Mycotic Posterior Inferior Cerebellar Artery Aneurysm Following Meningitis after Endoscopic Endonasal Transsphenoidal Surgery : Case Report and Review of the Literature

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Mycotic intracranial aneurysms (MIAs) are rare infection-mediated arterial wall destructions that result in focal vessel weakness and dilatation. They commonly involve the anterior cerebral circulation, usually following hematogenous embolization from infective cardiac vegetation, and are associated with an elevated risk of rupture. MIAs arising from a posterior inferior cerebellar artery (PICA) are uncommon, and those resulting from contiguous infections are extremely rare. Here, we present a case report and review the literature on rare MIAs involving the distal PICA segment following meningitis after endoscopic endonasal transsphenoidal surgery. A 75-year-old man presented with a 2-year history of progressive visual impairment of the left eye, for which initial cranial magnetic resonance imaging suggested optic perineuritis ; however, conservative management with high-dose steroid therapy did not improve the patient's condition. He subsequently had biopsy, which confirmed an optic nerve sheath meningioma, for which optic nerve decompression via the endoscopic endonasal approach (EEA) and follow-up radiation therapy was done. He developed postoperative meningitis and subsequently had rupture of left PICA mycotic aneurysm (angiography done a month earlier demonstrated normal left PICA). Risk factors for meningitis were invasive cranial intervention, prolonged steroid use, and radiation therapy. Coil embolization was successfully performed ; however, the patient succumbed to irreversible herniation and infection. MIAs arising from the PICA following meningitis are rare, but complications following surgical intervention and rupture are associated with high morbidity and mortality. A high index of suspicion and early intervention before rupture may prevent poor outcomes. *Shinshu Med J 71 : 415—422, 2023*

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I Introduction

Mycotic intracranial aneurysms (MIAs) are a focal weakening and dilatation of the arterial vessel walls mediated by microbial infections or toxin injury. They commonly follow septic embolization of bacterial or other microbes from infective cardiac vegetations[1)-3)]. Rarely do they occur due to the contiguous seeding of microbes onto the vascular wall, as observed in cases of meningitis or other parameningeal infection[4)5)]. The anterior cerebral circulation is commonly implicated with the middle cerebral artery (MCA), accounting for more than two-thirds in some series[3)-6)]. MIAs involving the vertebral-basilar system are uncommon and rarely reported to involve the posterior inferior cerebellar artery (PICA)[4)7)]. To the best of our knowl-

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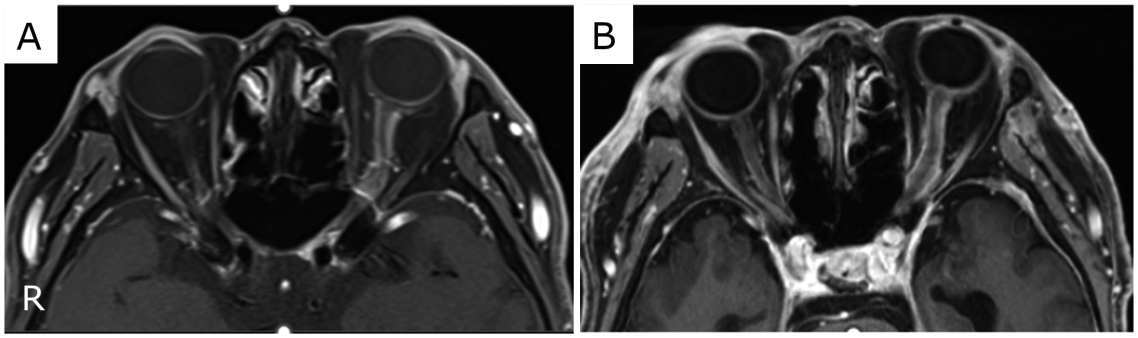

Fig. 1 Cranial contrast-enhanced MRI showing enlargement of the left optic nerve sheath with contrast enhancement, compared to the right (A). Repeat contrast cranial MRI 3 months later showed an enlarged optic nerve sheath with cavernous sinus involvement (B).

edge, this is the first reported distal PICA aneurysm arising from meningitis following endoscopic endonasal transsphenoidal surgery.

More than 70 % of patients present with catastrophic intracranial hemorrhage due to the friable nature of MIAs, which are therefore associated with high morbidity and mortality[1)3)5)]. Management is multidisciplinary, and options include clipping through craniotomy, endovascular coiling or trapping, and bypass surgery. For the optimal surgical decision, a variety of factors need to be considered, including the aneurysm location and peculiarities, comorbidities (especially cardiac disease) and the available facilities and expertise[1)5)6)8)9)]. Here we present a case report of a rare MIA involving the distal PICA following meningitis after endoscopic endonasal optic nerve decompression for optic nerve sheath tumors and a review of the related literature.

Ⅱ Case Presentation

A 75-year-old man presented with a 2-year history of progressively worsening visual impairment of the left eye. He had previously experienced fungal sinusitis, which had been managed with endoscopic rhinosinus surgery. He also reported to have gradually noticed double vision and left facial pain.

Clinical examination showed a corrected visual acuity of 1.2 in both eyes, and a progressive worsening on the left side at the follow-up. We also observed left cranial nerve IV and VI palsies with associated hypoesthesia involving the V1 and V2 divisions of the trigeminal nerve. Cardiovascular examination results were essentially normal, and echocardiography did not reveal any cardiac vegetation. Cranial magnetic resonance imaging (MRI) revealed enlargement of the left optic nerve sheath extending into the optic canal, with associated perioptic contrast enhancement **(Fig. 1A)**. The initial diagnosis was optic perineuritis. Other differentials excluded were anti-neutrophil cytoplasmic antibodies (ANCA)-associated orbital vasculitis (excluded by negative p-ANCA and c-ANCA), sarcoidosis (no hilar adenopathy and normal serum and cerebrospinal fluid (CSF) acetylcholinesterase) and IgG4-related ophthalmic disease (normal serum IgG4 concentrations). The neurology team placed the patient empirically on high-dose steroids (prednisolone 50 mg/day), after which he showed an initial improvement in vision.

A repeated cranial MRI was requested 1 month later because the patient's visual symptoms worsened, and he experienced progressive orbital and left hemifacial pain despite the high-dose steroid treatment ; we also observed further swelling of the optic nerve sheath with cavernous sinus involvement. Due to the non-improvement with steroids, a decision was made to obtain a biopsy via the left supraorbital keyhole approach, and histology revealed an optic nerve sheath meningioma with infiltrating cavernous sinus **(Fig. 2)**.

Endoscopic endonasal optic nerve decompression with left optic nerve canal release was performed 1 month later because the patient's left-eye vision had further worsened (to 0.05), and he subsequently underwent intensity-modulated radiotherapy. The patient noted some improvement after surgical release

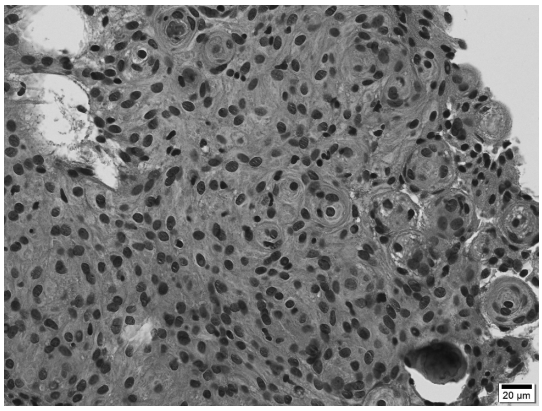

Fig. 2 Histopathological findings reveal the tumor cells have a fascicular arrangement with whorl formation and psammoma bodies, which were diagnosed as meningotherial meningioma. (H & E staining, ×40)

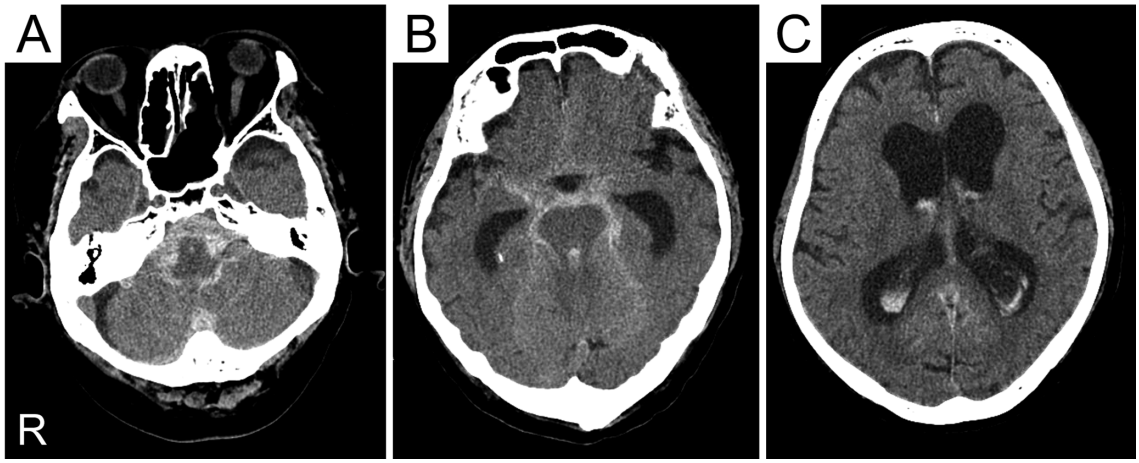

Fig. 3 CT showing subarachnoid hemorrhage involving the basal and the suprachiasmatic cisterns with associated intraventricular hemorrhage (A, B) and hydrocephalus with associated intraventricular haemorrhage (C).

and intensity-modulated radiotherapy ; however, 5 days later, he experienced a rebound of facial pain and rapidly deteriorating vision then involving both eyes. Orbital inflammation after radiation was considered, and high-dose steroids were recommended. This intervention resulted in some relief of orbital and hemifacial pain and some visual improvements.

About 1 month after surgery, the patient's vision had further worsened and he had completely lost vision in his left eye, while also experiencing debilitating orbital and hemifacial pain. Another repeat cranial MRI scan showed features suggestive of an optic sheath and canal infection extending to the cavernous sinus **(Fig. 1B)**. He became unwell with recurrent episodes of fever that were uncontrollable with antipyretics. Leukocytosis and differential neutrophilia were also observed. Periorbital infection following endoscopic endonasal transsphenoidal surgery was suspected. There were no features suggestive of CSF leakage. Therefore, he was hospitalized and antibiotics (CEZ) were initiated, which led to relief from fever and improvement in laboratory data. Five days later admission (7 weeks after surgery), the patient collapsed with loss of consciousness and respiratory distress. The immediate Glasgow Coma Scale score was E1V1M1, necessitating emergency intubation and transfer to the intensive care unit for ventilatory support. An emergency computed tomography scan showed features of an extensive subarachnoid hemorrhage (SAH) with an epicenter at the posterior fossa, associated with intraventricular hemorrhage and acute hydrocephalus **(Fig. 3)**.

Emergency computed tomography angiography (CTA) revealed a left distal PICA aneurysm with associated vasospasm. This contrasted with a similar CTA conducted 1 month earlier, which had been nor-

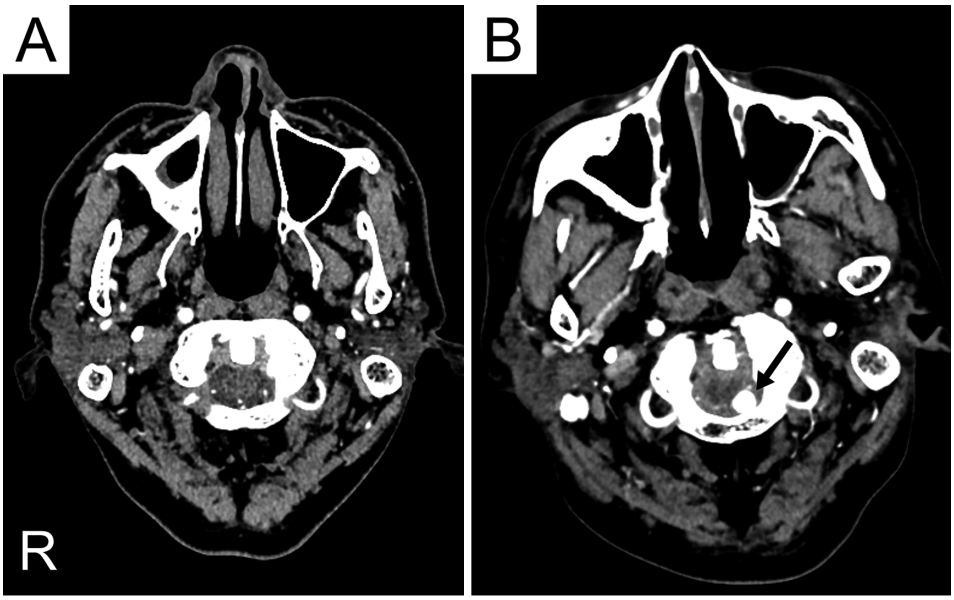

Fig. 4　A showing axial cut of CTA depicting the PICA without an associated aneurysm. B showing similar cut conducted 1 month later, revealing a left PICA aneurysm. The arrow indicates the aneurysm.

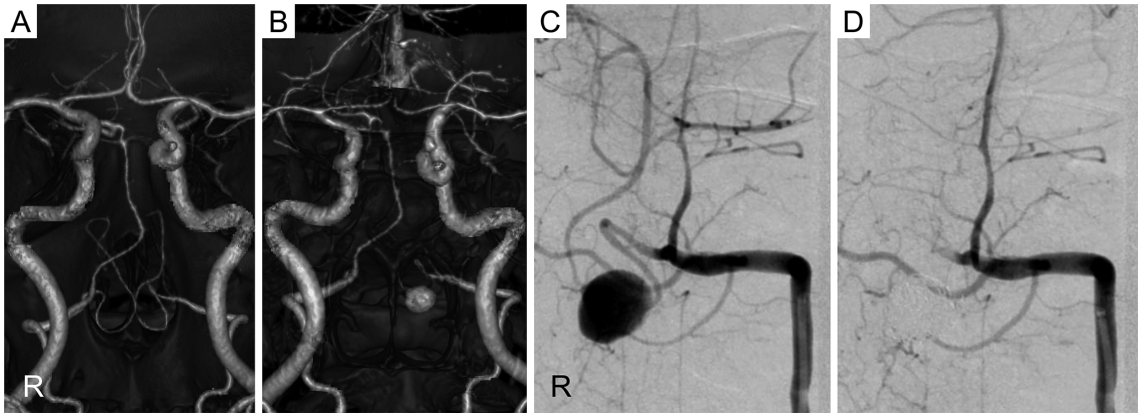

Fig. 5　CTA reconstruction showing both PICAs without associated aneurysms (A). CTA reconstruction conducted 1 month after the previous CTA showing a left PICA de-novo aneurysm with associated vasospasm (B). Catheter angiography via the transradial route showing a left PICA aneurysm (C) and complete coil embolization (D).

mal **(Fig. 4, 5)**. Based on this clinical course and findings of neuroimages, a diagnosis of a ruptured left PICA mycotic aneurysm with acute hydrocephalus (SAH World Federation of Neurological Surgeons (WFNS) grade 5) was made, and the patient's relatives were informed of the diagnosis and prognosis. The patient underwent emergency endovascular coil embolization of the left PICA aneurysm on the same day and external ventricular drainage to manage the hydrocephalus. Endovascular therapy was successful, and the aneurysm was well secured. However, the patient remained ventilator-dependent and showed no significant neurological recovery. Later, antibiotics were switched to sensitivity determined (MEPM) when CSF sampling revealed an increasing CSF cell count (55/μl) and decreasing CSF glucose (23 mg/dl), indicative of *Pseudomonas aeruginosa* infection. He passed away due to cardiac arrest 14 days after the initial incident.

Ⅲ　Discussion

MIAs account for 0.7-6.5 % of cerebral aneurysms,

although more than twice the incidence has been reported in autopsy series[1)5)8)]. The term "mycotic" was first described by William Osler in his *Gulstonian lectures*, referring to the mushroom appearance of the aneurysm resembling budding fungus on the aorta[8)10)]. Although the more accurate term should be "infected aneurysm", the older term has persisted in the literature. Here we present a case of a ruptured PICA mycotic aneurysm secondary to meningitis complicating transsphenoidal intervention, highlighting the extremely rare possibility of contiguous infection causing an aneurysm in the posterior circulation.

A Etiology and risk factors

Large population studies on MIAs are lacking due to their rarity ; however, an extensive systematic review of case reports and series by Alawieh et al. showed that infective endocarditis was the primary cause in almost 70 % of MIA cases, especially with vegetations in the left cardiac chamber[5)]. The authors also implicated dental infection as an important etiologic factor accounting for 10.7 % of cases. Other less common factors include meningitis, orbital cellulitis, mastoid infections, and cavernous sinus thrombosis[5)6)11)]. Immunosuppression from chronic steroid use and other immunosuppressants, especially seen in organ recipients or patients with acquired immunodeficiency syndrome, is a known risk factor and is frequently associated with fastidious organisms including fungi and protozoa[5)6)11)-13)]. Invasive cranial intervention such as endoscopic endonasal transsphenoidal surgery, prolonged steroid use, and radiation therapy were risk factors of meningitis in this index case that predisposed the patient to MIA.

B Pathoanatomy and microbiology of MIAs

The MCA is the most frequently implicated vessel, in 50–78 % of reported MIA cases, and are related to the higher differential flow from the internal carotid artery[1)3)5)-7)]. Most posterior circulation MIAs involve the posterior cerebral arteries, which are terminal branches of the basilar artery, but rarely the proximal tributaries[1)5)]. Piccirilli et al.[4)] reported the first case of an infective PICA aneurysm following dental infection treated approximately 2 years prior ; however, none have been reported following bacterial meningitis complicated by endonasal transsphenoidal surgery.

MIAs are distally located, often dysmorphic, friable, and have a wide or non-demonstrable neck. The fusiform morphology is the most common, accounting for 52.5 %, while the saccular type is seen in 45 % and may occur in multiples in up to 25 % of cases[1)5)6)]. The infectious cascade is triggered by embolization of the organism lodging in the distal intracranial vessels, causing septic infarction, or in the vaso-vasorum, triggering an inflammatory cascade. Neutrophil infiltration occurs within the media and adventitia, resulting in the release of cytokines and proinflammatory factors, including various proteases and matrix metalloproteins 1, 8, & 9[1)6)9)14)]. Degradation of the arterial wall occurs with accompanying intimal proliferation and fragmentation of the internal elastic lamina. The combination of vessel wall destruction and shear stress from the hydrostatic pressure of the blood flow results in focal dilatation of the vessels[1)9)14)].

Bacterial infections are the most common cause of MIAs, seen in 80 % of cases, and predominantly involve gram-positive cocci[1)5)6)]. In addition, almost one-third of cases are caused by gram-negative organisms, as seen in this index case, and usually follow contiguous infections[14)]. One systematic review has implicated fungal infections in 13.4 % of cases, with *Aspergillus* species being the most common and associated with immunosuppression[5)]. In rare cases, varicella zoster virus and HIV 1 and 2 are the causative organisms[1)6)].

C Clinical presentation and diagnosis

Most MIAs are noticed after rupture, resulting in subarachnoid and intraparenchymal hemorrhage (IPH)[8)11)15)]. IPH is more common in MIAs than in other berry aneurysms because of their friable nature and distal location within the brain parenchyma. Ruptured MIAs are usually catastrophic and present with a high WFNS grade, with mortality approaching 80 % in some series[1)3)15)16)]. Other authors have opined that minor focal deficits from distant embolization of septic foci are more frequent and usually go unnoticed[6)].

The diagnosis of MIA involves the demonstration of an intracranial aneurysm using an appropriate im-

Table 1　Validated criteria for diagnosis of mycotic intracranial aneurysm[17]

Mandatory criteria	Intracranial aneurysm on neurovascular imaging
Supportive criteria	**Presence of recent or predisposing infection :** (1) infective endocarditis, (2) meningitis, (3) orbital cellulitis, (4) cavernous sinus thrombophlebitis **Angiographic features :** (5) multiplicity, (6) distal location, (7) fusiform shape, (8) change is the shape and size of a new aneurysm on follow-up imaging. **Other contributory factors :** (9) age ＜45 years, (10) fever/history of fever ≥ 7 days, (11) recent lumbar puncture, (12) intraparenchymal haemorrhage in brain imaging.

Definitive MIA : presence of mandatory criteria and any three or more supportive criteria. Clinical probable MIA : mandatory criteria and two of the supportive criteria. Clinically probable MIA : mandatory criteria and one of the supportive criteria. Our patient had the mandatory criteria and four supportive criteria[9)17)].

aging modality along with the presence of predisposing factors, as described earlier. A scoring system devised by Kannoth et al. suggested that an intracranial aneurysm on neuroimaging with three or more associated supportive criteria indicates a definitive diagnosis of MIA **(Table 1)**[17]. The angiographic features of MIAs include their fusiform shape, distal location, multiplicity, dysmorphic nature, and change in shape or size on follow-up angiography[1)6)]. While digital subtraction angiography remains the gold standard for diagnosing MIAs, CTA and magnetic resonance angiography (MRA) are more commonly utilized due to their less invasive nature and easy availability of these modalities. However, in acute emergencies, a non-contrast computed tomography scan can demonstrate features of SAH, IPH, associated brain edema, hydrocephalus, and herniation syndrome, thereby guiding management. Identifying the causative organisms in the blood or CSF is pivotal in deciding the proper definitive antibiotic course, and blood cultures may be positive in 35–75 % of patients with infective endocarditis[1)6)14)]. Serial inflammatory marker assessment should be used to determine responses to antibiotic therapy and follow-up.

D　Management options for MIAs

There is lack of level-one evidence to create guidelines for the treatment of MIAs because of their rarity ; nevertheless, management options are guided by the aneurysmal characteristics, rupture status, presence of comorbidities, including concomitant cardiac disease, and need for cardiac surgery and availability of care facilities[1)2)5)6)8)9)]. Over the last decade, there has been rapid advancement in endovascular techniques (EVTs) for aneurysms, reflected in the increased number of MIAs treated with these techniques[1)5)8)18)]. EVTs offer numerous advantages, especially in high-risk patients with a high WFNS grade and significant anesthesia risk, can reach surgically inaccessible areas, and offer a cure for multiple aneurysms in one sitting. They also allow for early cardiac surgery in patients with valvular dysfunction, as anticoagulation therapy can be commenced as early as 24 hr after EVT[1)6)]. Various EVT options, including coil embolization, stent-assisted coiling, flow diverters, and liquid embolization agents, are available[1)2)5)6)8)19)]. The index case presented here underwent successful aneurysm coil embolization on the rupture day ; however, the patient succumbed to his illness due to irreversible herniation syndrome and infection.

Microsurgical clipping is the option of choice for ruptured MIAs with associated IPH, unfavorable aneurysm morphology, or failed EVT interventions[1)5)6)8)15)]. Additionally, microsurgical clipping is employed to raise intracranial pressure with associated herniation syndrome requiring decompression or CSF diversion. Microvascular clipping is more challenging in MIAs than in conventional aneurysms because of the friable wall and distal location of the former and the morphological complexity of the neck. Ohtake et al. analyzed 129 MIAs and noted that almost two-thirds of patients presented with ruptures and no relationship between rupture status and the location or size of their aneurysm[8)]. In addition, 63 patients in their se-

ries underwent surgical interventions (55.6 % underwent EVT procedures and 44.4 % had open surgery) ; however, no significant difference was noted in the outcome between both groups ($p = 0.867$). In contrast, a larger systematic review by Alawieh et al[5]. involving more patients showed the superiority of EVTs over open surgery in terms of mortality and overall outcomes.

Conservative therapy is reserved for unruptured aneurysms with a high surgical risk, defined by morphological characteristics, rendering them non-amenable to EVT and microvascular approaches[1)6)]. In such a scenario, antibiotic therapy based on culture results is commenced, followed by serial angiographic monitoring. Response to therapy is described as a reduction in the size or disappearance of the aneurysm. Therapy failure occurs when the MIA ruptures, increases in size, or remains the same despite antibiotic use or the occurrence of new aneurysms[1)6)]. Invasive therapy with microsurgical clipping or EVT procedures are then warranted. Matsubara and colleagues suggested a multimodal approach to the treatment of MIAs and possibly conservative treatment with antibiotics and serial imaging in unruptured and clinically stable patients[20)]. They noted disappearance without recurrence or rebleeding of seven unruptured MIAs managed following that protocol ; however, Ohtake et al. found that although antibiotic treatment is more effective in unruptured cases, it is associated with high mortality and most patients require additional surgery[8)].

Care for MIAs should be multidisciplinary and multimodal, with close collaboration among neurosurgeons, neurointerventionists, intensivists, and other care physicians, including cardiac surgeons. Decision making must involve the family and caregiver, and consideration of the patient's physical status, comorbidities, and aneurysm characteristics is essential. The prognosis for ruptured MIAs is poor, especially in moribund patients with cardiac disease.

Ⅳ Conclusions

MIAs arising from the PICA following meningitis are rare, but complications following surgical intervention and rupture are associated with high morbidity and mortality. Maintaining a high index of suspicion and pursuing early intervention before rupture could potentially prevent adverse outcomes. Patient care should be approached in a multimodal, multidisciplinary, and individualized manner. Notably, endovascular therapy stands as the treatment modality of choice, proving effective, particularly in high-risk cases of ruptured MIAs.

Compliance with Ethical Standards

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical Approval

All procedures described in this report were performed in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from the patient.

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