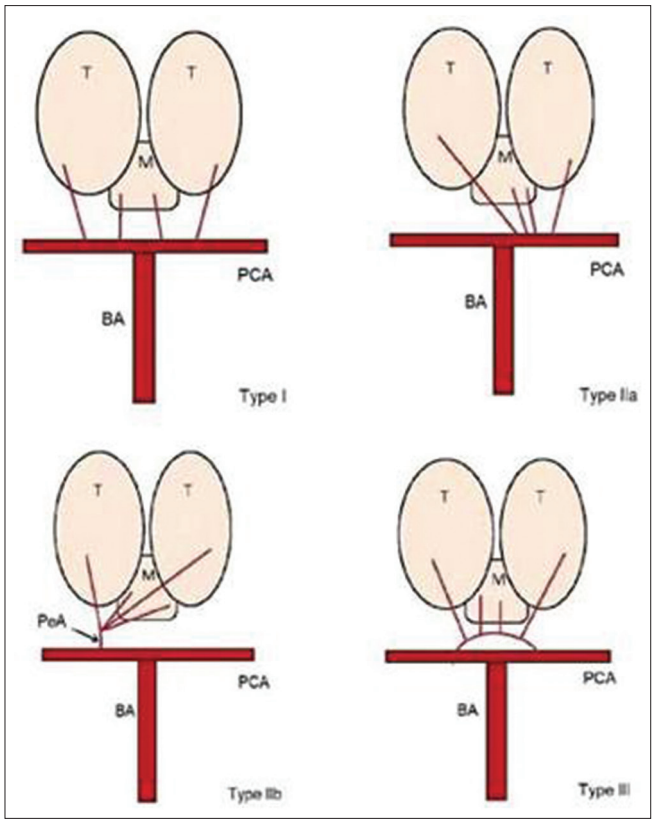

Figure 1: Normal and variant of arterial supply to the thalamus

Case Report

A 36-year-old nulliparous female with no comorbidities presented with intermittent headache for 1 month. She also had bitemporal vision disturbances for 1 month, pigmentation around the nape of the neck for 5 years, oligomenorrhea, infertility, and frequent change of footwear size. She also complained of transient giddiness and vertigo episodes, which were relieved by medications. Magnetic resonance imaging (MRI) was suggestive of a well-defined sellar extra-axial lesion which was isointense on T1 and hyperintense on T2 with homogeneous enhancement on contrast of size 11 mm × 9 mm and the pituitary stalk was displaced to the left. Hormonal profile showed elevated adrenocorticotropic hormone (ACTH) (78 pg/mL), elevated prolactin (310 ng/mL), normal growth hormone, insulin growth factor, cortisol, T3, T4, and thyroid-stimulating hormone. Visual fields showed bitemporal hemianopia. Routine blood investigations and cardiology parameters were normal.

The patient had a history of gallbladder stones and ureteric calculi for which she was operated a year back.

The patient was diagnosed as a case of multiple endocrine neoplasia 1 (MEN-I) syndrome and was referred from the endocrinology department with serum parathyroid hormone (105.3 pg/mL), serum calcium (10.2 mg/dL), and serum phosphorus (4.1 mg/dL) with fasting

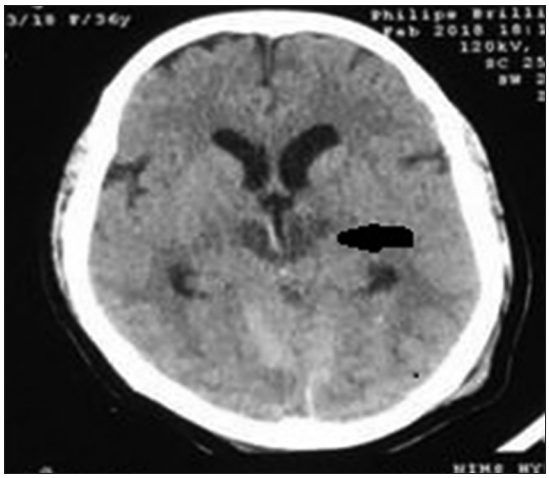

Figure 2: Computed tomography brain plain showing bilateral thalamic infarct (arrows)

blood sugar (111 mg/dL) and postprandial blood sugar (228 mg/dL). Tc^{99}sestamibi parathyroid scintigraphy with single-photon emission computed tomography (CT)-CT showed no parathyroid adenoma. Anti-cyclic citrullinated peptide IgG antibodies were negative.

In view of hyperparathyroidism, Cushing syndrome (increased ACTH and ACTH not suppressed by dexamethasone), prolactinoma (pituitary microadenoma), and diabetes diagnosis of MEN-1 syndrome were strongly considered.

Molecular genetic testing was done with full gene sequencing analysis of MEN-1 gene.[3,4] Polymerase chain reaction was used followed by Sanger DNA sequencing. Two novel variations namely *IVS 9c.1364 + 99C>G* and *EXON 10 c.1813 C>T (p. L605 L)* were detected.

The routine transsphenoidal approach was employed under general anesthesia to excise the tumor, and the tumor was excised completely. The surgery was uneventful other than some blood-mixed CSF leak during the procedure. Post excision, fat and tissue glue was packed. The patient did not recover from anesthesia and had bilateral dilated pupil with no oculocephalic reflex. In view of the delay for shifting to CT scan and as the patient was unstable, the nasal pack was removed and reexploration was done in search of hematoma, but none was found. Subsequently, MRI was done which showed bilateral thalamic and rostral mid-brain infarct.

Magnetic resonance angiography (MRA) suggested hypoplastic P1 segment of posterior cerebral artery (PCA) and dilated posterior communicating artery, suggestive of fetal PCA [Figure 1].

CT brain done 24 h after the surgery demonstrated a small amount of subarachnoid hemorrhage in the basal cisterns with minor bleed in the 4th ventricle and bilateral medial thalamic hypodensities which was suggestive of infarct [Figure 2 and 3].

Discussion

Bilateral thalamic infarction is rare, and that too after transsphenoidal surgery is even rarer. Blood supply to the medial thalamus is provided by paired paramedian thalamic perforators from the artery of Percheron, which arises from the P1 segments of each PCA.[7] Percheron also described a variation of this vascular pattern in which an unpaired perforating artery arises from the P1 segment on one side to supply the medial thalamus bilaterally. Bilateral paramedian thalamic infarction is thought to occur when such an unpaired artery of Percheron is occluded acutely.[8] In this case, digital subtraction angiography (DSA) was not available, however MRA was done postsurgery following the complication which showed hypoplastic P1 segment of PCA and dilated posterior communicating artery, suggestive of fetal PCA. In case of marked hypoplasia of a single P1 arterial segment or its complete absence (full fetal posterior cerebral artery), thalamoperforating arteries (TPAs) originate from the contralateral side and cross the midline to supply the medial aspects of both thalami and the rostral midbrain.[9] The hypothesis for such an event was vasospasm of this narrow-caliber single vessel due to subarachnoid hemorrhage. Furthermore, the presence of visual disturbances, occasional giddiness, and vertigo in such a small sellar tumor is also not explainable and points toward the possibility of any posterior circulation compromise. The occurrence of, however, Cushing's disease with high blood cortisol levels may

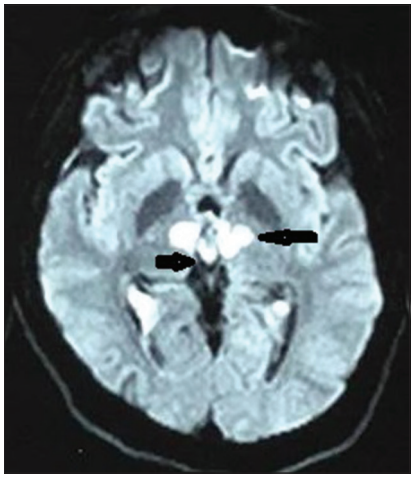

Figure 3: Magnetic resonance imaging diffusion-weighted imaging showing bilateral infarct postoperatively (arrows)

Table 1: Literature review of similar cases and hypothesis proposed

Literature	Clinical history	Outcome	Possible hypothesis postulated
Rao *et al*.[6] Journal of neurosciences in rural practice. 2014 Oct; 5 (04):434-6	A 42-year-old male underwent bifrontal craniotomy subfrontal approach and decompression for large pituitary adenoma	Developed infarct in the left thalamus on the 4th postoperative day	Postoperative vascular occlusion can be due to overzealous packing of sella or due to postoperative edema/hemorrhage in the residual tumor Postoperative vasospasm is also described as the possible mechanism of vascular infarcts
Tejas Sankar *et al*.[10] Case J. Neurol. Sci. 2008;35:522-25	A 50-year-old Caucasian female had a large sellar mass with suprasellar extension and underwent a subtotal transsphenoidal resection presented with recurrence and reoperated	Postoperatively, the patient was drowsy but stable; a CT scan at 48 h postoperative demonstrated a reduction in subarachnoid blood and ventricular size and bilateral medial thalamic hypodensities consistent with infarction	Indirect damage to theTPAs, and in particular the artery of Percheron, probably occurred intraoperatively; in large tumors with suprasellar extension, branches of the PCA may be adherent to the tumor capsule Thalamoperforator vasospasm; an intraoperative CSF leak allowed for blood to enter the subarachnoid space, possibly causing selective spasm of the small caliber artery of Percheron Transient intraoperative hypotension, which could have further limited thalamic perfusion through an already-disrupted or spastic artery of Percheron
Kuroyanagi *et al*.[3] A case report. Neurosurgical review. 1994 Jun 1;17 (2):161-5	A 59-year-old woman presented with a 5-year history of progressive bifrontal headache CT scan with contrast medium showed an enhanced intrasellar and suprasellar mass with a size of 1.5 cm×1.5 cm×2 cm	Immediately after surgery, the patient was somnolent and hemiparetic on the right side, and the left pupil was dilated without light reflex The CT scan showed a small infarcted area in the left thalamus	Subarachnoid hemorrhage with thalamic infarction is suspected to have been caused by intraoperative injury to the posterior TPAs

CT – Computed tomography; PCA – Posterior cerebral artery; CSF – Cerebrospinal fluid; TPAs – Thalamoperforating arteries

be an independent cause of atherosclerosis.[2,11] Probable mechanisms are modulation of vascular endothelial function, recruitment of monocytes to vascular wall, and transformation to macrophage foam cells, which lead to platelet aggregation and thrombus formation and stroke. To date, there have been very few case reports of bilateral thalamic infarct following transsphenoidal pituitary surgery. Table 1 illustrates literature review of such incident along with the hypothesis proposed by the authors.

The most likely mechanisms alone or in combination, likely contributed to bilateral thalamic and rostral midbrain infarct are, first, indirect damage to the TPA, in particular the artery of Percheron intraoperatively; the second mechanism is thalamoperforator vasospasm due to CSF leak which allows blood to enter the subarachnoid space and causes selective spasm of small caliber artery of Percheron; and the third mechanism could be intraoperative transient hypotension related to hypopituitarism and associated cortisol deficiency.

Conclusion

This case is reported in view of its unusual complication and to create awareness for such a fatal complication following transsphenoidal surgery for pituitary microadenoma and the importance of diligent approach to transsphenoidal surgery and to report novel genetic mutation of MEN-I gene.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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