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Selected Topics: Neurological Emergencies

INFECTIVE ENDOCARDITIS PRESENTING WITH INTRACRANIAL BLEEDING

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□ **Abstract—Background:** Infective endocarditis (IE) can be complicated by intracranial bleeding (ICB) caused by different pathologic mechanisms. The occurrence of ICB in patients with IE significantly influences therapeutic decisions and has a negative impact on outcome. **Case Report:** We describe the clinical courses of 3 patients with aortic prosthetic valve IE presenting with ICB. Patients 1 and 2 experienced subarachnoid hemorrhage (SAH) and intracerebral hemorrhage (ICH), respectively, caused by rupture of an intracranial infectious aneurysm (IIA). Both underwent endovascular treatment of IIA with good outcome. In patient 3, ICB was the hemorrhagic conversion of an acute ischemic lesion from septic brain embolization. In the subacute phase of the disease, aortic valve replacement was performed, with excellent outcome. **Why Should an Emergency Physician be Aware of This?:** ICB is a relevant complication and sometimes the first clinical feature of IE. Imaging of brain vessels should be performed to investigate the pathologic mechanism underlying ICB. The prevalence of IIA is probably underestimated and may influence the therapeutic strategy. Cerebrovascular imaging may therefore also be considered in asymptomatic subjects with left-sided IE. Withdrawal of anticoagulant treatment and delay of cardiac surgery are recommended in all cases of IE complicated by ICB. Because of the impact of ICB on IE management and outcome, a high level of clinical suspicion and prompt

recognition and treatment of this complication are necessary. © 2016 Elsevier Inc. All rights reserved.

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INTRODUCTION

Up to 40% of patients with infective endocarditis (IE) develop central nervous system involvement (1). Stroke is the most frequent neurologic complication of IE and the main cause of death after heart failure; it usually occurs in the early phase of the disease and in >50% of these patients represents the presenting symptom (2–4). In particular, intracranial bleeding (ICB) accounts for 30% of neurologic complications and has a negative impact on IE prognosis (1,5). Several mechanisms explain the occurrence of ICB in patients with IE (6). We describe 3 cases of IE presenting with different types of ICB.

CASE REPORTS

Patient 1

A 35-year-old man on oral anticoagulant therapy (OAT) for a mechanical prosthetic aortic valve presented with a thunderclap headache after a 3-day fever.

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Neuroimaging revealed a subarachnoid hemorrhage (SAH; [Figure 1A](#)) from a ruptured right pericallosal aneurysm and an unruptured aneurysm of the middle cerebral artery (MCA; [Figure 1C](#)). Laboratory findings revealed an elevated C-reactive protein level (457 nmol/L [normal, 0–48 nmol/L]) and *Enterococcus faecalis* was isolated from blood cultures. Prosthetic valve vegetation was identified on transesophageal echocardiography (TEE; [Figure 1B](#)) and a diagnosis of IE was made. OAT was promptly discontinued and the patient had good recovery after treatment of the ruptured aneurysm by endovascular occlusion of the parental artery ([Figure 1D](#)) and antibiotic therapy. Three months postdischarge, despite appropriate prolonged antimicrobial treatment, the unruptured aneurysm of the distal right MCA was unchanged. Therefore, the patient underwent endovascular

treatment by glue embolization of the parental artery ([Figure 1E](#)), with excellent outcome.

Patient 2

A 60-year-old man was admitted to our division for a right parieto-occipital intracerebral hemorrhage (ICH; [Figure 2A](#)). His vital signs and a general examination were unremarkable except for fever with chills. The patient's medical history was significant for the presence of a mechanical prosthetic aortic valve and OAT. Cerebral computed tomography angiography (CTA) and subsequent digital subtraction angiography (DSA) revealed the presence of an intracranial infectious aneurysm (IIA) originating from the right calcarine artery ([Figure 2B–D](#)), located at the base of the hematoma. IE

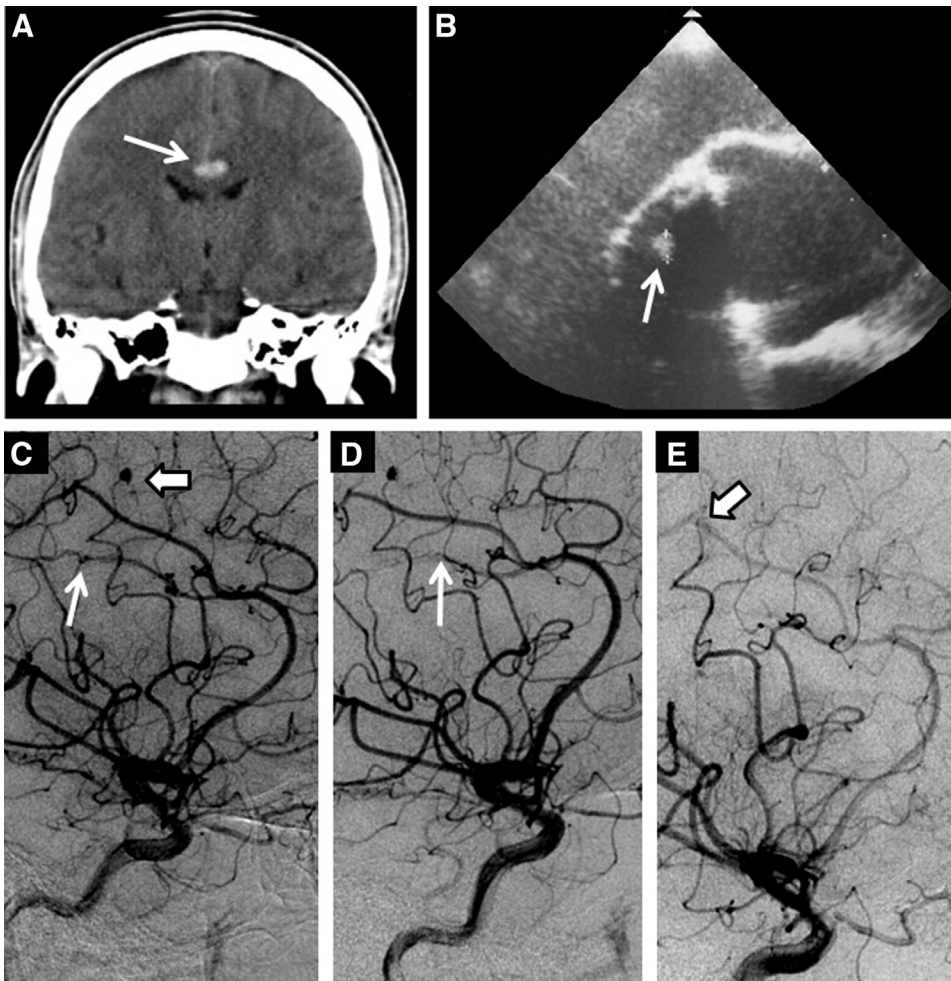


Figure 1. Coronal computed tomography scan of the brain showing subarachnoid hemorrhage in the supracallosal cistern (arrow, A) and transesophageal echocardiography with evidence of vegetation over the mechanical prosthetic aortic valve (arrow, B). Digital subtraction cerebral angiography revealing a ruptured aneurysm of the right pericallosal artery (thin arrow, C) and an aneurysm in the M4 division of the right middle cerebral artery (thick arrow, C). Digital subtraction cerebral angiography showing treatment of the infectious aneurysms with endovascular glue embolization of the parental artery (thin arrow, D and thick arrow, E).

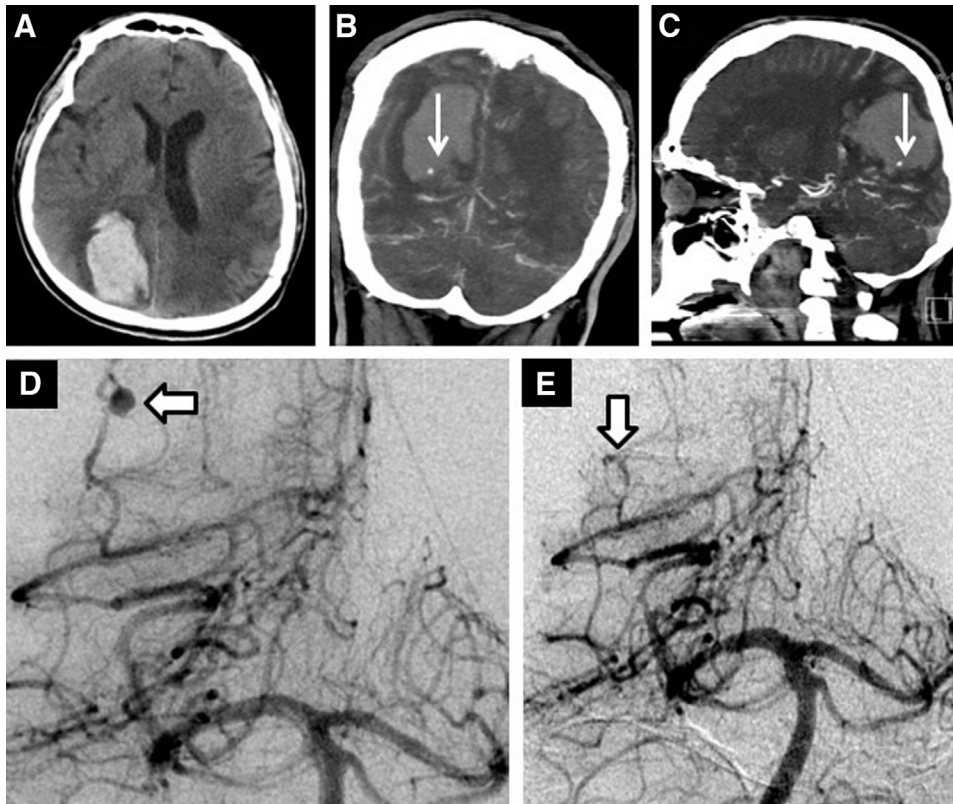


Figure 2. Axial computed tomography scan of the brain showing a large right parieto-occipital intracerebral hemorrhage (A). Computed tomography angiography showing an intracranial infectious aneurysm located at the base of the intracranial hematoma (arrows, B and C). Cerebral digital subtraction angiography revealing an aneurysm of the distal segment of the right calcarine artery before (arrow, D) and after (arrow, E) treatment by endovascular occlusion of the parental artery.

was suspected. Based on the simultaneous presence of fever, IIA, and a mechanical prosthetic valve, according to Duke Criteria, a diagnosis of possible IE was made, in spite of the negative results of TEE and blood cultures (4). Empiric antibiotic therapy was administered and endovascular occlusion of the IIA by glue embolization of the parental artery was successfully performed (Figure 2E), with good long-term outcome.

Patient 3

A 44-year-old man undergoing OAT for a mechanical prosthetic aortic valve was admitted with a 1-week history of fever with mild weight loss. Blood tests revealed the presence of normocytic anemia with significant elevation of the inflammatory markers (C-reactive protein, 1761 nmol/L [normal, 0–48 nmol/L]). The day after the admission the patient experienced a sudden onset of slurred speech and left hemiparesis. A CT scan of the brain was initially negative, but a follow-up CT scan revealed the presence of multifocal acute ischemic lesions (Figures 3A and 3B), with hemorrhagic transformation (Figure 3C). A CTA scan was unremarkable. The patient

underwent TEE with evidence of multiple aortic valve vegetations with severe valvular regurgitation and paravalvular abscess. *Staphylococcus aureus* was isolated from blood cultures, and the diagnosis of IE was made. Antibiotic treatment was started and OAT was withdrawn. Two months later, after complete disappearance of the ICB, aortic valve replacement was performed, with excellent outcome.

DISCUSSION

ICB is not an uncommon finding in patients with IE and can arise from variable pathologic mechanisms, such as hemorrhagic conversion of ischemic stroke, rupture of IIA, or pyogenic arteritis (7). In our case series, patients 1 and 2 experienced ICB from IIA rupture, while cerebral hemorrhage in patient 3 was caused by the hemorrhagic transformation of an acute embolic ischemic lesion.

IIA formation is the rarest neurologic complication of IE, occurring in 2% to 4% of cases (4,8). IIA are caused by septic embolization from infected heart structures and *S aureus* and viridans streptococci are the pathogens most frequently involved (9). Development of IIA is an

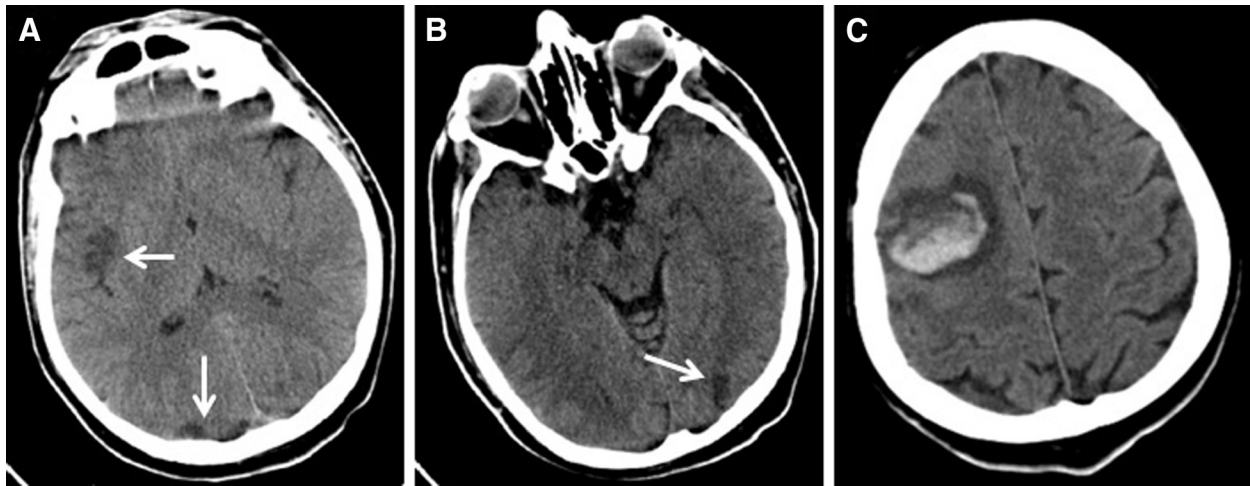


Figure 3. A computed tomography scan of the brain showing multifocal acute ischemic lesions (arrows, A and B) and right frontal infarction with hemorrhagic transformation (C).

uncommon finding in enterococcal endocarditis (10). Most patients with IIA present with fever, associated with headache, seizures, mental status impairment, or focal neurologic signs caused by an aneurysm rupture in the brain parenchyma or subarachnoid space (8). Fever and acute onset headache should raise the suspicion of IIA rupture in all patients with ICH or SAH, especially in those with predisposing conditions for IE, such as prosthetic heart valves.

Hemorrhagic conversion of a cerebral infarction was reported to be the most frequent cause of ICB in patients with IE (7). Overall, *S aureus* infection, prosthetic valve endocarditis, and OAT are the major risk factors for cerebral hemorrhagic complications of IE (5,11).

Although non-contrast CT scan of the brain is the preferred and most feasible initial imaging study in critical patients with IE and neurologic symptoms, cerebral vessel imaging is mandatory in all subjects (1,12). CTA and magnetic resonance angiography have excellent sensitivity for IIAs >5 mm; however, DSA is still considered the gold standard for the detection of IIA. IIAs are frequently multiple and have a predilection for the distal branches of the MCA. Unlike degenerative aneurysms, IIA size is not a predictor of rupture, and bleeding in the brain parenchyma is a common finding (8,9,13).

Magnetic resonance imaging (MRI) is the best imaging study to detect hemorrhagic conversion of an acute ischemic lesion. Moreover, systematic brain MRI evaluation of IE patients revealed that up to 80% of patients develop asymptomatic brain parenchymal lesions, such as small acute embolic ischemic lesions or microbleeds (14). However, the clinical impact of microbleed detection is still unclear, and asymptomatic central nervous system involvement has not been shown to have any influ-

ence on IE prognosis and management (1,2). Therefore, a routine brain MRI scan in all patients with IE is currently not recommended (1,12). In addition, MRI compatibility of the prosthetic device is a practical limitation in several cases.

Conversely, systematic brain vessel imaging with CTA may be considered in asymptomatic subjects with left-sided endocarditis (13). The prevalence of IIA is probably underestimated because small aneurysms may remain silent and resolve with antibiotic treatment (12,13). The identification of unruptured IIAs might have important clinical implications and guide the therapeutic strategy. First, the presence of IIA is included in the minor criteria for the diagnosis of IE, and IIA detection may therefore help in cases with nonspecific clinical presentation (4,13). Second, if early cardiac surgery is absolutely necessary, preoperative endovascular IIA treatment may be considered in order to prevent intraoperative IIA rupture (12). Third, endovascular treatment is warranted for ruptured IIA but also for IIA not resolved with appropriate medical treatment. Early identification of clinically silent IIA is therefore crucial and needs close imaging follow-up (12,13).

Surgical treatment of IIA and evacuation of the intracranial hematoma is usually reserved for bleeding with severe mass effect and intracranial hypertension (8,9,13).

Heart failure is the first cause of death in IE patients and the main indication for cardiac surgery in the acute phase of the disease (12). In subjects with IE complicated by ICB, cardiac surgery should be delayed for at least 4 weeks and all antithrombotic medications should be discontinued (3,12,13).

Early administration of empiric antibiotic therapy reduces the incidence of all cerebrovascular complications and is therefore warranted in all IE cases (12,13,15).

Finally, in patients with ischemic stroke related to IE, the potential benefits of intravenous thrombolysis administration should be balanced with the significantly increased risk of hemorrhagic transformation (16).

WHY SHOULD AN EMERGENCY PHYSICIAN BE AWARE OF THIS?

ICB is a common finding in IE, frequently occurring in the early phase of the disease and being the presenting sign in a relevant proportion of subjects. Various pathologic mechanisms can lead to ICB in subjects with IE, and brain vessel imaging is recommended in all patients with ICB in the setting of IE. The prevalence of IIA is probably underestimated and has a significant influence on IE management. Systematic imaging screening for IIA may be considered also in asymptomatic patients with left-sided endocarditis (13,17). Antithrombotic drugs should be discontinued and cardiac surgery delayed for at least 1 month in patients with an ICB caused by IE. Clinicians should therefore be aware of ICB in the setting of IE, in order to ensure prompt recognition and treatment of this dreadful complication.

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