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Cerebral vasospasm following subarachnoid hemorrhage: a rare complication after transsphenoidal surgery for pituitary macroadenoma

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Summary

Postoperative (PO) complications after transsphenoidal surgery (TSS) are rare when performed in pituitary referral centers. Partial hypopituitarism is more frequent and somewhat expected. Meningitis, cerebrospinal fluid leaks, and visual deficits are unusual. Cerebrovascular complications, including cerebral vasospasm are rare, usually under-appreciated and not mentioned to the patient prior to the surgery. This is a report of a 51-year-old male with a non-functioning pituitary macroadenoma presenting with partial hypopituitarism and visual field loss. The patient was submitted to an uneventful TSS. On the first PO day, he developed a left palpebral ptosis with unequal pupils and impaired consciousness (12 points on Glasgow Coma Scale). CT scan revealed a perimesencephalic subarachnoid hemorrhage (SAH) grade 1 according to the modified Fisher scale. High-dose dexamethasone (16 mg/day) was initiated and the patient became more alert (Glasgow 14). On the fifth PO day, due to progression of the neurological deficits (left III, IV, and VI cranial nerves palsy, ataxia, dysdiadochokinesia, right dysmetria, and dysarthria), a magnetic resonance angiography was obtained and revealed a recent mesencephalic infarct without evident vasospasm. Nevertheless, nimodipine 60 mg 4/4 h was initiated. No improvement was seen after 3 days of treatment. The patient was discharged and put on rehabilitation, returning to normal gait and balance after 7 months. This, therefore, is a case of an unexpected mesencephalic infarct probably due to vasospasm induced by minor SAH. Although exceptionally rare, informing the patient about this event prior to TSS is important due to its significant neurological impact. More data are needed considering preventive treatment with nimodipine as soon as SAH is detected after TSS and whether it would improve neurological outcomes.

Learning points

- Whenever neurological deficits arise after transsphenoidal surgery (TSS), systemic infection, meningitis, electrolyte imbalance, and evident hemorrhage must be promptly investigated.
- Although rare, cerebral vasospasm (CVS) after TSS is associated with high morbidity and high mortality rates.
- Vigilance for vasospasm is necessary for patients undergoing TSS for pituitary adenoma, especially those with significant suprasellar extension.
- Informing this event to the patient prior to TSS is essential due to its significant morbidity and mortality.
- Post-TSS subarachnoid hemorrhage and hemiparesis may be important clues indicating CVS and infarction.

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- There is limited evidence in the literature regarding post-TSS CVS surveillance and treatment strategies which could have an impact on clinical decisions.

Background

Transsphenoidal surgery (TSS) is the treatment of choice for pituitary adenomas, with the exception of prolactinomas, which are primarily treated with dopamine agonists. In recent years, TSS has undergone significant technical refinements, in particular with the introduction of endoscopic surgery.

Several studies show relatively better results with reduced rates of complications. Although post-TSS complications are rare, they certainly should not be overlooked. In addition to adenohypophyseal disorders, the most prevalent complications include postoperative (PO) cerebrospinal fluid leak (2.6–10.2%), severe bleeding (0.6–1.7%), permanent diabetes insipidus (1.9–4.3%), and meningitis (1.1–3.6%) (1, 2, 3). Cerebral vasospasm (CVS) after TSS is an even rarer event with a described incidence of 0.2% in a single-center TSS series (4). Less than 40 cases have been described in the literature, two-thirds being preceded by PO subarachnoid hemorrhage (SAH), which might result in delayed cerebral ischemia (DCI) and consequent neurologic deterioration (5, 6, 7, 8, 9, 10, 11).

The lack of knowledge of this condition makes it difficult to diagnose and manage, which can lead to a worse outcome.

Case presentation

A 51-year-old male patient was referred to our hospital due to erectile dysfunction and visual deficits. His physical examination was unremarkable except for obesity (BMI: 38 kg/m^2), a blood pressure of 130 × 80 mmHg, and visual field loss. Initial functional and imaging investigations revealed a non-functioning pituitary macroadenoma with suprasellar extension and compression of the optic chiasm (Fig. 1A). Partial hypopituitarism was confirmed with testosterone: 34 ng/dL (300–900), FSH: 18 mUI/mL (0.7–11.1), LH: 0.7 mUI/mL (0.8–7.6), TSH: 2.3 mUI/mL (0.4–4.5), FT4: 0.7 ng/dL (0.89–1.76), IGF-1: 38 ng/mL (42–214), prolactin: 9.1 ng/mL (5.0–25.0), basal cortisol: 12.5 µg/dL (5.0–22.0), and visual field testing showed right temporal hemianopia and left inferior temporal quadrantopia. The patient was then submitted to an uneventful TSS. The usual perioperative hydrocortisone stress dose was administered before and after TSS. On the first post-operative (PO) day, he developed an altered mental status (GCS 12), unequal pupils (left>right), and left palpebral ptosis. He had no hemodynamic instability throughout the PO period. On the sixth PO day, he had further neurological deterioration, now presenting with left III, IV, and VI cranial nerves palsy, ataxia, dysdiadochokinesia, right dysmetria, and dysarthria.

Investigation

A cranial CT was performed revealing a perimesencephalic subarachnoid haemorrhage (SAH) grade 1 according to the modified Fisher scale (Fig. 1B). Concomitant laboratory analysis showed no evidence of meningitis or electrolyte imbalance.

On the fifth PO day, due to the progression of the neurological deficits (left III, IV, and VI cranial nerves palsy, ataxia, dysdiadochokinesia, right dysmetria, and dysarthria), magnetic resonance image (MRI) was obtained and revealed a SAH, with blood surrounding the perforating arteries in the perimesencephalic cistern, with subacute infarction in the midbrain, evidenced by restriction in the diffusion sequence (Figs. 1C, D and E).

Treatment

High-dose i.v. dexamethasone was initiated on the first PO day and weaned off after 3 days. The patient became more alert and attentive (GCS 14), but his cranial nerve palsies persisted. Nimodipine 60 mg 4/4 h was initiated on the seventh PO day. As no improvement was seen after 3 days, treatment was stopped. The patient was discharged on hormone replacement therapy for hypopituitarism and put on rehabilitation.

Outcome and follow-up

After 7 months of follow-up, the patient showed significant gait improvement, as well as for ataxia, dysarthria, and right dysmetria. Left palpebral ptosis persisted. A subsequent MRI demonstrated a 15 mm residual pituitary tumor abutting the optic chiasm and small hematogenic remnants near the basilar artery and left mesencephalon peduncle suggestive of ischemic injury, in the chronic phase, already cavitated (Fig. 1F).

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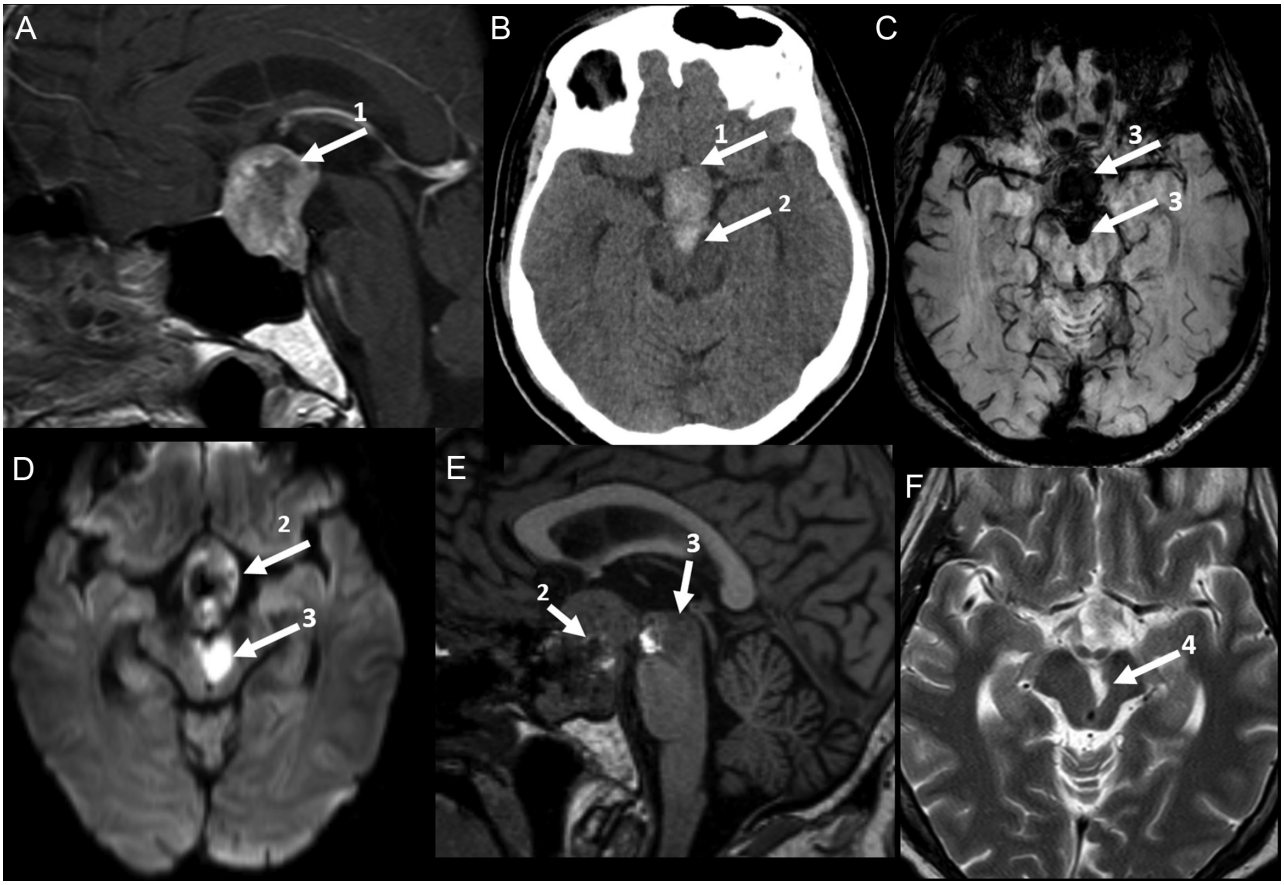

Figure 1
(A) Sagittal reconstruction of T1-w post-contrast-enhanced MRI. (B) Axial unenhanced CT scan reconstruction. (C) Axial SWI slice MRI. (D) Axial DWI slice through the suprasellar cistern. (E) Post-surgery MRI, sagittal T1-w non-contrast reconstruction. (F) Late follow-up axial T2-w slice through the mesencephalic infarct. Arrow 1 points to the non-functioning pituitary macroadenoma. Arrow 2 points to the SAH in the interpeduncular cisterna and the surgical cavitation. Arrow 3 points to the mesencephalic infarction in the subacute phase. Arrow 4 points to the chronic phase of the mesencephalic infarct, already cavitated.

Discussion

Well-known complications of TSS include anterior hypopituitarism, diabetes insipidus, hyponatremia, and more rarely, meningitis, cerebrospinal fluid leaks, and visual field loss. Close monitoring and replacement of the hormonal status, as well as water balance and electrolyte disturbances, are warranted. Whenever symptoms and signs of neurological impairment appear, a thorough investigation is necessary including screening for infection and imaging studies (1, 2, 3).

SAH is a rare complication of TSS (4). Symptomatic CVS are even rarer (5). Tumor size and suprasellar extension have been associated with PO complications in general (2). The posterior lesion extension into the interpeduncular mesencephalic cistern in the present case could also represent a risk factor for SAH. Interestingly, among the few cases described in the literature, two-thirds were preceded by PO SAH (6, 7, 8, 9, 10, 11). The average onset of symptomatic vasospasm was at 8.5 PO day (range: 2 to 16) (10). Diversely, in the case presented herein, neurological symptoms appeared on the first PO day. Laboratory studies excluded systemic infection, meningitis, and electrolyte imbalance. The cisternal grade 1 SAH around the upper brainstem was not deemed as the cause of neurological impairment of the patient, who was started on high-dose dexamethasone. The rationale for this therapy relies on its anti-edematous and anti-inflammatory effects and it has been shown to improve neurological function after surgery, reducing secondary brain injury. However, there are still controversies regarding the potential risks and benefits of steroids in different neurosurgical scenarios (12). Neurological symptoms further progressed, and an MRI scan revealed a mesencephalic infarct, but no direct evident vasospasm was detected because the small arteries involved are less than 300 microns, below MR angiography

resolution (13). Nevertheless, CVS with DCI was then suspected, possibly induced by the SAH, albeit grade 1.

The physiopathology of CVS post-TSS is unknown but presumed to be similar to the one seen in vasospasm after aneurysmal SAH where spasmogenic agents from blood degradation products lead to vessel spasm with sustained contraction of the arterial smooth muscle and consequent reduced cerebral blood flow and DCI (14, 15).

Accordingly, the majority of treatment strategies described to prevent vasospasm-associated DCI involve hemodilution, hypertension, and hypervolemia. In the context of SAH, nimodipine prophylaxis is often used to prevent CVS and its consequent ischemic effects (15).

The preventive protocol for vasospasm was started only on PO day 7. Such timing was likely late, considering SAH as the presumed etiology for CVS. Indeed, no further neurological improvement was achieved, most probably due to an already established cerebral infarct.

Other recognized etiologies of vasospasm include pituitary apoplexy, CSF leaks, hyponatremia, and syndrome of inappropriate antidiuretic hormone secretion (6, 16), none of those detected in the present case.

Due to its rarity, surveillance, and treatment strategies for vasospasm after TSS usually do not comprise systematic screening and treatment protocols. However, vigilance is paramount, especially in patients with large or giant pituitary adenomas with significant suprasellar tumor extension, especially posterior extension to the mesencephalon and basilar arteries.

Although exceptionally rare, patients that present such risk factors should be informed of this possibility prior to TSS, due to its significant morbidity and mortality.

In conclusion, in the event of neurological deterioration following TSS, after more frequent causes (systemic infection, meningitis, electrolyte imbalance, and evident hemorrhage) have been excluded, CSV should be considered, even with minor cerebral hemorrhage, preferably with a magnetic resonance angiography study.

The presence of post-TSS SAH associated with hemiparesis may be an important clue indicating an increased risk for CVS.

There is limited evidence in the literature regarding CVS surveillance and treatment strategies, which has a clear impact on clinical decisions.

Declaration of interest

There is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported. A C Moreira is a Senior Editor of *Endocrinology, Diabetes & Metabolism Case Reports*. A C Moreira was not involved in the peer review or editorial process for this paper, on which he is listed as an author.

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Patient consent

Written informed consent was obtained for publication containing clinical details as well as clinical images including patient's photograph.

Author contribution statement

P C Lamparelli Eliaswas the neuroendocrinologist who supervised case conduction, revised literature, wrote and revised the manuscript; Ma Volpon and H Machado were the neurosurgeons who supervised the case and helped with manuscript revision; G de Gobbi Azevedo and G H M Gonçalves were the medical residents responsible for the case and helped with manuscript revision; A C Santoswas the neurorradiologist who supervised the imaging studies and helped with manuscript revision; L M Mermejo, M de Castro and A C Moreira were the neuroendocrinologists who supervised the case and helped with manuscript revision.

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