SUBARACHNOID HEMORRHAGE REVEALING A BACTERIAL ENDOCARDITIS: CASE REPORT WITH LITERATURE REVIEW

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Abstract

We present a case of subarachnoid haemorrhage (SAH) caused by ruptured infectious intracranial aneurysms secondary to endocarditis. The patient presented with neurological signs of a SAH. Fever and the presence of a previously undiagnosed heart murmur were reasons to obtain blood cultures and initiate further diagnostic workup for endocarditis. Using this case as illustration, we want to draw attention to the dangerous neurological complications that can occur during an episode of endocarditis and call for timely evaluation.

Key words: Subarachnoid haemorrhage, bacterial endocarditis.

Introduction

Mycotic aneurysms (MAs), also known as infective or microbial aneurysms, are rare inflammatory neurovascular lesions that account for 0.7–6.5% of all intracranial aneurysms (12). Mycotic aneurysms are unique in their natural history and pathologic findings, with distinct angiographic features, and frequently develop at terminal arterial branches. Because their spontaneous rupture results in subarachnoid and intracerebral hemorrhage, they are associated with significant morbidity and mortality, as high as 60%–90% in earlier case studies, and 12–32% in more recent literature reviews (12, 28). The following is a case report coupled with a methodical review of the presentation, diagnosis, complications, and management of MAs.

Case report

A 29-year-old woman was admitted to the emergency department of our hospital with sudden loss of consciousness. Her initial Glasgow coma score (GCS) was 3, 6 and 4 for eye opening, best motor response and best verbal response, respectively (E3M6V4). She had right-sided hemiparesis. Her medical history revealed no previous illnesses or hospital admission. There was no evidence to suggest intravenous drug abuse. Heteroanamnesis revealed that she had been suffering from general malaise and arthralgia for the past few months. On physical examination at our hospital, her blood pressure was 120/70 mmHg, pulse rate 70 beats per minute, and temperature 38.5° C. Inspection of the mouth and throat revealed no abnormalities. Her lungs were clear on auscultation and a new onset systolic heart murmur degree III/VI, punctum maximum (p.m.) apically radiating to the left axillar region, was found. Examination of the skin and nails revealed no stigmata of endocarditis. Neurological

examination showed a GCS of E4V2M6 with a left hemiparesis. A computed tomogram (CT) scan (Figure 1) showed intracerebral haemorrhage with blood in the Fissura Sylvii, indicative of SAH. Cerebral angiography on admission (Figure 2) showed an aneurysm of 3.7 mm distally on the left middle cerebral artery. Laboratory studies included: C-reactive protein (CRP) 94.9 mg/l (0-5 mg/l), WBC 18.0×10^9/l ($4.0\text{-}10 \times 10^9$/l), Hb 8.6 g/dl, and prothrombin time 16.0s (10-13.5s). All other laboratory studies were within normal range. Blood cultures obtained at the time of admission revealed *Staphylococcus hominis*. Transoesophageal echocardiography confirmed the clinical suspicion of endocarditis. Intravenous (IV) cefalotin 2g three times a day and gentamycin 120 mg once a day, were started immediately. The cerebral angiography after 6 weeks of that intravenous treatment showed no aneurysm (Figure 3).
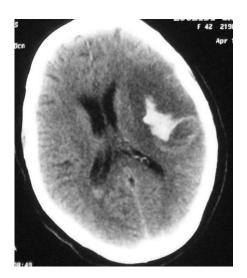

Figure 1: Intracerebral haemorrhage with blood in the Fissura Sylvii, indicative of SAH
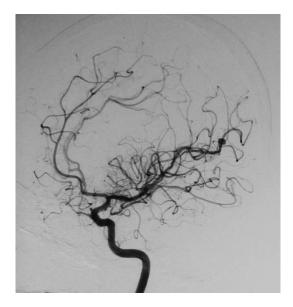
Figure 2: Cerebral angiogram showing a distally aneurysm on the left middle cerebral artery.

Figure 3 : Repeat cerebral angiogram after 6 weeks of IV antibiotics.

Discussion

Epidemiology

In the pre-antibiotic era, 86% of all infectious intracranial aneurysms (IIA) were associated with bacterial endocarditis, commonly arising in patients with prosthetic valves, nosocomially acquired blood stream infections, or a history of intravenous drug use (20). While the advent of antibiotic therapy has substantially decreased the occurrence of endocarditis in the developed world, endocarditis persists due to the increasing use of prosthetic valves, intravenous drug abuse, and degenerative valve diseases, with the vast majority of mycotic aneurysms originating from left-sided bacterial endocarditis (5, 20). In fact, IIA are clinically recognized in 3–10% of patients with infective endocarditis (20, 24). However, as IIA are often clinically silent but discovered in 5–10% of autopsy cases, their incidence may actually be higher than current estimates (1). Less commonly, IIA result from direct extension of intracranial bacterial infections such as meningitis, cavernous sinus thrombophlebitis, and orbital cellulitis, often in patients who are immunosuppressed (14, 20).

Pathogenesis

Mycotic aneurysms develop in infective endocarditis (IE) when friable cardiac vegetations give rise to septic emboli that lodge in intracranial vessels at branching points and distal branches. These emboli may occlude vessels, cause cerebral infarction, or promote infection (17). The vasa vasorum theory is the most widely accepted mechanism of pathogenesis. It proposes that bacteria from septic emboli escape through the vasa vasorum and cause severe inflammation of the adventitia. The infection then spreads inwardly (19, 2). The arterial pulsation against the weakened vessel wall eventually results in aneurysm formation and enlargement. The resulting aneurysms are usually fusiform and eccentric, without saccular characteristics, and are more common in the anterior circulation (18). Histologically, MAs are

characterized by acute neutrophilic infiltration, along with marked intimal proliferation and internal elastic lamina destruction. The responsible organism may be identified with appropriate staining (12). Although a wide variety of bacteria, mycobacteria, viruses, and fungi may cause mycotic aneurysms, *Streptococcus viridans* and *Staphylococcus aureus* are the most common etiologic organisms (12).

Natural History, Clinical Presentation and Diagnosis

Given the lack of population-based studies, the natural history of IIA is unknown, although a high case fatality has been previously described (10). Even unruptured IIA are associated with significant mortality, reaching 30%, with a significant increase in mortality to almost 80% should the aneurysm subsequently rupture (27). Although many cases remain asymptomatic, the majority of symptomatic IIA patients present with symptoms related to rupture of the aneurysm and to its causative etiology (26). For instance, patients with endocarditis and unruptured IIA often initially present with minor focal deficits due to septic embolization to the intracranial vasculature. Additional presentations for unruptured IIA are diverse and often insidious, including a subacute history of fever, chills, and malaise (14, 29). The clinical presentation for ruptured IIA includes severe unremitting localized headaches, dizziness, seizures, altered mental status, and focal neurological deficits related to subarachnoid hemorrhage (15). Most commonly, IIA present clinically following aneurysm rupture (21). It is the clinical presentation of our case.

In a large case series by Kannoth et al. 25 patients with infectious intracranial aneurysms presented with initial symptoms of headache (83%), fever (67%), vomiting (50%), ocular palsy (25%), seizures (21%), behavioral changes (21%), hemiparesis (21%), drowsiness (17%), and loss of consciousness (17%) (11). Almost half the patients met Duke's criteria for IE and gave a history of either rheumatic or congenital heart disease.

A scoring system based on the presence of specific clinical and radiographic findings has been proposed for the diagnosis of MA. Points are given for the presence of clinical markers, such as IE, meningitis, orbital cellulitis, cavernous sinus thrombophlebitis, persistent fever, age less than 45, recent lumbar puncture, and radiographic evidence of aneurysm multiplicity, distal location, fusiform shape, and change in size (12). The sensitivity and specificity of this value are 100% and 87.4%, respectively.

Supporting evidence of IIA includes leukocytosis, elevated erythrocyte sedimentation rate, and elevated C-reactive protein. Results of these laboratory tests should be evaluated in conjunction with radiographic studies in order to improve the diagnostic yield (29).

Radiographic Imaging Modalities

Cerebral vascular imaging is available through CT angiograhy (CTA), Magnetic Resonance Angiography (MRA), and Digital Subtraction Angiography (DSA). DSA, until recent decades, was the gold standard in intracranial aneurysm diagnosis (6). The advent of Multidetector CT imaging (MDCT) has increased the resolution of CTA, allowing for complete visualization of the intracranial vascular tree. This imaging modality carries a lower contrast burden and risk of permanent neurologic deficits than DSA. When compared to DSA, CTA had a sensitivity of 90% and specificity of 86% in recent systematic meta-analysis (8).

Management and Treatment

Given the relative rarity of this disease, current recommendations regarding the management and treatment of MA have largely been restricted to a limited number of case reports. Over the past decade, the management of infective intracranial aneurysms has been divided into medical, endovascular, and surgical treatment. The medical intervention that is uniformly

recommended is long- term intravenous antibiotic therapy for at least 6 weeks (13). In 1984, Morawetz and Karp observed that unruptured MAs could undergo spontaneous thrombosis, suggesting that MAs could resolve completely with antibiotic therapy alone (17). In a review of 20 cases of MAs over a ten year period by Chun in 2001, seven patients were initially treated conservatively with IV antibiotics alone and followed by serial angiography (4). In this series, the aneurysms in two patients decreased in size, one did not change, two achieved successful thrombosis, and the remaining two enlarged. Based on this review, the conclusion regarding unruptured MAs is that medical management with 6 weeks of IV antibiotic therapy is reasonable if closely followed by serial angiography. The goal of serial angiography would be to demonstrate improvement in aneurysm size and resolution. Zhao et al. reported a case in which a MA failed to show radiographic decrease in size after 2 weeks of medical therapy, and was successfully treated with endovascular therapy (30). Endovascular therapy has rapidly evolved in its efficacy and ability to access more distal aneurysms. The safety profile of this intervention is difficult to interpret, as it is based only on anecdotal and case-report data. A meta-analysis was performed on 16 patients in previously published cases who underwent endovascular treatment; 69% had a good outcome, while none had procedural-related complications (4). However, parent artery sacrifice was much more common in patients who underwent endovascular treatment versus open craniotomy with surgical ligation. This affects the management of diseased vessels supplying eloquent brain parenchyma, such as areas that involve language, sensorimotor cortex, visual cortex, hypothalamus, thalamus, cerebral peduncles, and brain stem. In a retrospective review performed on 14 patients with intracranial MAs who underwent endovascular intervention between 1991 and 1999 at a major French hospital (3), no deaths or complications were reported, 11 of the 14 patients showed stable lesions on follow up angiography 6–24 months after endovascular embolization, and 9 had complete resolution of their presenting neurologic deficit (3).

Indications for the surgical and/or endovascular treatment of IIA remain controversial and the success of such intervention is highly dependent on aneurysm morphology, the overall health of the patient, and the presence of concomitant intracerebral hemorrhage (24).

Valvular repair in the setting of intracranial septic emboli

The purpose of cardiac surgery is to remove the source of cerebral emboli and to improve hemodynamics (17). Whether the aneurysm has ruptured influences the timing and sequence of cardiothoracic and neurosurgery (12). Cardiac surgery is relatively safe if the MA is unruptured. Cardiopulmonary bypass, even with its requirement for heparinization, does not impose additional risks of rupture perioperatively (22). In the absence of a hemorrhagic infarct, valve replacement can be performed with very little risk of perioperative stroke (25). However, if the MA has ruptured and there is mass effect from an intracerebral hematoma or abscess, the intracranial aneurysm should be repaired first (17). In the presence of cerebral infarction, the danger of hemorrhagic transformation warrants a 2-3 week postponement of cardiac surgery (12). The exception to this rule would be if left heart failure were to develop as a consequence to IE. The presence of left heart failure would compromise cerebral perfusion, thus negating the benefits of any prior interventions performed on an intracranial MA. Hashimoto et al. reported a case in which a 24-year-old female with mitral valve IE and ruptured intracranial MA, safely underwent urgent mechanical mitral valve replacement for worsening congestive heart failure 10 days after suffering from an intracerebral hemorrhage. Neither the IE nor MA recurred in the postoperative 4 year follow up period (9). Shiraishi et al. reported a similar case in a 55 year old patient who presented with ruptured MA and left heart failure from aortic valve IE. In this case the patient underwent emergent bioprosthetic aortic valve replacement and did well with resolution of MA 9 months postoperatively (23).

Prognosis and outcome

The general consensus in the current literature is that ruptured MAs carry a worse prognosis than unruptured MAs; however, the rarity of intracranial MAs makes it difficult to ascertain prognostic markers that may help predict likely outcomes. A comprehensive review of 27 clinical series and 287 patients with intracranial MA diagnosed between 1950 and 2009 was recently conducted by Ducruet et al. The analysis, while limited due to heterogeneity of presentations and variable follow up duration, concluded that in all treatment modalities combined, 62% of patients had a positive outcome, 20% faced further neurological decline, 5% died before an invasive intervention could be performed, and 12% died immediately after an intervention was performed whether surgical or endovascular (7).

In conclusion we want to state that SAH can be a dangerous complication of endocarditis that is known to increase morbidity and mortality. Using this case, we want to create awareness that the formation of infectious intracranial aneurysms and SAH can occur during an episode of endocarditis. Neurological symptoms during an episode of endocarditis should always prompt thorough neurological investigations. Furthermore, since SAH can be the first presenting symptom of endocarditis, a diagnostic workup for endocarditis is justified in SAH patients presenting with fever upon admission.

Authors declare there is no conflict of interest.

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