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PRIMARY BACTERIAL INFECTION OF THE MYOCARDIUM

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1. ABSTRACT

Primary bacterial infection of myocardial tissue without associated endocarditis occurs only rarely. It is generally seen in the setting of overwhelming bacteremia. The most common bacterial cause of myocarditis is *Staphylococcus aureus*, although infections with a broad range of bacterial pathogens have been described. Pathologically, the disease process is characterized by multifocal studding of the myocardium with tiny abscesses, and the left ventricle is most commonly involved. Complications include cardiac dysfunction, rhythm disturbances, and myocardial rupture with secondary purulent pericarditis. Since virtually all information regarding primary bacterial myocarditis originates from autopsy studies conducted in the pre-antibiotic era, little is known about the modern approach to diagnosis and management of this clinical entity.

2. INTRODUCTION

Intact muscle tissue is generally not fertile soil for bacterial infections. Primary infections of heart muscle, like skeletal muscle, occur infrequently. William Osler recognized the entity of bacterial myocarditis in his medical text when he stated that "In pyaemia the smaller branches of the coronary arteries may be blocked with septic emboli and cause infarcts in the myocardium in the form of miliary abscesses, varying in size from a pea to a pin's head. These may not cause any disturbance, but when large they may perforate into the ventricle or into the pericardium, forming what has been called acute ulcer of the heart ." (1)

This review will restrict its discussion to primary bacterial infection of cardiac muscle. Since most bacterial infections of myocardial tissue present as localized collections, this review will use the terms bacterial myocarditis and myocardial abscess interchangeably. Autoimmune myocarditis triggered by bacterial infections, myocarditis that occurs as a consequence of endocarditis, myocarditis caused by bacterial toxins, and myocardial infections caused by mycobacteria and spirochetes will not be discussed. Rickettsial causes of myocarditis are discussed in another chapter.

3. HISTORY AND EPIDEMIOLOGY

Descriptions of bacterial myocarditis in the medical literature date back to at least 1846, when a case of myocardial rupture originating from a myocardial abscess was described at autopsy in an eight year old boy (2). The most recent reported substantial series of cases was published in 1981 (3). For obvious reasons, all conclusive descriptions of this condition in the older literature are from autopsy studies. The few published studies of bacterial myocarditis describe prevalences at post-mortem ranging from 0.2% to 1.5% (3-7). Most of these studies include cases of bacterial myocarditis secondary to endocarditis. Predisposing factors for primary bacterial myocarditis described in the early reports included bacteremia, neutropenia, myocardial infarction, osteomyelitis, and recent surgical procedures. The impact of antimicrobial therapy, modern diagnostic techniques, and modern surgical approaches (including cardiac transplantation) on the epidemiology of bacterial myocarditis has not been defined.

4. ETIOLOGIC AGENTS

The range of bacterial pathogens reported to cause primary bacterial myocarditis are summarized in Table 1.

Staphyloccocus aureus is the most common recognized cause of bacterial myocarditis. Flaxman, in 1943, described 23 cases of staphylococcal myocardial abscesses; 6 were due to bacterial endocarditis, 7 due to acute osteomyelitis and 10 were due to cellulitis, acute tonsillitis, mediastinitis, lung abscess, and peritonitis (5). Sanson, in 1963, reported 14 cases of *S. aureus* myocardial abscess five of which were due to endocarditis (6).6 An association with osteomyelitis was not observed. In a

Table 1. Organisms known to cause primary bacterial myocarditis

Organism	References
Staphylococcus aureus	3,5-8
Streptococcus pyogenes (Group A streptococci)	5,7
Streptococcus agalactiae (Group B streptococci)	9,10
Viridans streptococci	6,7
Streptococcus pneumoniae	5,7
Neisseria meningitidis	3,11
Escherichia coli	6
Proteus species	3,6
Klebsiella species	3,6
Pseudomonas species	3
Listeria monocytogenes	12
Bacteroides fragilis	13
Clostridium perfringens	6,14
Salmonella species	15
Chlamydia psittaci	16

single case, *S. aureus* myocarditis was implicated as a mimic of acute myocardial infarction in a young man, although in this case, the bacteriium was isolated only from the pharynx (17). *S. aureus* infection of infarcted myocardial tissue has been described (8). Myocardial perforation due to *S. aureus* abscess has also been reported in several series (4,6,7).

While *Streptococcus pyogenes* generally affects the heart by eliciting an immunologic reaction manifested as rheumatic fever, cases of direct invasion of cardiac muscle by this organism have also been described (4,7). Group B streptococcus has been reported as a cause of primary bacterial myocarditis in two separate case reports (9,10). Viridans streptococci have been included in lists of causes of myocardial abscess in some series, but it is not clear whether this process has occurred in the absence of bacterial endocarditis (5-7). *Streptococcus pneumoniae* is another recognized cause of bacterial myocarditis, generally occurring in the setting of pneumococcal bacteremia (5,7,18). Fatal rupture of a pneumococcal abscess into the pericardium has been reported (7).

Saphir described two fatal cases of *Neisseria meningitidis* meningitis with myocarditis. Autopsy revealed an intense polymorphonuclear cell infiltrate with gram-negative diplococci in the myocardium with involvement of the bundle of His (11). Brasier et al. reported a case of clinically and electrocardiographically diagnosed myopericarditis in a patient with meningococcal meningitis and bacteremia (19). The patient recovered with antibiotic therapy, but the authors speculated that bacterial seeding of the myocardium had occurred. One additional case of meningococcal infection of the myocardium was reported in the series of Abela et al (3).

An assortment of other bacteria may cause myocardial abscesses. *Escherichia coli* was a common cause of myocardial abscess in the series of Sanson et al., generally occurring in the aftermath of an acute gastrointestinal process (usually surgery or a perforated viscus) (6). Proteus, Klebsiella, and Pseudomonas species were responsible for myocardial abscesses in the series of Abela et al (3). *Listeria monocytogenes* (12), *Bacteroides fragilis* (13), and *Clostridium perfringens* (14) have all seeded infarcted myocardial tissue in isolated cases. Myocardial abscess is a rare extraintestinal complication of salmonella infection. Cohen et al. reported two cases of salmonella myocardial abscess in patients with ventricular aneurysms (15). Finally, Jannach described a case of *Chlamydia psittaci* infection with inclusion bodies characteristic of psittacosis in plasma cells invading the myocardium (16).

5. PATHOPHYSIOLOGY

There are several distinct pathophysiologic patterns of bacterial myocarditis. In their review of the pathogenesis of myocardial abscess, Tennant and Parks (14), described three groups of patients. First, and most common, were myocardial abscesses that occurred in the setting of overwhelming sepsis, in which there were generally other organs with abscesses, but no evidence of endocarditis. The likelihood of incidental involvement of the myocardium in patients with overwhelming bacteremia was highlighted by the statement of Saphir in his classic review of myocarditis, "As a matter of fact, in every instance of pyemia abscesses may be expected in the myocardium." (4) The second group were patients with endocarditis who developed myocardial abscess by direct extension. The third group were patients who seeded their myocardium, but not any other organ, from a suppurative focus elsewhere. A subgroup of the latter category included rare patients who seeded an injured area of the heart, e.g. an infarct or a ventricular aneurysm. An additional group, not mentioned in the Tennant and Parks review, are patients with diffuse bacterial infiltration throughout the myocardium without discrete abscess formation. The gross and microscopic findings of myocardial abscess are demonstrated in Figures 1 and 2.

Most of what is known about bacterial infection of the myocardium is derived from four autopsy series. Flaxman described 29 cases among 14,160 autopsies performed between 1929 and 1942 (5). Thirteen (45%) of the cases occurred in patients less than 18 years old, and five (17%) occurred in infants. Only three (10%) patients were older than 50. Twenty-one (72%) patients had myocardial abscesses in the absence of endocarditis. All had remote foci of infection, especially osteomyelitis and cellulitis. Saphir noted 32 cases of myocardial abscess among 240 cases of myocarditis, all occurring in the presence of pyemia, but few other details were provided (4). Sanson et al. described 23 cases of myocardial abscess among 2,897 autopsies performed between 1940 and 1961 (6). Their population was older than the earlier study with only one patient (4%) younger than 18, and 13 (57%) patients older than 50. In 17 of 23 (74%) cases the myocardial abscesses developed in the absence of endocarditis. Most patients had proven bacteremia, and a recent history of surgery and/or malignant disease was common. Disseminated abscesses were noted in 21

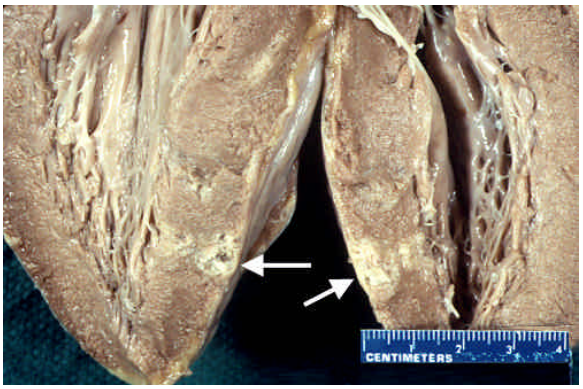

Figure 1. Myocardial abscess (arrows)

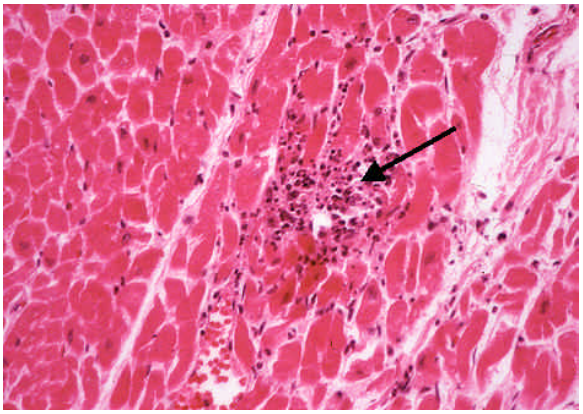

Figure 2. Acute bacterial myocarditis (arrows)

patients (91%), while the heart alone was involved in only two (9%). The most common extra-cardiac sites of abscess were, in order, kidneys, lungs, brain, liver, and adrenal glands. In the myocardium, abscesses were almost always multiple, with an average of four per slide, and the left ventricle was involved in all patients. While left ventricular involvement was most common, myocardial abscesses of all four chambers occurred. Most abscesses were minute, and were described grossly as "yellow flecks, usually surrounded by a zone of hemorrhage." Four patients (17%) had abscesses that were larger than 6mm in size. Finally, Abela et al. described 14 cases of myocardial abscess unassociated with infective endocarditis from an autopsy series of 3,084 patients between 1967 and 1977 (3). Two of these cases were fungal and not bacterial. The median age of their patients was 50. Sixty-four percent of patients had disseminated abscesses, while the heart alone was involved in 36%. The most common extra-cardiac sites of abscess were, in order, the lungs, adrenal glands, thyroid gland, and parietal pericardium. The authors observed that the routine autopsy procedure of examining only a single, randomly selected section of myocardium is inadequate, and that the true prevalence of this condition at post-mortem is underestimated.

Other more unusual presentations of bacterial myocarditis, including infection of infarcted tissue, abscess associated myocardial rupture, and diffuse myocardial infiltration by bacteria are encountered in the medical literature in the form of case reports. Bacterial abscesses may occur both in old infarcts (17) and in acutely infarcted myocardium (7,12,13). While the pathophysiologic sequence of events leading to this rare occurrence has not been established, most authors believe that it is a consequence of bacterial seeding of abnormal myocardium. Contrary to Dr. Osler's view, the bacteremia is probably not the cause of both infarct and infection in most cases, because in many cases the infarcts are old, the involved vessels often demonstrate severe atherosclerosis, and septic emboli within the coronary arteries are not generally seen. Rupture of the myocardium is a rare complication of myocardial abscess. It has been described within each of the pathophysiologic groups, although anecdotal evidence suggests that it is more common in abscesses involving infarcted tissue (14). A final, seemingly distinct presentation, is diffuse bacterial myocarditis without discrete abscess formation. This exceedingly rare pathologic type has been seen with meningococcal (11) and Group B streptococcal myocarditis (9).

6. CLINICAL PRESENTATION

The patient's clinical presentation may be dominated by the symptoms and signs of overwhelming infection or by the manifestations of cardiac involvement. Most patients are febrile and present with some elements of the sepsis syndrome. Symptoms of cardiac dysfunction may include angina, dyspnea, and orthopnea. Physical examination may reveal signs of congestive heart failure, including tachycardia, hypotension, distended neck veins, gallop rhythms, and rales on lung exam (12,13,17). Pulsus paradoxus and pericardial rub may be present in cases of myocardial rupture (19).

Routine laboratory testing may reveal leukocytosis with band forms. Blood cultures are generally positive, and biochemical markers of cardiac injury may be present. Common findings on chest roentgenogram include cardiomegaly and pulmonary edema (12,13).

Electrocardiograms demonstrate a range of abnormalities. Tachycardia is common as are non-specific ST-T wave changes which may be a consequence of direct cardiac injury, or may results from alterations in the host physiologic and metabolic state, i.e. hyperpyrexia, electrolyte abnormalities and respiratory and central nervous system disturbances which may produce hypoxia (6). Acute myocardial ischemia may be seen (17), and patients with pericardial involvement may present with electrocardiographic evidence of pericarditis (19). Arrhythmias and conduction abnormalities, the latter suggesting bacterial invasion of the conduction system, have been described (11,12).

Since the last published review of primary bacterial myocarditis a number of new tests have been developed to diagnose inflammation and damage of myocardial cells. Nuclear imaging techniques, such as gallium citrate and indium-labeled antimyosin antibody scanning may be useful for visualizing leukocytic infiltrates

and myocardial necrosis respectively. These tests have been used in the setting of viral myocarditis (21,22), but we are not aware of published reports of their use for myocardial abscess. Similarly, magnetic resonance imaging and spin echo imaging of viral myocarditis, but not, to our knowledge, primary bacterial myocarditis, have been reported (23,24).

7. TREATMENT

There have been no organized studies of treatment strategies for primary bacterial infection of the myocardium. Common sense would dictate that patients should receive intensive supportive therapy for hemodynamic instability. Aggressive antimicrobial therapy directed at the suspected or proven pathogen is in order. If a primary focus of bacteremia is identified drainage is indicated. The role of surgical removal or drainage of localized myocardial abscesses is not well defined, although the usual multifocal distribution of tiny abscesses would militate against the effectiveness and feasibility of surgical intervention in most cases.

8. SUMMARY

Primary bacterial infection of the myocardium is a devastating complication of bacteremia. It may be caused by a broad range of organisms in a wide variety of clinical settings. Clinical presentation is dominated by sepsis and cardiac dysfunction. Since almost all information on bacterial myocarditis originates from autopsy studies largely conducted in the pre-antibiotic era, little is known about the role of modern diagnostic and treatment modalities in the management this disorder.

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