SAGE Open Medical Case Reports
Volume 8: 1–6

DOI: 10.1177/2050313X20948714
journals.sagepub.com/home/sco
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Persistent hyperprolactinemia, transient hypopituitarism, and transient contralateral third nerve palsy after endovascular treatment of an internal carotid artery aneurysm: Case report and review of the literature

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Abstract

Intracranial aneurysms have an estimated prevalence of about 3%. A rare subgroup are aneurysms of the internal carotid artery that develop medially into the sellar region. Due to the risk of rupture with subsequent subarachnoid hemorrhage and of compression of surrounding structures, mechanical occlusion is advised. Hypopituitarism is not a rare disease and most often related to pituitary adenoma. Only 0.17% of cases with hypopituitarism are caused by unruptured intracranial aneurysms. Today, the predominant treatment of these aneurysms is endovascular coiling or application of flow diverting stents. We present the case of a 60-year-old female patient, who was treated with endovascular coiling for a right-sided, intracavernous, incidental internal carotid artery aneurysm. On postinterventional day 6, she was readmitted with contralateral third nerve palsy, mild hyponatremia und thyreotropic insufficiency. The symptoms recovered after anti-edematous treatment with corticosteroids; only an asymptomatic hyperprolactinemia persisted. To the best of our knowledge, this is the first case report of transient contralateral cranial nerve palsy combined with transient hypopituitarism after endovascular treatment of an internal carotid aneurysm. As treatment we propose corticosteroids, if necessary in combination with nonsteroidal anti-inflammatory drugs, in order to inhibit inflammatory reactions of the aneurysm wall compromising the nearby, partially compressed neural structures.

Keywords

Internal carotid artery aneurysm, hypopituitarism, hyperprolactinemia, third nerve palsy

Date received: 20 April 2020; accepted: 15 July 2020

Introduction

Intracranial aneurysms occur with a prevalence of 3%–5%.[1] Most aneurysms remain asymptomatic, until rupture or mass effect occurs. The most dangerous complication is subarachnoid hemorrhage after rupture of the aneurysm. Therefore, depending on the risk of rupture, mechanical occlusion is usually necessary. Only 1%–2% of intracranial aneurysms are located in the sellar region close to the pituitary gland.[2] These aneurysms can become symptomatic by diplopia or vision impairment due to affection of cranial nerves as well as by endocrinological symptoms.

As *Van 'T Hoff et al.* and *White et al.* have pointed out in their literature reviews in 1961, intrasellar aneurysms can simulate symptoms of pituitary tumors and must not be confused with them. They identified the first case report dating back to 1887.[3–5] Through a PubMed-based literature search, we could identify 34 further case reports and case series of hypopituitarism associated with unruptured

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Table 1. Case reports published after the reviews by *Van 'T Hoff et al.* and *White et al.*

Authors	Year	Onset of hypopituitarism	Cases	Treatment of aneurysm	Recovery of pituitary function
Gilman et al.[6]	1962	Before treatment	1	No	No
Dussault et al.[7]	1969	Before treatment	2	No	No
Shantharam[8]	1974	Before treatment	1	No	No
Verbalis et al.[9]	1982	Before treatment	1	Clipping and decompression	Yes
Ooi and Russell[10]	1986	Before treatment	1	No	No
Nukta and Taylor[11]	1987	Before treatment	1	No	No
Chien et al.[12]	1989	Before treatment	1	No	No
Michils et al.[13]	1991	Before treatment	1	No	No
Heshmati et al.[14]	2001	Before treatment	7	Surgery	No
Ray et al.[15]	2002	Before treatment	1	No	No
Miljic et al.[16]	2003	Before treatment	1	No	No
Gondim et al.[17]	2004	Before treatment	1	No	No
Finny et al.[19]	2005	Before treatment	1	Coiling	No
Klose et al.[18]	2005	Before treatment	1	Clipping	No
Carrera et al.[20]	2006	Before treatment	1	Balloon occlusion	No
Lawson et al.[21]	2008	Before treatment	1	No	No
Goto et al.[22]	2008	Before treatment	1	No	No
Partridge et al.[23]	2010	Before treatment	1	No	No
Lee et al.[24]	2010	Before treatment	1	Not reported	Not reported
Orozco et al.[26]	2011	Before treatment	1	Coiling	No
Tungaria et al.[25]	2011	Before treatment	1	No	No
Munarriz et al.[27]	2013	Before treatment	1	No	No
Ding et al.[28]	2014	Before treatment	1	Pipeline flow-diverting stent	No
Tan et al.[29]	2014	Before treatment	1	Flow-diverting stent	Yes
Seok et al.[30]	2015	Before treatment	1	No	No
Gungor et al.[31]	2015	Before treatment	1	Flow-diverting stent and coiling	No
Hall et al.[32]	2015	After treatment	1	Flow-diverting stent and coiling	No
Ono et al.[33]	2017	Before treatment	1	High-flow bypass	Yes
Higgoda et al.[34]	2017	Before treatment	1	No	No
Lamback et al.[35]	2017	Before treatment	1	Flow-diverting stent	No
Wijethunga et al.[36]	2018	Before treatment	1	Coiling	No
Ambulkar et al.[37]	2018	Before treatment	1	Flow-diverting stents	No
Katsuhiro et al.[38]	2019	Before treatment	1	Low-flow bypass	No
Kageyama et al.[39]	2020	Before treatment	2	No	No

intracranial aneurysms.[6–39] In only one of these cases, hypopituitarism occurred after treatment.[32]

Usually, pituitary insufficiency is detected before treatment, or even initially leads to the diagnosis of the aneurysm. The therapy remains challenging, since in only three of the published cases hypopituitarism recovered after occlusion of the aneurysm[9,29,33] (Table 1).

More generally, hypopituitarism is not an uncommon disease with a prevalence of 45.5/100.000 and can be accompanied by hyperprolactinemia due to pituitary stalk affection. Most cases (70%) are caused by tumorous lesions.[40,41] Only 0.17% are caused by intracranial aneurysms.[14] While hypopituitarism can lead to unspecific symptoms such as chronic fatigue, loss of libido or hyponatremia, the accompanying hyperprolactinemia can cause galactorrhea, breast swelling or hypogonadism. Untreated hypopituitarism eventually ends with coma, cardiac arrythmia and death. The treatment of hypopituitarism consists in hormone substitution and, if possible, removal of the sellar tumor. This is especially true for pituitary adenomas, except for prolactinomas, which can be treated more efficiently with dopamine agonists.

Case report

A 60-year-old female presented to her general practitioner because of intermittent headaches. Computed tomography of the head brought up the suspicion of a right-sided internal carotid artery (ICA) aneurysm of 25 mm, protruding into the sellar region, which was confirmed by magnetic resonance imaging (MRI).

After digital subtraction angiography, endovascular coiling was recommended and the patient agreed to the intervention. Two months later, the aneurysm was densely packed

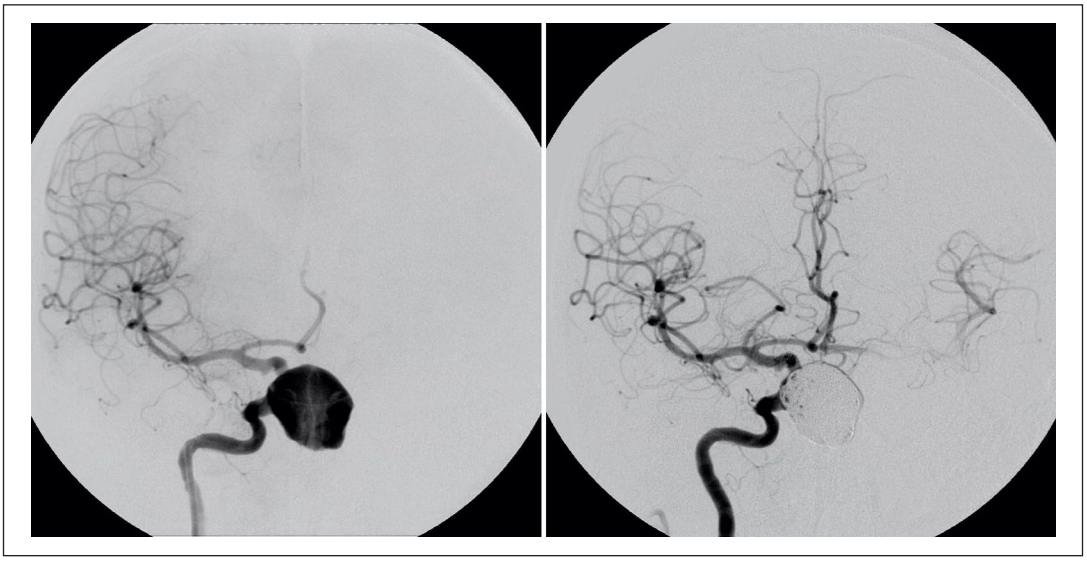

Figure 1. Left: Anterior–posterior digital subtraction angiography of the right ICA before treatment. The aneurysm develops medially into the sellar region and measures 25 mm. After interdisciplinary discussion, endovascular treatment was recommended and performed with application of 24 coils (Penumbra 400) with assistance of a self-expanding stent (Neuroform EZ, 4.5 × 20). Right: Control series at the end of the first intervention.

Table 2. Serum concentrations of sodium (Na^+), thyroid-stimulating hormone (TSH), free triiodthyronine (fT3), and free thyroxine (fT4) before treatment (2013), on postinterventional day 6 (onset of symptoms, 2014), and after completion of treatment (2017, no symptoms).

	Before first coiling, 2013	Postinterventional day 6, 2014	August 2017	Reference value
Na^+ (mmol/L)	140.2	133.0	140.8	135–145
TSH (mU/L)	1.65	0.859	2.05	0.4–3.77
fT3 (pmol/L)	4.96	1.88	4.18	3.1–6.79
fT4 (pmol/L)	5.29	5.83	12.18	12.8–20.4

TSH: thyroid-stimulating hormone.
Note that hyponatremia and thyreotropic insufficiency resolved after completion of treatment.

with 24 platin coils (Penumbra 400) with assistance of a self-expanding stent (Neuroform EZ, 4.5 × 20). Final control showed complete occlusion of the aneurysm; no residual inflow could be detected (Figure 1). The patient was observed for four further days on our neurosurgical ward and then was dismissed home without neurological deficit.

On postinterventional day 6, she was readmitted to the emergency room because of diplopia. Clinical examination revealed unilateral palsy of the left oculomotor nerve, contralateral to the site of the aneurysm. Endocrinological work-up disclosed new mild hyponatremia (133 mmol/L) and new thyreotropic insufficiency (Table 2). MRI on postinterventional day 7 did not detect subarachnoid hemorrhage or increased compression of neural structures, but revealed inflammatory signals in the aneurysm wall with contact to the pituitary stalk and the left oculomotor nerve (Figure 2). Anti-edematous treatment with dexamethasone led to full recovery of clinical symptoms and normalization of sodium and thyroid-stimulating hormone (TSH) serum levels within 1 week.

Subsequently, the patient needed multiple treatments for reperfusion of the aneurysm. In August 2014, 6 months after first intervention, 25 additional platin coils (Penumbra 400) were applied. In October 2015, 20 months after first intervention, two flow-diverting stents (Phenox p64, 3.5 × 15 and 3.5 × 21) were inserted. In February 2017, 3 years after first intervention, another flow-diverting stent (Phenox p64, 3.5 × 18) was administered. Consecutively, the aneurysm then was permanently occluded, as shown in the digital subtraction angiography from August 2017, 42 months after first treatment (Figure 3). In contrast to the first intervention, the subsequent steps went without further complications.

Meanwhile, the patient has received L-thyroxine from her general practitioner due to primary hypothyroidism with normal TSH serum levels. Asymptomatic serological hyperprolactinemia is persisting, which only came to attention as

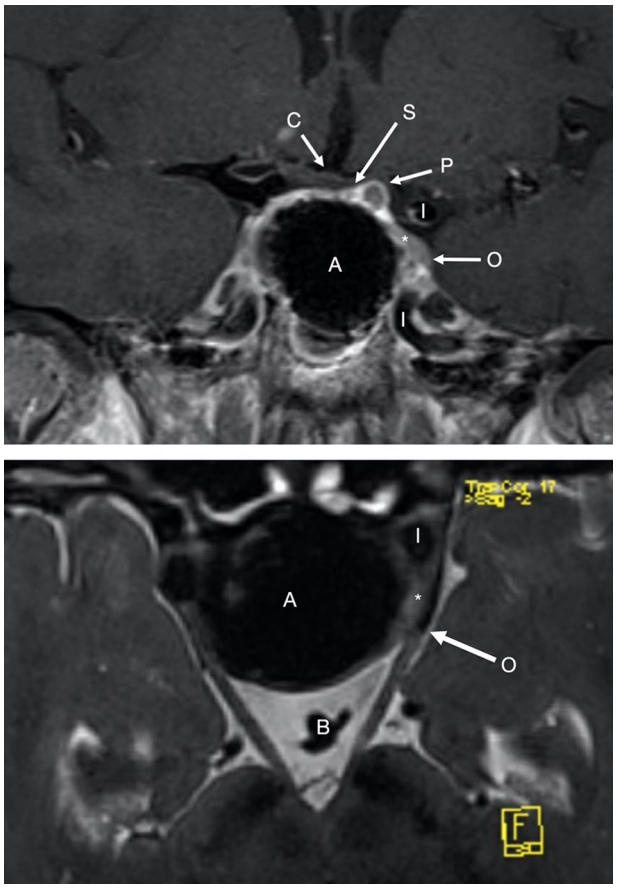

Figure 2. Magnetic resonance imaging on postinterventional day 7. The mass effect of the aneurysm compromises all structures in proximity to the sella turcica. Note the strong inflammatory signal close to the left oculomotor nerve and the pituitary stalk, as well as around the whole wall of the aneurysm. Top: Coronal contrast enhanced T1 sequence of the sellar region. A: giant aneurysm of the right ICA after occlusion, I: left ICA, C: optic chiasm, S: pituitary stalk, P: pituitary, O: left oculomotor nerve in the wall of the cavernous sinus, *: inflammatory signal. Bottom: Axial T2 sequence of the sellar region. A: giant aneurysm of the right ICA after occlusion, I: left ICA, B: head of the basilar artery, O: left oculomotor nerve, *: inflammatory signal.

late as November 2018, 5 years after diagnosis of the aneurysm and 21 months after permanent occlusion (Table 3).

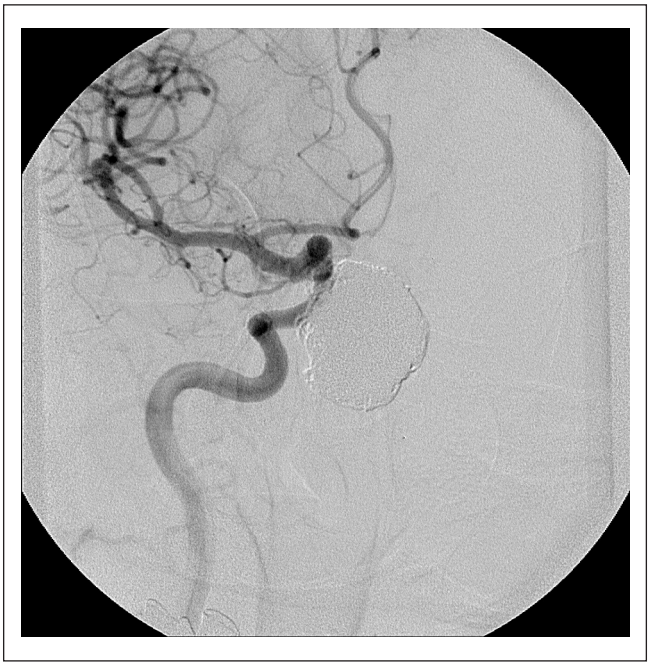

Figure 3. Anterior–posterior digital subtraction angiography of the right ICA 42 months after first treatment. In addition to the first intervention, 25 platinum coils (Penumbra 400) and three flow-diverting stents (Phenox p64, 3.5 × 15, 3.5 × 21 and 3.5 × 18) have been applied in three additional interventions. In contrast to the first intervention, the subsequent steps went without further complications.

Table 3. Pituitary hormones after completion of treatment at 57 and 61 months after first coiling.

	November 2018	March 2019	Reference value
Prolactin (mU/L)	2328.0	2148.0	102–496
LH (U/L)	1.65	1.45	7.7–58.5
FSH (U/L)	3.37	3.12	25.8–134.8
Estradiol (pmol/L)	<37	<37	<92
Random cortisol (nmol/L)	216.0	238.9	158–810
IGF-1 (isys, µg/L)	66.60	72.00	NA
IGF-1 SDS (isys)	−0.76	−0.56	−2.0 to +2.0

LH: luteinizing hormone; FSH: follicle-stimulating hormone.
Note that hyperprolactinemia was diagnosed only after completion of treatment and remained asymptomatic, even in the presence of low values for LH and FSH.

Discussion

Hypopituitarism and impairment of cranial nerves in the cavernous sinus are well-known symptoms when diagnosing a tumor of the sellar region. The case presented here points to an important differential diagnosis and fits well into the existing reports of ICA aneurysms provoking these deficits.

However, these symptoms usually stand at the beginning of the diagnostic work-up that finally detects the aneurysm, whereas in our case, the symptoms occurred within 1 week after endovascular treatment. Most likely, mass effect and inflammatory reactions of the aneurysmal wall lying in closest vicinity to the involved structures led to metabolic dysregulation and induced the deficits (Figure 2). This can explain the contralateral oculomotor nerve palsy and the resolution of symptoms by anti-edematous treatment with dexamethasone.

Literature research identified only one further case report, in which hypopituitarism occurred after treatment.[32] In that

case, hypopituitarism was delayed by 18 months after the placement of a flow-diverting stent and did not recover, rather suggesting a late ischemic event than inflammation as etiology. However, compression of surrounding structures by coil material or induced by intra-aneurysmal microbleeding has to be taken into account, too, since non-ischemic cerebral enhancing lesions occur in only 0.5% of endovascular interventions.[42]

Recovery of pituitary function after occlusion of an ICA aneurysm as the underlying cause is rare and relies on residual pituitary function before treatment. Interestingly, the mode of occlusion seems to be unrelated, since recovery has been achieved by clipping and decompression,[9] flow-diverting stent,[29] high-flow bypass surgery,[33] as well as, in our case, by anti-edematous treatment after endovascular coiling.

Conclusion

Hypopituitarism and cranial nerve impairment can occur after endovascular treatment of asymptomatic sellar aneurysms of the ICA. Treatment of choice comprises corticosteroids.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Funding

We acknowledge support from Leipzig University for Open Access Publishing.

Informed consent

Written informed consent was obtained from the patient for publication of this case report.

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References

1. Etminan N and Rinkel GJ. Unruptured intracranial aneurysms: development, rupture and preventive management. *Nature Rev Neuro* 2016; 12: 699–713.
2. Hanak BW, Zada G, Nayar VV, et al. Cerebral aneurysms with intrasellar extension: a systematic review of clinical, anatomical, and treatment characteristics: a review. *J Neurosur* 2012; 116: 164–173.
3. White JC and Ballantine HT Jr. Intrasellar aneurysms simulating hypophyseal tumours. *J Neurosurg* 1961; 18: 34–50.
4. Van 'T Hoff W, Hornabrook RW and Marks V. Hypopituitarism associated with intracranial aneurysms. *BMJ* 1961; 2: 1190–1194.
5. Bramwell B. Two enormous intracranial aneurisms. *Edinburgh Med J* 1887; 32: 911–922.
6. Gilman S, Braverman LE, Starr A, et al. Intracranial aneurysm causing panhypopituitarism, blindness, seizures, and dementia. *Ann Intern Med* 1962; 57: 639–646.
7. Dussault J, Plamondon C and Volpe R. Aneurysms of the internal carotid artery simulating pituitary tumours. Report of two cases. *Can Med Assoc J* 1969; 101: 51–56.
8. Shantharam VV. Suprasellar aneurysm. An unusual cause of hypopituitarism. *J Am Med Assoc* 1974; 229: 1473.
9. Verbalis JG, Nelson PB and Robinson AG. Reversible panhypopituitarism caused by a suprasellar aneurysm. *Neurosurgery* 1982; 10: 604–611.
10. Ooi TC and Russell NA. Hypopituitarism resulting from an intrasellar carotid aneurysm. *Can J Neurol Sci* 1986; 13: 70–71.
11. Nukta EM and Taylor HC. Panhypopituitarism secondary to an aneurysm of the anterior communicating artery. *Can Med Assoc J* 1987; 137: 413–415.
12. Chien WY, Wang PW, Huang HS, et al. Aneurysm of the internal carotid artery simulating pituitary tumor with panhypopituitarism—a case report. *Chang Yi Xue Za Zhi* 1989; 12: 161–166.
13. Michils A, Balériaux D and Mockel J. Bilateral carotid aneurysms unmasked by severe hypopituitarism. *Postgrad Med J* 1991; 67: 285–288.
14. Heshmati HM, Fatourechi V, Dagam SA, et al. Hypopituitarism caused by intrasellar aneurysms. *Mayo Clin Proc* 2001; 76: 789–793.
15. Ray A, Leach P and Vafidis J. Spontaneous thrombosis of a giant internal carotid aneurysm in a patient who presented with hypopituitarism. *Br J Neurosurg* 2002; 16: 590–592.
16. Miljic D, Damjanovic S, Petakov M, et al. Case report of hypopituitarism with suspected syndrome of inappropriate VP secretion (SIADH) due to a large aneurysm of the internal carotid in the sellar region. *J Endocrinol Invest* 2003; 26: 450–452.
17. Gondim J, Schops M and Ferreira E. Hypopituitarism and amenorrhea- galactorrhea syndrome caused by thrombosis of both internal carotid artery and giant intrasellar aneurysm: case report. *Arq Neuropsiquiatr* 2004; 62: 158–161.
18. Klose S, Kopf D and Lehnert H. Giant intrasellar carotid aneurysm—an unusual cause of panhypopituitarism. *Exp Clin Endocrinol Diabetes* 2005; 113: 551–553.
19. Finny P, Rao N, Shyamkumar NK, et al. A vascular cause for hypopituitarism. *J Postgrad Med* 2005; 51: 334–335.
20. Carrera MJ, Salar A, Pascual J, et al. Hypopituitarism associated with mycotic aneurysm of the cavernous carotid artery in a renal transplant recipient. *Nephrol Dial Transplant* 2006; 21: 3299–3300.
21. Lawson EA, Buchbinder BR and Daniels GH. Hypopituitarism associated with a giant aneurysm of the internal carotid artery. *J Clin Endocrinol Metab* 2008; 93: 4616.
22. Goto A, Takahashi Y, Kishimoto M, et al. Hypopituitarism caused by bilateral internal carotid artery aneurysms with a carotid-cavernous fistula. *Intern Med* 2008; 47: 815–816.

23. Partridge H, Armitage M and Richardson T. An unusual cause of hypopituitarism. *Postgrad Med J* 2010; 86: 189.
24. Lee I, Hackman K, Liubinas S, et al. A giant aneurysm of internal carotid artery causing hypopituitarism. *Intern Med J* 2010; 40: 464–465.
25. Tungaria A, Kumar V, Garg P, et al. Giant, thrombosed, sellar–suprasellar internal carotid artery aneurysm with persistent, primitive trigeminal artery causing hypopituitarism. *Acta Neurochir (Wien)* 2011; 153: 1129–1133.
26. Orozco LD and Buciuc RF. Balloon-assisted coiling of the proximal lobule of a paraophthalmic aneurysm causing panhypopituitarism: technical case report. *Surg Neurol Int* 2011; 2: 59.
27. Munarriz PM, Paredes I, Cicuendez M, et al. Acute confusional syndrome and hypopituitarism produced by a giant aneurysm of internal carotid artery. *Am J Med Sci* 2013; 346: 147.
28. Ding D, Mehta GU and Liu KC. Pituitary insufficiency from large unruptured supraclinoid internal carotid artery aneurysm. *Br J Neurosurg* 2014; 28: 290–292.
29. Tan LA, Sandler V, Todorova-Koteva K, et al. Recovery of pituitary function following treatment of an unruptured giant cavernous carotid aneurysm using Surpass flow-diverting stents. *Case Reports* 2014; 2014: bcr2014011233–bcr2014011233.
30. Seok H, Park H-N, Kim G-H, et al. A giant carotid aneurysm with intrasellar extension: a rare cause of panhypopituitarism. *Korean J Intern Med* 2015; 30: 265–266.
31. Gungor A, Gokkaya N, Bilen A, et al. Pituitary insufficiency and hyperprolactinemia associated with giant intra- and suprasellar carotid artery aneurysm. *Case Rep Med* 2015; 2015: 536191–536193.
32. Hall J, Caputo C, Chung C, et al. Delayed pan-hypopituitarism as a complication following endovascular treatment of bilateral internal carotid artery aneurysms. A case report and review. *Br J Neurosurg* 2015; 29: 303–305.
33. Ono H, Inoue T, Kunii N, et al. Giant cavernous carotid aneurysm causing pituitary dysfunction: pituitary function recovery with high-flow bypass. *Surg Neurol Int* 2017; 8: 180.
34. Higgoda RA, Lokuketagoda K, Perera D, et al. An unusual cause of panhypopituitarism. *Ceylon Med J* 2017; 62: 246–247.
35. Lamback EB, Gouveia HR and Bulzico DA. Into the void: a giant aneurysm mimicking a macroprolactinoma. *Endocrine* 2017; 58: 394–395.
36. Wijethunga WMUA, Dissanayake HA, Perera S, et al. Intra cavernous aneurysm of internal carotid artery masquerading as a pituitary adenoma: a case report. *BMC Res Notes* 2018; 11: 237.
37. Ambulkar S, Tayde P, Sarda P, et al. Panhypopituitarism due to internal carotid artery branch aneurysm compressing pituitary gland. *J Assoc Physicians India* 2018; 66: 92–93.
38. Katsuhiro T, Fujimaro I, Satoru T, et al. Transient aggravation of hypopituitarism after parent artery occlusion with low-flow bypass for unruptured giant cavernous carotid aneurysm. *World Neurosurg* 2019; 123: 339–342.
39. Kageyama K, Kinoshita N, Terui K, et al. Two cases of hypopituitarism caused by intrasellar aneurysm. *Intern Med* 2020; 59: 677–681.
40. Schneider HJ, Aimaretti G, Kreitschmann-Andermahr I, et al. Hypopituitarism. *Lancet* 2007; 369: 1461–1470.
41. Regal M, Páramo C, Sierra SM, et al. Prevalence and incidence of hypopituitarism in an adult Caucasian population in northwestern Spain. *Clin Endocrinol* 2001; 55: 735–740.
42. Shotar E, Law-Ye B, Baronnet-Chauvet F, et al. Non-ischemic cerebral enhancing lesions secondary to endovascular aneurysm therapy: nickel allergy or foreign body reaction? Case series and review of the literature. *Neuroradiology* 2016; 58: 877–885.