Case Study

A 45-year-old man presented to the emergency department with acute right-sided weakness and aphasia. Computed tomography (CT) showed an evolving left middle cerebral artery infarct with some hemorrhagic transformation. Thrombolytic treatment was considered but withheld due to the presence of partial hemorrhage on CT.

According to his family he had been in excellent health until the last three to six months, when he developed periods of confusion, intermittent fever, and weight loss. His family physician had performed some basic investigations and found no specific cause for his symptoms.

Once in hospital, he developed swinging fever and tachypnea. He showed decreased air entry in his lungs and tachycardia without a heart murmur. His electrocardiogram was normal. Chest x-ray showed no pneumonia. Blood cultures were drawn and he was started on broad-spectrum antibiotics.

Three days after admission he suddenly became comatose and showed bilateral upper and lower limb weakness. Magnetic resonance imaging (MRI) showed infarction of the mid and left pons and midbrain with patchy areas of increased signal in the distribution of the basilar and posterior cerebral arteries. Echocardiography revealed friable vegetations on the aortic valve consistent with infectious endocarditis (IE). *Staphylococcus aureus* was cultured and the antibiotics were appropriately adjusted. After 48 hours in the intensive care unit, he did not regain consciousness and had lost all of his brainstem reflexes including a positive apnea test. After consultation with the family, ventilatory support was withdrawn and he died.

This case illustrates the insidious nature of the development of IE in a previously healthy individual. The occurrence of an acute neurological event in the context of a three-month history of nonspecific constitutional symptoms should alert the clinician to the possibility of IE. A delay in the diagnosis and treatment must be avoided to improve the outcome of these patients.

Introduction

The occurrence of a neurological event due to IE can be sudden and catastrophic. It is frequently perceived as an unfortunate but generally unavoidable event. However when one looks at the sequence of the pathophysiologic process of the disease, often there are telltale systemic and neurological signs and symptoms prior to the main event, which could be essential in making an early diagnosis. Early diagnosis may lead to measures, which could be useful to mitigate the catastrophic event.

This chapter is an attempt to document the sequence of the pathophysiologic processes in which the nervous system gets progressively involved in the disease process of IE. Infective
endocarditis will be the primary focus, but a brief discussion of marantic endocarditis will be included.

Full appreciation of the different neurological events in IE must take into consideration the pathophysiological processes, the etiological agent and the neurological localization over the dimension of time from preclinical defining event, to the defining event and to the evolutionary changes following the defining clinical event. This chapter provides a neurological diagnostic framework for the practicing clinician based on the current literature.

**Historical Perspective**

The clinical triad of fever, heart murmur and stroke were recognized by Osler and others before him to indicate the presence of IE [1,2]. However, present-day clinicians strive to recognize the endocarditis complex before permanent damage to heart, brain, and other target organs has occurred. Despite the use of modern imaging, there remains a significant delay in diagnosis and treatment in many IE patients.

The major historical milestones in the diagnosis and treatment of IE have been the development of antibiotics; cardiac imaging, including angiography and echocardiography; and the various options of surgical treatment from valve replacement or repair to extensive reconstruction of aortic or mitral annulus.

From a neurological standpoint, advancements in imaging, including CT, MRI, and digital cerebral angiography, have helped enormously in terms of localization of lesions and treatment planning. These are usually employed after the defining event has occurred. More attention has to be paid to the use of these tools earlier in the course of the disease before the defining event to provide information which may mitigate the event. Treatment from a neurological standpoint may include in selected cases the use of thrombolytics to hasten resolution of a septic embolus and the use of valve surgery to prevent an impending embolic stroke.

The use of neurological interventional techniques to deal with septic aneurysms has lead to the development of aneurysm hardware for coiling and clipping mycotic aneurysms. There are many case reports on treatment of these aneurysms using neuroradiological interventional techniques. However, there are no clinical trials to assist the clinical determination of the best treatment of these aneurysm from a risk benefit standpoint.

**Epidemiology**

The occurrence of neurological complications in IE is 20–40% [3]. Neurological deficits have been reported in up to 40% of patients with endocarditis of the left side of the heart [4]. Once neurological damage has occurred a mortality rate of 50% has been reported versus 21% in patients with IE without neurological complications [5]. Therefore prevention of neurological complications must become a priority.

Neurological complications are either the chief complaint or one of the major presenting symptoms in about a quarter of patients with IE [5]. The presence of congestive heart failure and non-cardiac shock with neurological damage increases the mortality and morbidity significantly [6,7].

**Pathophysiological Mechanisms**

The first matter to consider is the sequence of the pathophysiological processes by which IE affects the nervous system either directly or indirectly (Table 14.1). The life history of IE starts with the development of damage to the endocardium in particular the heart valve with the initiation of an inflammatory process on the surface of a valve, which then leads to progressive destruction of the endocardial, then myocardial and conducting system tissue.

In the early stages, the inflammatory process does not usually lead to the formation and liberation of thromboembolic material but rather initiates more nonspecific inflammatory responses, which affect the nervous system indirectly. In the preclinical-event stage, there is release of inflammatory cytokines such as IL-8 and tumor necrosis factor as well as other humoral responses. These humoral factors can affect the brain often causing nonspecific encephalopathic responses such as fatigue, anorexia and malaise. The detection of the presence of these cytokines could be used as markers...