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DEVELOPMENT OF INTERNAL CAROTID ARTERY ANEURYSM AFTER SUCCESSFUL CONSERVATIVE TREATMENT OF PROLACTINOMA

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Background. The problem of concomitant pituitary adenomas and intracranial aneurysms is extensively covered in literature. According to various authors, the prevalence of such a combination of lesions is as high as 9 %, most commonly involving hormone-producing pituitary adenomas and aneurysms of the anterior circulation, up to 69 % of which originate from the carotid artery.
Aim. To analyze and demonstrate the treatment of patients with developed internal carotid artery aneurysm (ICA) against the background of successful conservative therapy of prolactinoma.
Materials and methods. In this article we review the literature and present two clinical cases of patients with development of internal carotid artery (ICA) aneurysms after successful conservative treatment of prolactinomas.
Results. In both of the described cases, ICA aneurysms with intrasellar extension developed after successful conservative treatment of large invasive prolactinomas. In both cases ICA occlusion were performed and in one of them extra-intracranial bypass surgery was performed as well.
Conclusion. The presented clinical cases suggest potential direct destructive effect of tumor tissue on vessel walls. Currently, it seems reasonable to carry out computed tomography angiography in all patients with adenomas invading the cavernous sinus.

Keywords: pituitary adenoma, cerebral aneurysm, endovascular aneurysm occlusion

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INTRODUCTION

The problem of concomitant pituitary adenomas and intracranial aneurysms is quite extensively covered in modern literature. According to various authors, the average incidence of this combination of lesions is 9 % [1–6]. The most common combination is hormone-producing pituitary adenomas and aneurysms of the anterior circulation: 69 % of these aneurysms originate from the carotid artery [1, 2, 6–20]. Less common are intrasellar aneurysms which can be contiguous with the tumor, non-contiguous or incorporated into the tumor [6, 14–16, 21]. Usually, aneurysm is detected at the same time as pituitary tumor, and adequate treatment tactics are developed taking this fact into account. Sometimes both the tumor and the aneurysm are diagnosed due to aneurysm rupture which can lead to hemorrhage into the tumor, nasal bleeding, formation of carotid-cavernous fistula, or subarachnoid hemorrhage in cases of destruction of the base of the skull structures by the tumor [22–27]. Somatotropinomas and prolactinomas are frequently associated with aneurysms [1–6]. The latter comprise about 40 % of all pituitary adenomas, and the treatment of choice for them are dopamine agonist therapy (in particular, cabergoline 1.8 %) with effectiveness of about 80 % [28]. Among complications of conservative treatment with prolactin are cerebrospinal fluid rhinorrhea, pulmonary fibrosis, constrictive pericarditis [29–31].

We describe 2 clinical cases of development of aneurysms of the cavernous segment of the internal carotid artery (ICA) after successful conservative treatment with prolactin. The true causes of these aneurysms are unknown. We have not encountered articles describing this combination and discussing possible partial destruction of the vascular wall by the tumor in the location of the aneurysm.

CLINICAL CASE 1

Female patient K., *65 years old, since 2009 have been receiving cabergoline at maximal dose 2 mg/week due to giant prolactinoma (baseline serum prolactin level 289,656 mIU/L (40–530)) diagnosed due to headaches and visual impairment (OD (oculus dexter) – finger counting, OS (oculus sinister) – 0.9; field of vision: OD – in the narrow field in the nasal part, central vision impaired, OS – narrowing in the temporal part for all colors) (Fig. 1).*

In 4 months after the start of prolactinoma treatment, serum prolactin level normalized (410 mIU/mL) and the tumor became smaller. In 2013, tumor regressed almost completely, secondarily empty sella formed, visual acuity improved to 0.6 on the right and 0.7 on the left with normal field of vision (Fig. 2).

In 2019 (the whole previous year the patient took cabergoline and was followed up at the place of residence) at routine MRI exam, endo-supra-laterosellar lesion interpreted as

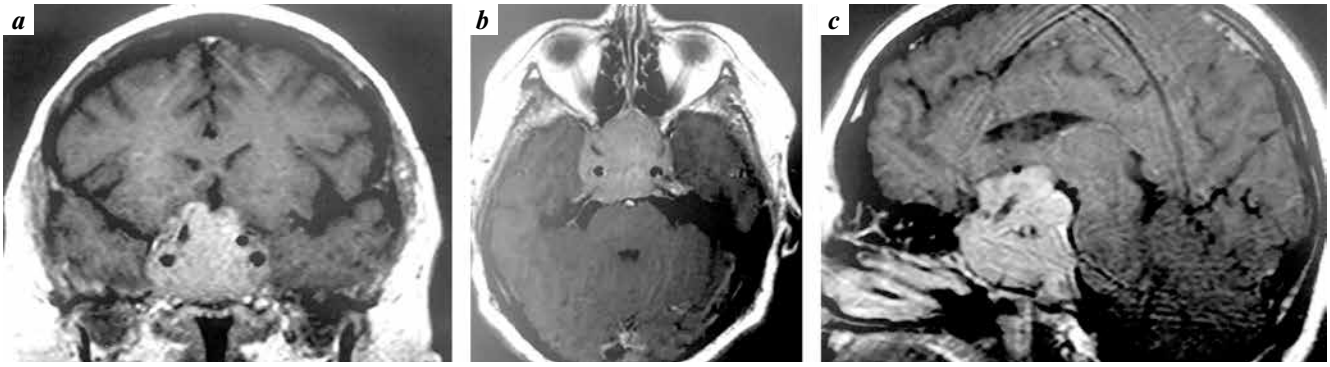

Fig. 1. *Magnetic resonance imaging of the brain of patient K. before the start of therapy with dopamine agonists in frontal (a), axial (b) and sagittal (c) projections. An invasively growing pituitary tumor of large size is determined*

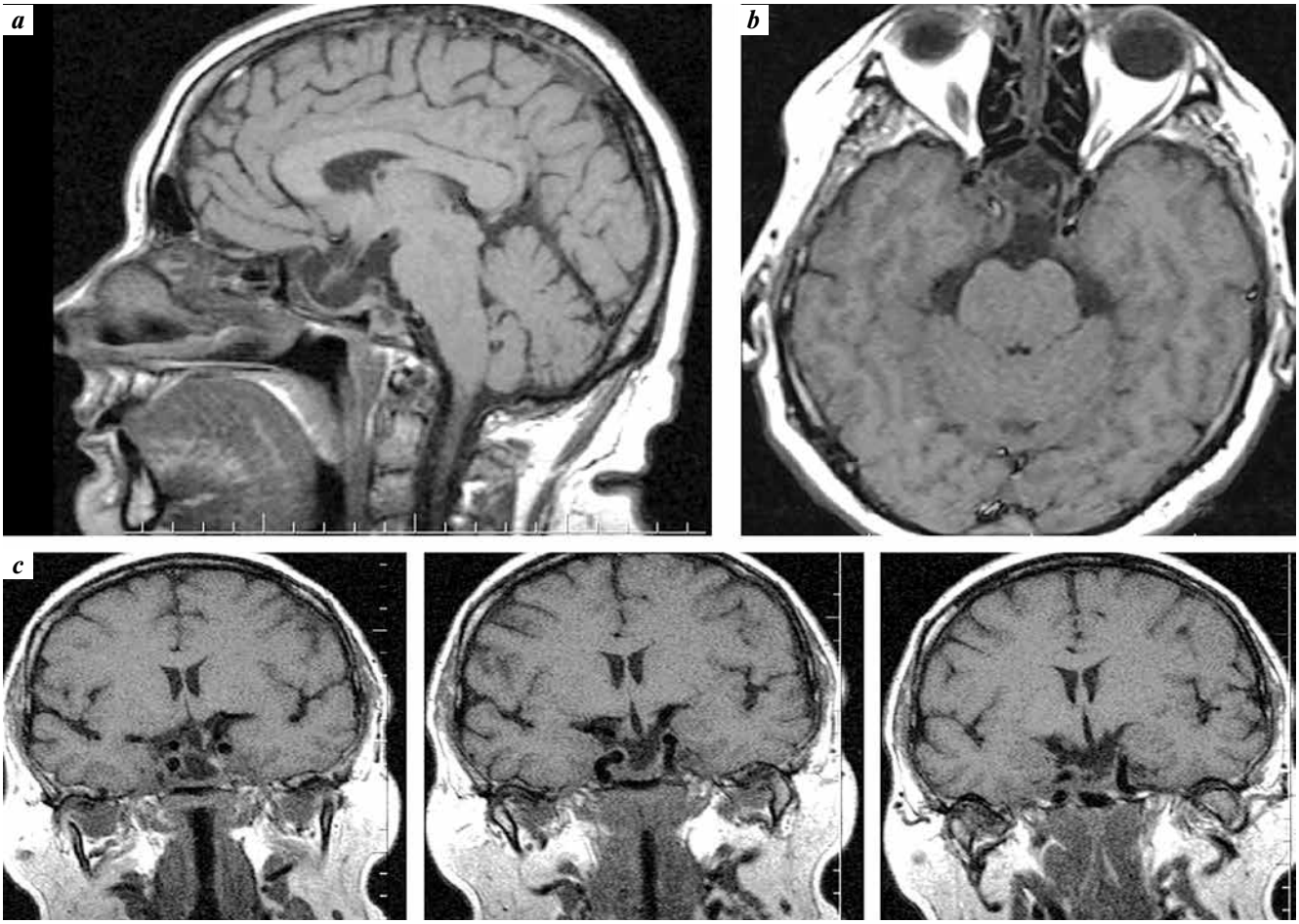

Fig. 2. *Magnetic resonance tomograms of the brain of patient K. 4 years after the start of cabergoline therapy in sagittal (a), axial (b) and frontal (c) projections*

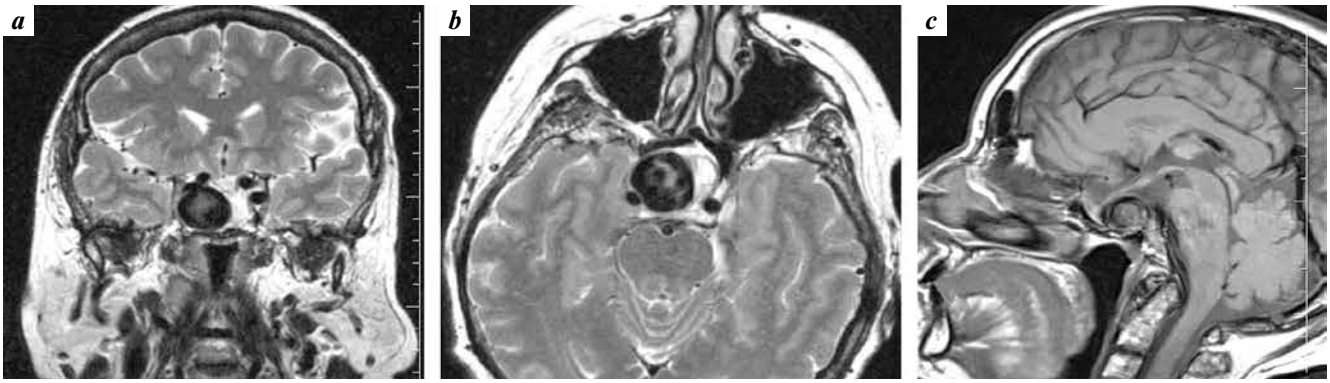

Fig. 3. *Magnetic resonance tomograms of the brain of patient K. from 2019 in frontal (a), axial (b) and sagittal (c) projections. Determined by endo-supralaterosellar formation*

tumor progression was found, and cabergoline dose was increased with normal prolactin levels in the patient (Fig. 3).

At the end of 2020, due to progressing visual impairment (OD – finger counting close to the face on a limited area in the temporal field paracentrally, OS – 0.9) spiral computed tomography angiography (CTA) was performed which showed giant aneurysm of the cavernous segment of the right ICA (Fig. 4). The patient was admitted to the N.N. Burdenko Scientific Research Institute of Neurosurgery for endovascular treatment.

Installation of a flow diverter was planned, but attempts at catheterization of the right ICA distally from the giant aneurysm were unsuccessful during two surgeries due to complex anatomical characteristics of the aneurysm and the artery. Additionally, insufficiency of collateral blood flow through the posterior communicating artery was observed. During conservative hormonal therapy with hydrocortisone after second unsuccessful attempt at endovascular treatment, the patient developed acute psychosis with symptoms of delusions. Two weeks after stabilization of the patient's condition, preventive installation of extra-intracranial bypass and ICA occlusion at the aneurysm level were performed (Fig. 5). After the surgery, the patient's condition is satisfactory with no dynamics in neurological status.

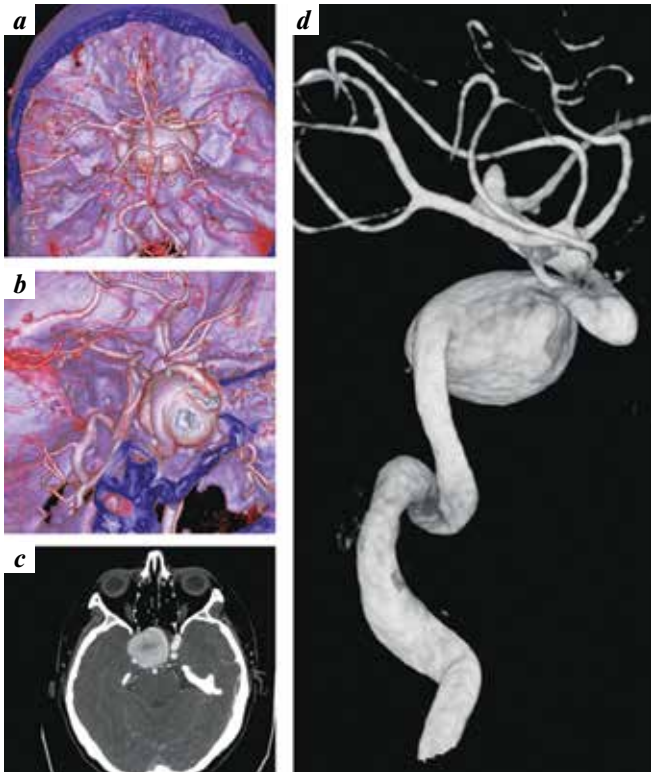

Fig. 4. *Giant aneurysm of the cavernous segment of the right ICA detected in patient K.: a–c – spiral computed tomography angiograms; d – 3D angiography of the right internal carotid artery*

CLINICAL CASE 2

Male patient M., *58 years old, underwent MRI due to visual impairment and hypopituitarism which showed large invasively growing pituitary adenoma (Fig. 6).*

Due to increased prolactin level (above 5,000 mIU/L, specific number unknown), patient was prescribed cabergoline 1 mg/week with positive effect in the form of tumor shrinkage and serum prolactin level normalization (Fig. 7).

Since 2020 (after 13 years of continuous cabergoline therapy, the patient was not followed up since 2008), the patient has developed amaurosis on the right, and his vision on the left decreased to 0.6 (with correction) with loss of the temporal part of the field. Spiral CTA showed giant partially thrombosed aneurysm of the cavernous segment of the right ICA (Fig. 8).

Due to anatomic and topographic characteristics of the aneurysm (almost complete vascular wall dysplasia, acute angle of ICA branching distally from the aneurysm), reconstructive surgery with flow diverter was not possible. Therefore, a decision to perform deconstructive surgery was made. Functional sampling showed good development of the anterior and posterior communicating arteries. Deconstruction with microcoils was performed (Fig. 9).

On day 3 after surgery the patient was discharged in satisfactory condition without dynamics in the neurological status.

DISCUSSION

In both above-described cases, intrasellarly advancing ICA aneurysm developed after successful drug treatment

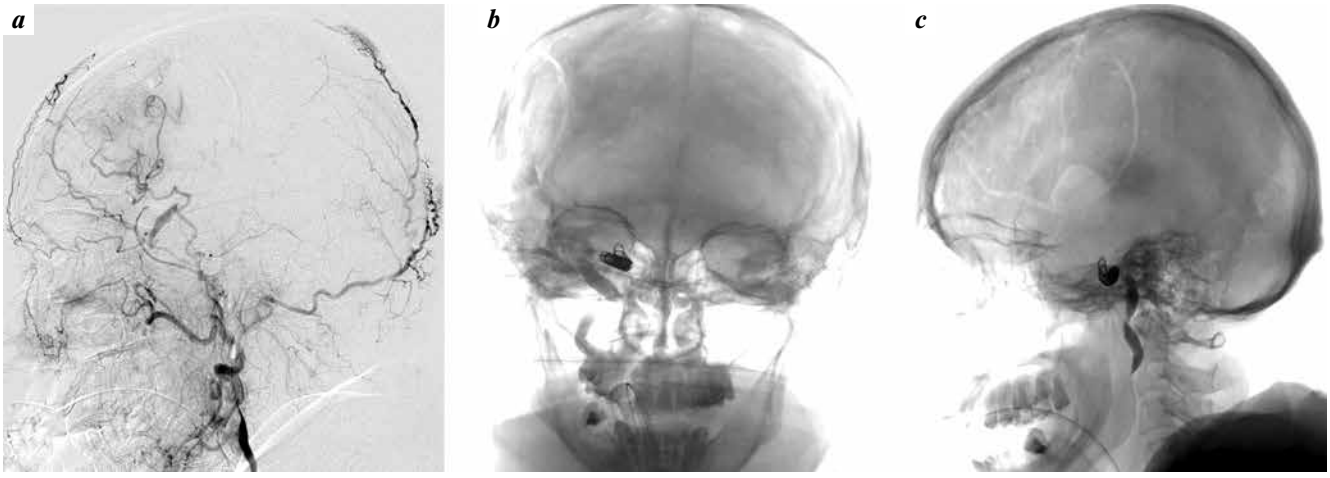

Fig. 5. *Angiograms of the cerebral vessels of patient K.: a – the right common and external carotid arteries after extra-intracranial bypass; b, c – the right internal carotid artery after deconstructive surgery (occlusion with microspirals)*

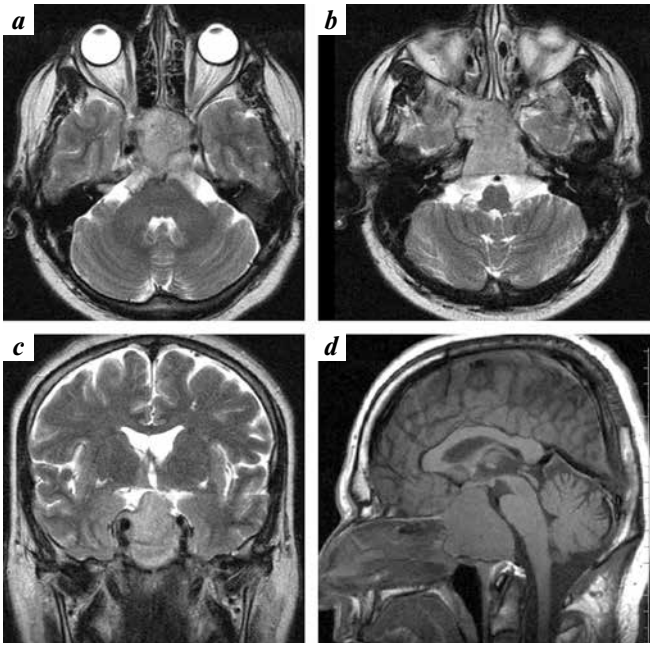

Fig. 6. *Magnetic resonance tomograms of the brain of patient M. prior to cabergoline therapy in axial (a, b), frontal (c) and sagittal (d) projections. An invasively growing pituitary tumor of large size is determined*

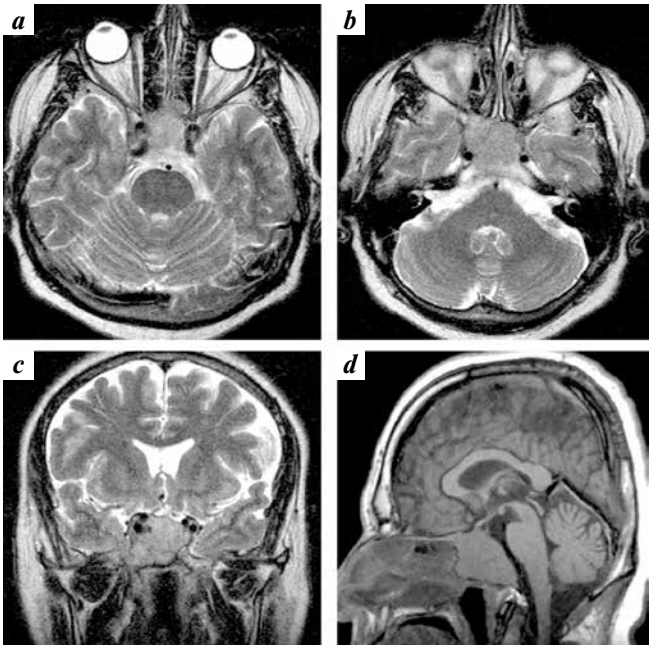

Fig. 7. *Magnetic resonance tomograms of the brain of patient M. 3 months after the start of cabergoline therapy in axial (a, b), frontal (c) and sagittal (d) projections. There is a decrease in the size of the tumor*

of invasively growing large prolactinomas. The mechanism of action of dopamine agonists is based on the direct binding of the drug to type 2 dopamine receptors on lactotrophic tumor cells leading to inhibition of cell proliferation [32–34], decrease in tumor size and serum prolactin level [35, 36]. In 40 % of cases, pituitary adenomas, prolactinoma in particular, are characterized by invasive growth: tumors can grow in any direction from the sella turcica affecting the cavernous sinus, bones and dura mater [37, 38]. Invasion into the surrounding structures is dependent on such factors as presence of disintegrin and metalloprotease, transforming tumor growth factor, vascular endothelial growth factor, etc. In combination, these factors theoretically create a possibility of tumor affecting ICA wall, which is one theory explaining concomitant intrasellar aneurysms and pituitary adenomas together with such factors as local circulatory stress, endocrine effects and mechanical effects [22, 39, 40]. In the cases presented in this article, pituitary adenoma in all likelihood partially destroyed ICA wall, and after tumor shrinkage its carcass function disappeared which led to predisposition for aneurysm development.

In such cases, correct interpretation of the 3D process in the chiasmal-sellar area is very important, as specific anamnesis immediately suggests drug resistance and continued tumor growth or hemorrhage into the residual tumor. Aneurysm can be distinguished from the tumor on MRI by

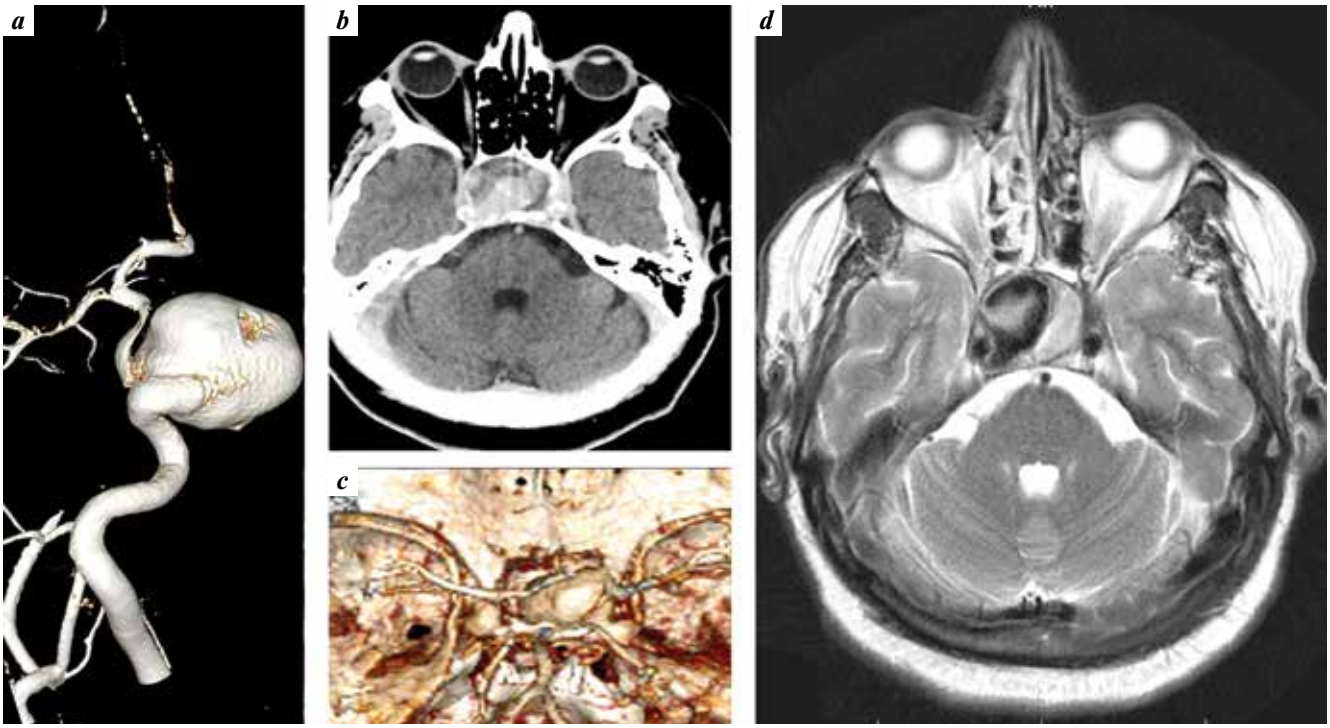

Fig. 8. *Giant partially thrombosed aneurysm of the cavernous segment of the right internal carotid artery, detected in patient M.: a – 3D angiograms of the right internal carotid artery; b, c – spiral computed tomographic angiograms; d – magnetic resonance tomogram in T2 mode in axial projection*

Fig. 9. *Angiogram of the right internal carotid artery after reconstructive surgery (microspiral occlusion)*

the presence of blood flow void in T1- and T2-weighted images; however, aneurysm thrombosis can complicate differential diagnosis, and in such cases spiral CTA is recommended.

Treatment tactics for intrasellar aneurysms depend on their size and shape. Both deconstructive surgeries in case of adequate collateral blood flow [26, 27, 41] and vasculature-preserving surgeries in the form of coiling or installation of flow diverters if anatomical characteristics are permissible are possible [42]. In the above-described cases, selective intraoperative angiography showed practically full ICA dysplasia at the aneurysm level, severely unfavorable anatomical characteristics of the aneurysm including inconvenient ICA branching angle distally from the aneurysm which did not allow to perform reconstructive surgery using flow diverters and led to deconstructive surgeries.

CONCLUSION

The described clinical cases allow to assume direct destructive effect of the tumor on the vascular wall. Two observations do not allow to confidently state if it is characteristic of prolactin or can happen for any tumor with hormonal activity. This, in turn, once again poses the question of the mechanism of development of aneurysms of the ICA cavernous segment during pituitary adenoma invasion into the cavernous sinus. Possibly, the structure of the walls of such aneurysms differ from aneurysms caused by other factors. Additionally, these two clinical cases allow to assume the presence of thinning of ICA walls during tumor invasion into the cavernous sinus with absence of changes in ICA according to MRI and spiral CTA, which, in turn, increases the risk of ICA wall rupture during tumor resection from the cavernous sinus.

At this stage, it seems reasonable to perform spiral CTA for all patients with adenoma invasion into the cavernous sinus, and to take into account the possibility of ICA wall rupture during tumor resection from the cavernous sinus due to the loss of tumor carcass function, and formation of an aneurysm in the postoperative period.

REFERENCES

1. Pant B., Arita K., Kurisu K. et al. Incidence of intracranial aneurysm associated with pituitary adenoma. Neurosurg Rev 1997;20(1):13–7. DOI: 10.1007/BF01390519
2. Housepian E.M., Pool J.L. A systematic analysis of intracranial aneurysms from the autopsy file of the Presbyterian Hospital, 1914 to 1956. J Neuropathol Exp Neurol 1958;17(3):409–23. DOI: 10.1097/00005072-195807000-00001
3. Imamura J., Okuzono T., Okuzono Y. Fatal epistaxis caused by rupture of an intratumoral aneurysm enclosed by a large prolactinoma – case report. Neurol Med Chir 1998;38(10):654–6. DOI: 10.2176/nmc.38.654
4. Manara R., Maffei P., Citton V. et al. Increased rate of intracranial saccular aneurysms in acromegaly: an MR angiography study and review of the literature. J Clin Endocrinol Metab 2011;96(5):1292–300. DOI: 10.1210/jc.2010-2721
5. Onishi H., Ito H., Kuroda E. et al. Intracranial mycotic aneurysm associated with transsphenoidal surgery to the pituitary adenoma. Surg Neurol 1989;31(2):149–54. DOI: 10.1016/0090-3019(89)90330-3
6. Oh M.C., Kim E.H., Kim S.H. Coexistence of intracranial aneurysm in 800 patients with surgically confirmed pituitary adenoma. J Neurosurg 2012;116(5):942–7. DOI: 10.3171/2011.12.JNS11875
7. Xia X., Ramanathan M., Orr B.A. et al. Expanded endonasal endoscopic approach for resection of a growth hormone-secreting pituitary macroadenoma coexistent with a cavernous carotid artery aneurysm. J Clin Neurosci 2012;19(10):1437–41. DOI: 10.1016/j.jocn.2011.11.032
8. Berker M., Aghayev K., Saatci I. et al. Overview of vascular complications of pituitary surgery with special emphasis on unexpected abnormality. Pituitary 2010;13(2):160–7. DOI: 10.1007/s11102-009-0198-7
9. Bulsara K., Karavadia S., Powers C., Paullus W. Association between pituitary adenomas and intracranial aneurysms: an illustrative case and review of the literature. Neurol India 2007;55(4):410. DOI: 10.4103/0028-3886.33307
10. Curto L., Squadrito S., Almoto B. et al. MRI finding of simultaneous coexistence of growth hormone-secreting pituitary adenoma with intracranial meningioma and carotid artery aneurysms: report of a case. Pituitary 2007;10(3):299–305. DOI: 10.1007/s11102-007-0011-4
11. Fujiwara S., Fujii K., Nishio S., Fukui M. Diagnosis and treatment of pituitary adenoma with adjacent carotid artery aneurysm. J Neurosurg Sci 1991;35(1):41–6.
12. Hori T., Muraoka K., Hokama Y. et al. A growth-hormone-producing pituitary adenoma and an internal carotid artery aneurysm. Surg Neurol 1982;18(2):108–11. DOI: 10.1016/0090-3019(82)90366-4
13. Revuelta R., Arriada-Mendicoa N., Ramirez-Alba J., Soto-Hernandez J.L. Simultaneous treatment of a pituitary adenoma and an internal carotid artery aneurysm through a supraorbital keyhole approach. Minim Invasive Neurosurg 2002;45(2):109–11. DOI: 10.1055/s-2002-32488
14. Seda Jr L., Cukiert A., Nogueira K.C. et al. Intrasellar internal carotid aneurysm coexisting with GH-secreting pituitary adenoma in an acromegalic patient. Arq Neuropsiquiatr 2008;66(1):99–100. DOI: 10.1590/S0004-282X2008000100026
15. Yamada S., Yamada S.M., Hirohata T. et al. Endoscopic extracapsular removal of pituitary adenoma: the importance of pretreatment of an adjacent unruptured internal carotid artery aneurysm. Case Rep Neurol Med 2012;2012:1–3. DOI: 10.1155/2012/891847
16. Sade B., Mohr G., Tampieri D., Rizzo A. Intrasellar aneurysm and a growth hormone-secreting pituitary macroadenoma. J Neurosurg 2004;100(3):557–9. DOI: 10.3171/jns.2004.100.3.0557
17. Salpietro F.M., Longo M., Alafaci C. et al. Co-existing pituitary tumour and intracavernous asymptomatic aneurysm: management implications. Acta Neurochir (Wien) 1997;139(8):791–2. DOI: 10.1007/BF01420056
18. Tsuchida T., Tanaka R., Yokoyama M., Sato H. Rupture of anterior communicating artery aneurysm during transsphenoidal surgery for pituitary adenoma. Surg Neurol 1983;20(1):67–70. DOI: 10.1016/0090-3019(83)90110-6
19. Li M.-H., Cheng Y.-S., Li Y.-D. et al. Large-cohort comparison between three-dimensional time-of-flight magnetic resonance and rotational digital subtraction angiographies in intracranial aneurysm detection. Stroke 2009;40(9):3127–9. DOI: 10.1161/STROKEAHA.109.553800
20. Wanke I., Doerfler A., Stolke D., Forsting M. Carotid cavernous fistula due to a ruptured intracavernous aneurysm of the internal carotid artery: treatment with selective endovascular occlusion of the aneurysm. J Neurol Neurosurg Psychiatry 2001;71(6):784–7. DOI: 10.1136/jnnp.71.6.784
21. Sasagawa Y., Tachibana O., Shiraga S. et al. [A clinical feature and therapeutic strategy in pituitary adenomas associated with intracranial aneurysms.] No Shinkei Geka 2012;40(1):15–21 (in Japanese). DOI: 22223518
22. Nakahara M., Uozumi Y., Chiba Y. et al. Direct carotid cavernous fistula due to rupture of a cavernous carotid aneurysm embedded within a prolactinoma after cabergoline administration. World Neurosurg 2019;122:495–9. DOI: 10.1016/j.wneu.2018.11.071
23. Peng Z., Tian D., Wang H. et al. Epistaxis and pituitary apoplexy due to ruptured internal carotid artery aneurysm embedded within pituitary adenoma. Int J Clin Exp Pathol 2015;8(11):14189–97.
24. Khalsa S.S., Hollon T.C., Shastri R. et al. Spontaneous subarachnoid hemorrhage due to ruptured cavernous internal carotid artery aneurysm after medical prolactinoma treatment. BMJ Case Rep 2016;2016:bcr2016012446. DOI: 10.1136/bcr-2016-012446
25. Suzuki H., Muramatsu M., Murao K. et al. Pituitary apoplexy caused by ruptured internal carotid artery aneurysm. Stroke 2001;32(2):567–9. DOI: 10.1161/01.STR.32.2.567
26. Khalsa S.S., Hollon T.C., Shastri R. et al. Spontaneous subarachnoid hemorrhage due to ruptured cavernous internal carotid artery aneurysm after medical prolactinoma treatment. J Neurointerv Surg 2017;9(3):e9. DOI: 10.1136/neurintsurg-2016-012446.rep
27. Gillam M.P., Molitch M.E., Lombardi G., Colao A. Advances in the treatment of prolactinomas. Endocr Rev 2006;27(5):485–534. DOI: 10.1210/er.2005-9998
28. Bhatt M.H., Keenan S.P., Fleetham J.A., Calne D.B. Pleuropulmonary disease associated with dopamine agonist therapy. Ann Neurol 1991;30(4):613–6. DOI: 10.1002/ana.410300416
29. Delgrange E., Daems T., Verhelst J. et al. Characterization of resistance to the prolactin-lowering effects of cabergoline in macroprolactinomas: a study in 122 patients. Eur J Endocrinol 2009;160(5):747–52. DOI: 10.1530/EJE-09-0012
30. Ling L.H., Ahlskog J.E., Munger T.M. et al. Constrictive pericarditis and pleuropulmonary disease linked to ergot dopamine agonist therapy (Cabergoline) for Parkinson's disease. Mayo Clin Proc 1999;74(4):371–5. DOI: 10.4065/74.4.371
31. Usiello A., Baik J.-H., Rougé-Pont F. et al. Distinct functions of the two isoforms of dopamine D2 receptors. Nature 2000;408(6809):199–203. DOI: 10.1038/35041572
32. Lin S., Zhang A., Zhang X., Wu Z.B. Treatment of pituitary and other tumours with cabergoline: new mechanisms and potential broader applications. Neuroendocrinology 2020;110(6):477–88. DOI: 10.1159/000504000
33. Spada A., Nicosia S., Cortelazzi L. et al. In vitro studies on prolactin release and adenylate cyclase activity in human prolactin-secreting pituitary adenomas. Different sensitivity of macro- and microadenomas to dopamine and vasoactive intestinal polypeptide. J Clin Endocrinol Metab 1983;56(1):1–10. DOI: 10.1210/jcem-56-1-1

34. Lin S.J., Leng Z.G., Guo Y.H. et al. Suppression of mTOR pathway and induction of autophagy-dependent cell death by cabergoline. Oncotarget 2015;6(36):39329–41. DOI: 10.18632/oncotarget.5744
35. Leng Z.G., Lin S.J., Wu Z.R. et al. Activation of DRD5 (dopamine receptor D5) inhibits tumor growth by autophagic cell death. Autophagy 2017;13(8):1404–19. DOI: 10.1080/15548627.2017.1328347
36. Yang Q., Li X. Molecular network basis of invasive pituitary adenoma: a review. Front Endocrinol (Lausanne) 2019;10:7. DOI: 10.3389/fendo.2019.00007
37. Wang J., Zhang Z., Li R. et al. ADAM12 induces EMT and promotes cell migration, invasion and proliferation in pituitary adenomas via EGFR/ERK signaling pathway. Biomed Pharmacother 2018;97:1066–77. DOI: 10.1016/j.biopha.2017.11.034
38. Soni A., De Silva S.R., Allen K. et al. A case of macroprolactinoma encasing an internal carotid artery aneurysm, presenting as pituitary apoplexy. Pituitary 2008;11(3):307–11. DOI: 10.1007/s11102-007-0063-5
39. Chuang C.C., Chen Y.L., Pai P.C. A giant intracavernous carotid artery aneurysm embedded in pituitary macroadenoma presenting with pituitary apoplexy. Cerebrovasc Dis 2006;21(1-2):142–4. DOI: 10.1159/000090450
40. Peng Z., Tian D., Wang H. et al. Epistaxis and pituitary apoplexy due to ruptured internal carotid artery aneurysm embedded within pituitary adenoma. Int J Clin Exp Pathol 2015;8(11):14189–97. DOI: 26823732
41. Sun Y., Wan B., Li Q. et al. Endovascular treatment for cavernous carotid aneurysms: a systematic review and meta-analysis. J Stroke Cerebrovasc Dis 2020;29(6):104808. DOI: 10.1016/j.jstrokecerebrovasdis.2020.104808

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K.G. Mikeladze: software, visualization, literature research;
S.B. Yakovlev: writing an article, reviewing, editing;
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