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Case Report

Fungal symptomatic intracranial aneurysm treated with a flow diverting stent: A case report

Yosuke Fujimi[1], Tomohiko Ozaki[2], Nobuyuki Izutsu[1], Shin Nakajima[1], Yonehiro Kanemura[1,3], Tomoki Kidani[1], Saki Kawamoto[1], Naoki Nishizawa[1], Koji Kobayashi[1], Toshiyuki Fujinaka[1]

[1]Department of Neurosurgery, National Hospital Organization (NHO) Osaka National Hospital, Osaka, [2]Department of Neurosurgery, Osaka University Graduate School of Medicine, Suita, [3]Department of Biomedical Research and Innovation, Institute for Clinical Research, National Hospital Organization (NHO) Osaka National Hospital, Osaka, Japan.

E-mail: Yosuke Fujimi - yosukef@hotmail.co.jp; Tomohiko Ozaki - tomohikoozaki@gmail.com; *Nobuyuki Izutsu - hoheitai8@gmail.com; Shin Nakajima - nakajima.shin.tf@mail.hosp.go.jp; Yonehiro Kanemura - kanemura.yonehiro.hk@mail.hosp.go.jp; Tomoki Kidani - kkkkidani@ybb.ne.jp; Saki Kawamoto - carame1ize.0128@gmail.com; Naoki Nishizawa - n.nishizawa44@gmail.com; Koji Kobayashi - k.072914er@gmail.com; Toshiyuki Fujinaka - fujinaka.toshiyuki.pn@mail.hosp.go.jp

***Corresponding author:**
Nobuyuki Izutsu,
Department of Neurosurgery,
NHO Osaka National Hospital,
Osaka, Japan.

hoheitai8@gmail.com

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ABSTRACT

Background: Intracranial infectious aneurysms (IIAs) are very rare, and fungal aneurysms are infrequently reported. We report a case of an unruptured IIA caused by fungal rhinosinusitis and treated with a flow-diverting stent.

Case Description: An 81-year-old woman visited the ophthalmology department with impaired eye movement and ptosis and was placed under follow-up. A week later, she also developed a headache; magnetic resonance angiography revealed an aneurysm measuring 2 mm in the C4 portion of the right internal carotid artery. A 3-week follow-up with contrast-enhanced magnetic resonance imaging showed an increase in its size to 10 mm, and a contrast lesion was observed surrounding the right cavernous sinus. The patient started treatment with voriconazole and steroids on the same day. Ten weeks later, despite improvements in inflammation, the size of the aneurysm was unchanged; we, therefore, treated the aneurysm with a flow-diverting stent. Oculomotor nerve palsy improved, and the patient was discharged to a rehabilitation hospital 28 days after the placement, with a modified Rankin Scale of 4. A 1-year follow-up angiogram showed a partial decrease in the size of the aneurysm, with an O'Kelly-Marotta grading scale of B3.

Conclusion: IIAs grow rapidly, and the risk of rupture is high due to the weakening of the aneurysmal wall. To reduce the risks of rupture and recurrence after treatment, the infection should be treated before inserting a flow-diverting stent. Flow-diverting stent placement may be an effective treatment for IIA once the original infection has been cured.

Keywords: Flow diverting stent, Intracranial fungal aneurysm, Intracranial infectious aneurysm

INTRODUCTION

Intracranial infectious aneurysm (IIA) is a rare disease[14], of which 72.8% of cases are caused by bacterial infection; infectious endocarditis is the major predisposing factor.[26,30] Only 13.2% of IIA cases are caused by fungal pathogens.[26] Treatments for fungal IIA remain controversial, and many different approaches have been used. Surgical treatments include trapping,[31] excision,[17] and clipping,[4,20,22] whereas endovascular treatments include coiling,[8,10] placing of a detachable balloon,[8] and liquid embolization.[8] However, the endovascular treatment of fungal

IIA using a flow-diverting stent has rarely been reported. Herein, we report a case of unruptured IIA caused by fungal rhinosinusitis, which we treated with a flow-diverting stent.

CASE DESCRIPTION

An 80-year-old woman with a medical history of cerebral infarction, ovarian cancer, and breast cancer noted sudden right eye ptosis and abduction. She visited her local ophthalmology department for a check-up and was placed under follow-up. One week later, she had a gradually worsening headache and was taken by ambulance to a local hospital. Magnetic resonance angiography revealed a 2-mm aneurysm in the C4 portion of the right internal carotid artery (ICA); however, the relationship between the aneurysm and her symptoms was unclear [Figures 1a and b]. Follow-up magnetic resonance imaging revealed an increase in the size of the aneurysm to 10 mm within two weeks [Figures 1c and d]; the patient was referred to our hospital for further evaluation. Contrast-enhanced magnetic resonance imaging revealed a contrast-enhanced lesion from the right cavernous sinus to the orbital apex, which was suspected of communicating with the sphenoid sinus [Figures 1e and f].

Moreover, the cavernous portion of the right ICA was dilated with wall irregularities caused by vascular invasion [Figures 2a and b]. Laboratory examination revealed elevated β-d-glucan (33.1 pg/mL); white blood cell counts and C-reactive protein levels were within normal ranges. The patient was diagnosed with an invasive fungal sinus infection with a fungal ICA aneurysm and was hospitalized for medical treatment. She started steroid treatment with intravenous hydrocortisone followed by oral prednisolone, as well as antifungal treatment with voriconazole. Although she was afebrile and her β-d-glucan levels lowered after medical treatment, the size of the aneurysm was enlarged, and its shape changed [Figures 2c and d]. We considered surgical treatments. A balloon occlusion test was not performed due to her mild cognitive impairment and restlessness. Parent artery occlusion with extracranial to intracranial bypass seemed too invasive for her general condition. We, therefore, planned an endovascular treatment using flow diverting stent to maintain distal cerebral perfusion. She started dual antiplatelet therapy with daily aspirin (100 mg) and clopidogrel (75 mg). Three weeks later, on hospital day 47, she received a flow-diverting stent (Pipeline Flex with Shield Technology 4 × 35 mm, Medtronic) and had an O'Kelly-Marotta grading scale of B2. Her ptosis and eye movement gradually improved after flow-diverting stent placement, and she was discharged to a rehabilitation hospital with a modified Rankin Scale of 4, which was the same score as at admission. Her symptoms almost completely recovered six months after the surgery. Follow-up angiograms at six months and one year showed a partial decrease in aneurysm size, with O'Kelly-Marotta grading scales of B2 and B3, respectively [Figures 2e and f]. The patient finished antifungals at one year, and steroid treatment was tapered off over two years. She is currently in a nursing home with no complications.

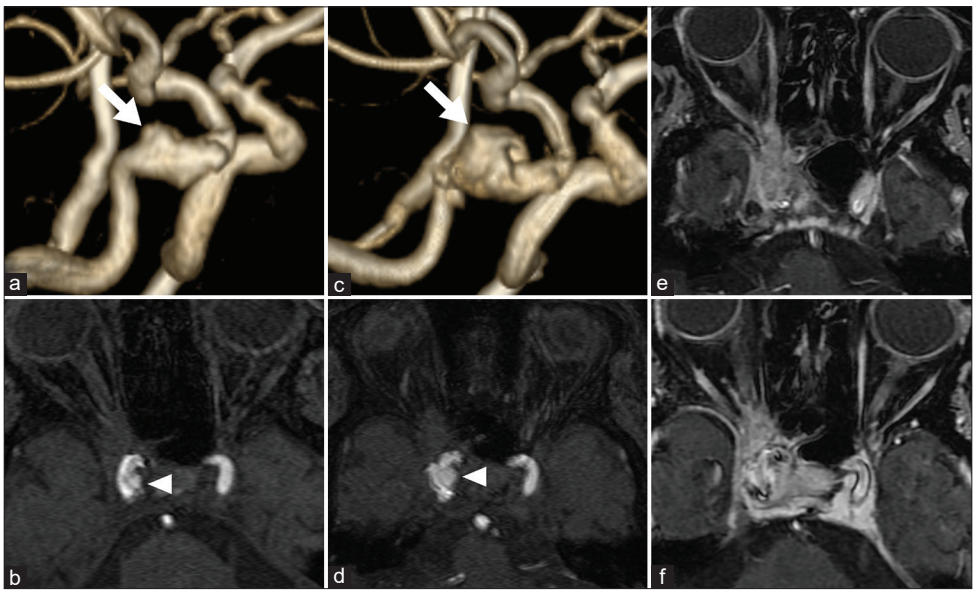

Figure 1: (a and b) First magnetic resonance angiography of the aneurysm, with a size of approximately 2 mm (arrow and arrowhead). (c and d) The aneurysm size increased to 10 mm in 2 weeks (arrow and arrowhead). (e and f) Contrast-enhanced magnetic resonance imaging demonstrates a contrast-enhanced lesion from the right cavernous sinus to the orbital apex, which communicates with the sphenoid sinus.

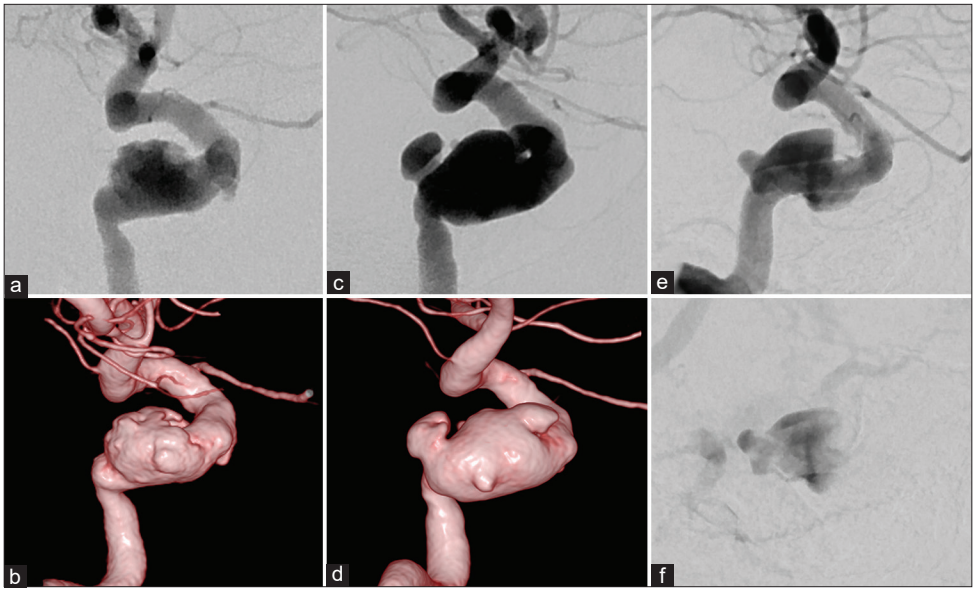

Figure 2: (a and b) First angiogram demonstrating the aneurysm in the cavernous portion of the right internal carotid artery with wall irregularities. (c and d) Angiogram after six weeks of medical treatment exhibiting the aneurysm dilatation and shape change. (e and f) Arterial phase and venous phase of angiogram one year after flow diverting stent placement. O'Kelly-Marotta grading scale: B3.

DISCUSSION

IIA often occurs in patients with conditions such as poorly controlled diabetes mellitus, leukemia, ongoing chemotherapy, or steroid therapy.[7,9,13,17,18,31] The present case had no pre-existing diabetes mellitus and was not on steroids. Although she had recently undergone treatment for breast cancer, she received surgical resection and hormone therapy only, with no chemotherapy. However, the breast cancer itself may have compromised her immune system through carcinoma-associated fibroblasts, which are reportedly associated with immunosuppression.[9]

Infective endocarditis is the most common cause of IIA[3], and patients usually have some clinical symptoms. However, in some cases, patients have negative results for various examinations. For example, blood cultures may be negative[3,7,17,29] multiple times,[24] as can be urine, sputum,[24] spinal fluid, and ascitic cultures.[29] It has been reported that 12.7% of patients with IIA have negative results for blood cultures.[3] Some cases of intracranial fungal aneurysm have C-reactive protein levels and white blood cell counts within a normal range[17,18], and some show negative results for β-d-glucan or aspergillus antigen.[7,17] After resection of intracranial fungal aneurysms, histopathologic findings may directly demonstrate the existence of fungus, for example, by detecting coenocytic hyphae.[17] However, in some cases, only the thickening or destruction of vessel walls is detected.[29] Okawa *et al*. diagnosed a case of IIA based on clinical symptoms, imaging findings, and reduced serum inflammation after initiating antibiotics despite various negative culture results.[24] In the present case, although we did not detect any signs of infection, we made the diagnosis of intracranial fungal aneurysm based on a comprehensive evaluation of laboratory data and imaging findings.

Different IIAs are thought to have distinct characteristic locations. For example, intracranial bacterial cerebral aneurysms are often caused by infective endocarditis[3,30], in which infections in the intracardiac space are transported by the bloodstream. The infections then settle into peripheral intracranial arteries and use them as scaffolds to enlarge and form cerebral aneurysms. Intracranial bacterial aneurysms, therefore, tend to form in small peripheral arteries. In contrast, intracranial fungal aneurysms often occur in a slightly different manner; fungal infections are thought to directly invade and infect adjacent organs rather than travel through the bloodstream.[3,7,18,31] Intracranial fungal aneurysms thus tend to form in main arteries, such as the ICA, through direct invasion from the sinuses and other organs. In autopsy cases, bone destruction of the sinus wall has been observed near the neck of the aneurysm[18], and a pouch has been detected in the sphenoid sinus in connection with an ICA cavernous segment with multiple aneurysms.[13]

There is no established duration of antifungal medical treatment for intracranial fungal aneurysms. According to

a retrospective cohort study of the use of antifungals and outcomes of invasive aspergillosis or mucormycosis, the average duration of antifungal treatment was 41 days.[27] In two previously reported cases of intracranial fungal aneurysms treated with flow-diverting stents, the duration of antifungal treatment was 3 and 6 weeks.[10,16] These results may indicate that six weeks of antimicrobial treatment before performing endovascular treatment is appropriate. Concerning the duration of antimicrobial treatment after stent placement, some reported cases have continued antifungals until β-d-glucan levels were within normal limits,[31] some were treated until week 6,[5] and some continued treatment for more than two years.[13] In the current case, with an aim to decrease aneurysm size, we first administered antifungal treatment for seven weeks before performing endovascular treatment. However, because the aneurysm size remained unchanged, we then inserted a flow-diverting stent and continued antifungal treatment for one year.

IIAs rapidly grow and deform, thus inducing destruction and necrosis of the surrounding organs.[17] Invasive fungal sinus infection can also lead to artery stenosis as well.[28] In a case reported by Koiso *et al*., elastic fibers had disappeared from the aneurysm wall, and only fibrotic tissue was observed.[17] Such aneurysms rapidly grow over a few weeks to a few months[5,24,30], and this rapid growth makes the vessel walls fragile and prone to rupture. Treatment is difficult when the walls rupture. Intracranial fungal aneurysms tend to form in proximal, larger-diameter main arteries; once ruptured, they can be fatal. Although coil embolization can obtain an earlier aneurysmal flow reduction than flow-diverting stent placement, flow-diverting stent placement has been performed in some cases of recurrence after acute phase coil embolization.[15] As shown in Table 1, IIAs have been treated using flow diverting stent, with favorable outcomes. Complete occlusion was achieved in 75% of those cases. In the present case, although the aneurysm remained even one year after flow-diverting stent placement, the aneurysm decreased in size and remained unruptured. Predictive factors were reported, such as older age (>70 years),[12,19] aneurysm with mass effect, aneurysm location other than vertebral artery,[1] and fusiform morphology.[19] These factors were consistent with the present case and seemed to be the cause of incomplete occlusion. Parent artery occlusion is another treatment method that can provide more immediate aneurysm obliteration than flow-diverting stent placement [11,21]. However, the complication rate for unruptured cerebral aneurysms is 21.8%, which includes ischemic complications at 17.5%.[23] To maintain distal cerebral perfusion in our case, we, therefore, decided to insert a flow-diverting stent.

Table 1: A literature review of intracranial infectious aneurysms treated with a flow diverter stent

Author, year	Age (year)/ Sex	Site of aneurysm	Pathogen	Antimicrobials	Antimicrobial duration before EVT	Total antimicrobial duration	Treatment	Outcome
Appelboom *et al*., 2010[5]	10/F	ICA (C4)	*Streptococcus*	CTRX/AMC	6 weeks	6 weeks	Silk	CO
Kobets *et al*., 2018[16]	41/F	ICA (C4)	*Actinomyces/ A. fumigatus*	broad spectrum antibiotics/ Amphotericin	3 weeks	N.A.	Pipeline	CO
Imamura *et al*., 2019[14]	35/M	ICA (C4)	*Brucella*	Doxycycline	2 weeks	N.A.	Pipeline	CO
Ares *et al*., 2019[6]	2/M	BA	N.A.	N.A.	N.A.	N.A.	Pipeline	CO
Aguilar-Perez *et al*., 2020[2]	50/M	MCA	N.A.	N.A.	N.A.	N.A.	p48MW HPC	Enlargement
Samples *et al*., 2021[26]	10/F	MCA	*S. aureus/ S. anginosus*	CTRX	4 weeks	6 weeks	Pipeline	CO
Dalai *et al*., 2021[10]	28/M	ICA (C4)	Fungal smear positive	LAmB/Posaconazole	6 weeks	N.A.	FRED	Near CO
Kashkoush *et al*., 2023[15]	45/M	MCA	*Streptococcus*	N.A.	N.A.	6 weeks	Pipeline	CO
	33/F	MCA/PCA	*Streptococcus*	N.A.	N.A.	8 weeks	Pipeline	CO
	24/M	PCA	*Streptococcus*	N.A.	N.A.	8 weeks	Pipeline	CO
Osuki *et al*., 2023[25]	64/F	ICA (C3/4)	*S. milleri*	Penicillin G	6 weeks	6 weeks	Pipeline	Enlargement
Present case, 2023	80/F	ICA (C4)	N.A.	Voriconazole	7 weeks	1 year	Pipeline	CO

A. fumigatus: Aspergillus fumigatus, AMC: Amoxicillin clavulanic acid, BA: Basilar artery, C3: Clinoidal segment, C4: Cavernous segment, CO: Complete obliteration, CTRX: Ceftriaxone, EVT: Endovascular treatment, F: Female, HPC: Hydrophilic polymer coating, ICA: Internal carotid artery, M: Male, MCA: Middle cerebral artery, N.A.: Not available; PCA: Posterior cerebral artery, S. aureus: Staphylococcus aureus, S. anginosus: Streptococcus anginosus, S. milleri: Streptococcus milleri, HPC: Hydrophilic polymer coating

CONCLUSION

Flow-diverting stent placement may be an effective treatment for symptomatic intracranial fungal aneurysms once the original infection has been cured.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Abdel-Tawab M, Abdeltawab AK, Abdelmonem M, Moubark MA, Taha MA, Morsy A, *et al.* Efficacy and safety of flow diverters in posterior circulation aneurysms and comparison with their efficacy in anterior circulation aneurysms: A systematic review and meta-analysis. Interv Neuroradiol 2021;27:609-21.
2. Aguilar-Perez M, Hellstern V, AlMatter M, Wendl C, Bazner H, Ganslandt O, *et al.* The p48 flow modulation device with hydrophilic polymer coating (HPC) for the treatment of acutely ruptured aneurysms: Early clinical experience using single antiplatelet therapy. Cardiovasc Intervent Radiol 2020;43:740-8.
3. Alawieh A, Chaudry MI, Turner RD, Turk AS, Spiotta AM. Infectious intracranial aneurysms: A systematic review of epidemiology, management, and outcomes. J Neurointerv Surg 2018;10:708-16.
4. Allen LM, Fowler AM, Walker C, Derdeyn CP, Nguyen BV, Hasso AN, *et al.* Retrospective review of cerebral mycotic aneurysms in 26 patients: Focus on treatment in strongly immunocompromised patients with a brief literature review. AJNR Am J Neuroradiol 2013;34:823-7.
5. Appelboom G, Kadri K, Hassan F, Leclerc X. Infectious aneurysm of the cavernous carotid artery in a child treated with a new-generation of flow-diverting stent graft: Case report. Neurosurgery 2010;66:E623-4; discussion E4.
6. Ares WJ, Tonetti DA, Greene S, Sharma MS, Xavier F, Jankowitz BT, *et al.* Pipeline embolization of an infectious basilar artery aneurysm in a 2-year-old child: Case report, discussion of the literature and perioperative considerations. Oper Neurosurg (Hagerstown) 2019;17:E224-8.
7. Azar MM, Assi R, Patel N, Malinis MF. Fungal mycotic aneurysm of the internal carotid artery associated with sphenoid sinusitis in an immunocompromised patient: A case report and review of the literature. Mycopathologia 2016;181:425-33.
8. Chapot R, Houdart E, Saint-Maurice JP, Aymard A, Mounayer C, Lot G, *et al.* Endovascular treatment of cerebral mycotic aneurysms. Radiology 2002;222:389-96.
9. Costa A, Kieffer Y, Scholer-Dahirel A, Pelon F, Bourachot B, Cardon M, *et al.* Fibroblast heterogeneity and immunosuppressive environment in human breast cancer. Cancer Cell 2018;33:463-79.e10.
10. Dalai S, Datla AV, Francis AA, Dannana NK, Parappil H. Endovascular management of mucormycotic aneurysms of the internal carotid artery in post-COVID-19 patients. Cureus 2021;13:e20812.
11. Fang YB, Lin A, Kostynskyy A, Agid R, Tymianski M, Radovanovic I, *et al.* Endovascular treatment of intracranial vertebrobasilar artery dissecting aneurysms: Parent artery occlusion versus flow diverter. Eur J Radiol 2018;99:68-75.
12. Hiramatsu R, Yagi R, Kameda M, Nonoguchi N, Furuse M, Kawabata S, *et al.* Treatment outcomes of 94 cases of pipeline embolization device in a single center: Predictive factors of incomplete aneurysm occlusion. J Neuroendovasc Ther 2023;17:217-23.
13. Hot A, Mazighi M, Lecuit M, Poiree S, Viard JP, Loulergue P, *et al.* Fungal internal carotid artery aneurysms: Successful embolization of an *Aspergillus*-associated case and review. Clin Infect Dis 2007;45:e156-61.
14. Imamura H, Sakai N, Alexander MJ. Flow-diverter stenting of intracavernous internal carotid artery mycotic aneurysm. J Stroke Cerebrovasc Dis 2019;28:e81-2.
15. Kashkoush A, El-Abtah ME, Achey R, Hussain MS, Toth G, Moore NZ, *et al.* Flow diversion as destination treatment of intracranial mycotic aneurysms: A retrospective case series. Oper Neurosurg (Hagerstown) 2023;24:492-8.
16. Kobets AJ, Scoco A, Nakhla J, Brook AL, Kinon MD, Baxi N, *et al.* Flow-diverting stents for the obliteration of symptomatic, infectious cavernous carotid artery aneurysms. Oper Neurosurg (Hagerstown) 2018;14:681-5.
17. Koiso T, Komatsu Y, Matsumaru Y, Ishikawa E. Difficulty of diagnosing a mucor-induced aneurysm arising in segment P4 of the posterior cerebral artery - A case report. Surg Neurol Int 2022;13:111.
18. Komatsu Y, Narushima K, Kobayashi E, Tomono Y, Nose T. *Aspergillus* mycotic aneurysm--case report. Neurol Med Chir (Tokyo) 1991;31:346-50.
19. Maragkos GA, Ascanio LC, Salem MM, Gopakumar S, Gomez-Paz S, Enriquez-Marulanda A, *et al.* Predictive factors of incomplete aneurysm occlusion after endovascular treatment with the Pipeline embolization device. J Neurosurg 2019;132:1598-605.

20. Matsubara N, Miyachi S, Izumi T, Yamanouchi T, Asai T, Ota K, *et al.* Results and current trends of multimodality treatment for infectious intracranial aneurysms. Neurol Med Chir (Tokyo) 2015;55:155-62.
21. Miyachi S, Ohnishi H, Hiramatsu R, Izumi T, Matsubara N, Kuroiwa T. Innovations in endovascular treatment strategies for large carotid cavernous aneurysms-the safety and efficacy of a flow diverter. J Stroke Cerebrovasc Dis 2017;26:1071-80.
22. Nakahara I, Taha MM, Higashi T, Iwamuro Y, Iwaasa M, Watanabe Y, *et al.* Different modalities of treatment of intracranial mycotic aneurysms: Report of 4 cases. Surg Neurol 2006;66:405-9; discussion 9-10.
23. Nishi H, Ishii A, Satow T, Iihara K, Sakai N, Japanese Registry of Neuroendovascular Therapy investigators. Parent artery occlusion for unruptured cerebral aneurysms: Results of the Japanese registry of neuroendovascular therapy 3. Neurol Med Chir (Tokyo) 2019;59:1-9.
24. Okawa S, Hanazono A, Sugawara M, Takahashi S, Yanagiwsawa T, Mizoi K, *et al.* Cavernous sinus thrombosis with infectious intracranial aneurysms: A case report. Jpn J Stroke 2010;32:307-13.
25. Osuki T, Ikeda H, Uezato M, Kinosada M, Kurosaki Y, Chin M. *De novo* expansion formation in the outer curvature of the internal carotid artery after flow diverter deployment for an infectious cavernous carotid aneurysm: Illustrative case. J Neurosurg Case Lessons 2023;5:CASE23124.
26. Samples DC, Ravindra VM, Thoms DJ, Tarasiewicz I, Grandhi R. Successful flow diversion treatment of ruptured infectious middle cerebral artery aneurysms with the use of Pipeline Flex with Shield technology. Interv Neuroradiol 2021;27:225-9.
27. Stull K, Esterberg E, Ajmera M, Candrilli S, Kitt TM, Spalding JR, *et al.* Use of antifungals and outcomes among inpatients at risk of invasive aspergillosis or mucormycosis in the USA: A retrospective cohort study. Infect Dis Ther 2019;8:641-55.
28. Terada E, Nishida T, Fujita Y, Maeda Y, Hayama M, Takagaki M, *et al.* Percutaneous transluminal angioplasty and stenting for progressive intracranial carotid artery stenosis secondary to invasive sphenoid sinus aspergillosis: A case report. NMC Case Rep J 2023;10:215-20.
29. Tokuda T, Ono Y, Nishiya H, Aoki M, Yamanouchi S, Kunii O, *et al.* An autopsy case of fungal (Mucor) cerebral aneurysm. Kansenshogaku Zasshi 1995;69:438-43.
30. Tokunaga H, Kamada K, Hoshida T, Kawaguchi S, Uranishi R, Shiomi K. The treatment for the bacterial aneurysm. Surg Cereb Stroke 1991;19:476-81.
31. Yamaguchi J, Kawabata T, Motomura A, Hatano N, Seki Y. Fungal internal carotid artery aneurysm treated by trapping and high-flow bypass: A case report and literature review. Neurol Med Chir (Tokyo) 2016;56:89-94.

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