ANNALS OF CLINICAL AND LABORATORY SCIENCE, Vol. 23, No. 3
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Haemophilus parainfluenzae Endocarditis in a Patient with Mitral Valve Prolapse*

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ABSTRACT

Haemophilus parainfluenzae is a frequent cause of “culture-negative” endocarditis (i.e., endocarditis owing to a fastidious organism which may require longer incubation periods and/or enrichment media for detection compared to traditional pathogens). More cases will probably be identified with improvements in growth and isolation techniques. A case of H. parainfluenzae endocarditis is presented in a patient with mitral valve prolapse, which illustrates the difficulty in diagnosing endocarditis when initial blood cultures are negative. Particularly, it emphasizes the difficulty in selecting appropriate antibiotic therapy since beta-lactamase producing organisms are being isolated with increased frequency. This report is unique in that it documents successful treatment with a cephalosporin and what is, to our knowledge, the third reported case of a beta-lactamase producing H. parainfluenzae causing endocarditis. The authors believe that beta-lactamase stable second or third generation cephalosporins should constitute initial treatment of H. parainfluenzae endocarditis until sensitivity studies become available, since beta-lactamase production by this organism would nullify the effect of the previous agent of choice, ampicillin.

Introduction

Endocarditis caused by Haemophilus parainfluenzae is an uncommon entity,2,6,12,14 representing 0.5 to 1 percent of all cases of endocarditis.10 The organism is a non-motile, non spore-forming, pleomorphic, gram-negative coccobacillus. It is a normal inhabitant of the nasopharynx and oropharynx, isolated in 5 to 25 percent of cultures from normal subjects.7 This fastidious organism requires coenzyme 1 (NAD or V factor) for growth, and its isolation in blood cultures may take up to 18 days.6 Subculture onto chocolate agar and incubation with CO₂ enrichment, however, can accomplish isolation in 18 to 24 hours. In fact, blood cultures might not be recog-
nized as positive until there is subculture to suitable agar, either chocolate agar or Fildes peptic digest of blood agar. Some behaviours of this particular microbe which may contribute to a decrease in isolation rates include adherence to glass at the glass-fluid interface in broth culture bottles with the formation of "puff balls," and affinity for erythrocytes with which it settles to the bottom of broth bottles. The advent of effective antibiotic therapy has decreased mortality from this entity from 100 percent prior to 1940, to 12 percent at present. The first reported cure was in a 46-year-old woman who was treated with penicillin and sulfadiazine by Hunter and Dwane. During the subsequent 40 years, penicillin G and streptomycin or a sulfa agent were most often used. Ampicillin and streptomycin became the drugs of choice during the last 10 years until Calio et al reported success in treatment with a long-acting cephalosporin. These authors also reported the second case of beta-lactamase production by *H. parainfluenzae* which rendered the organism resistant to ampicillin. It is hereby reported what is, to our knowledge, the third case of beta-lactamase production by an *H. parainfluenzae* organism involved in endocarditis and the second case of *H. parainfluenzae* endocarditis which was successfully treated with a cephalosporin.

**Case Report**

A 36-year old school teacher had mitral valve prolapse diagnosed during a routine physical examination 13 years prior to admission and subsequently confirmed by echocardiogram. She remained asymptomatic and was not on any therapy except for endocarditis prophylaxis during surgical or dental procedures. During the next 13 years, her only complaint was that of anxiety and some morning nausea prior to the beginning of a new school teaching position. About one month later, the patient developed a severe febrile illness with chills, headache, and backache. This occurred two days after her son experienced a similar illness, during which she spent two nights caring for the child. She was placed on oral penicillin without response and was then hospitalized for intravenous ampicillin administration. Once the patient defervesced, she was discharged on oral cefaclor, which was subsequently changed to amoxicillin/clavulanate owing to a recurrence of fevers. Blood cultures subsequently became positive for *H. parainfluenzae* in three out of three sets, and she was readmitted to the hospital for intravenous antibiotics. Pertinent physical findings during hospitalization included a regular heart beat with a systolic click but without murmurs, and a single splinter hemorrhage under the left third fingernail, in an otherwise well-nourished, white lady. Remarkable laboratory findings during hospitalization included a white blood cell count of 2.9 with 60 percent polymorphonuclear leucocytes, 2 percent bands, 26 percent lymphocytes and 8 percent eosinophils. Hemoglobin was 12.2 grams and the erythrocyte sedimentation rate was 28. Chest X ray and urinalysis were normal. Echocardiogram revealed a redundant mitral valve with marked prolapse of anterior and posterior leaflets, but without vegetations. The *H. parainfluenzae* was beta-lactamase positive and sensitive to erythromycin, tetracycline, aztreonam, ampicillin/sulbactam, gentamicin, and imipenem. It was resistant to penicillin, ampicillin, and clindamycin. The patient was treated with I.V. cefamandole for six weeks. She remained asymptomatic afterwards, with no evidence of recurrence.

**Discussion**

The fastidious growth requirements of *H. parainfluenzae* have made it a frequent cause of "culture negative" endocarditis, accounting for 7 to 28 percent of such cases. The infection is usually insidious in nature and is superimposed on pre-existing cardiac lesions associated with rheumatic or congenital heart disease, prosthetic valves, or mitral valve prolapse. Average age of onset is the 20 to 40 year-old age group with a 2:1 female to male ratio. This differs from the 2:1 male to female ratio reported in cases of subacute bacterial endocarditis. Frequent findings include: duration of symptoms in two-thirds of cases of less
than two months before diagnosis is made, febrile illness, anemia and hematuria, and petechiae occurring in 50 percent of the cases.\textsuperscript{11} Roth spots, Osler nodes and Janeway lesions are uncommon findings.

Similar to fungal endocarditis, large vegetations may be produced which may lead to major occlusive disease, as noted in 29 to 85 percent of patients.\textsuperscript{1} As reported by Chunn et al, microscopy demonstrated \textit{H. parainfluenzae} growing in long mat-like chains which resembled the long branching hyphae and/or pseudohyphae seen with \textit{Candida} or \textit{Aspergillus}.\textsuperscript{3} Cerebrovascular emboli account for approximately 57 to 66 percent of embolic events in these patients, in whom it is the leading cause of mortality.\textsuperscript{11,13} This contrasts with the reported 6 to 25 percent risk of peripheral embolization in cases of subacute bacterial endocarditis caused by more frequently isolated organisms such as the viridans streptococci.\textsuperscript{13} Another complication is congestive heart failure secondary to damaged heart valves, where early surgical intervention may decrease mortality from 80 percent to 35 percent.\textsuperscript{10}

This case constitutes the second report of successful treatment of \textit{H. parainfluenzae} endocarditis with a cephalosporin, and the third report of a beta-lactamase positive, ampicillin-resistant, \textit{H. parainfluenzae}. Several aspects about this patient’s presentation were similar to other reports of \textit{H. parainfluenzae} endocarditis: (1) insidious onset of disease, with symptoms first developing more than a month following a routine dental procedure; (2) difficulty in isolating the offending organism, which required from five to seven days before growth became detectable; and (3) the presence of mitral valve prolapse in this patient. In one series of patients with endocarditis, 11 percent of cases had mitral valve prolapse.\textsuperscript{4} That the patient’s illness coincided with a similar illness in her child was probably incidental given the speed of onset of her symptoms, which occurred within one to two days of exposure to the sick child.

This patient’s presentation differed significantly from prior reports in the absence of valvular vegetations and absence of embolization, with its potential for high morbidity and mortality. As a member of the “HACEK” (\textit{Haemophilus sp.}, \textit{Actinobacillus actinomycetemcomitans}, \textit{Cardiobacterium hominis}, \textit{Eikenella corrodens}, and \textit{Kingella kingae}) group of etiological agents, which frequently cause “culture-negative” endocarditis, \textit{H. parainfluenzae} can be difficult to diagnose and may cause significant morbidity and possibly mortality if not recognized promptly.

In the past, ampicillin plus gentamicin was the treatment of choice for endocarditis caused by the “HACEK” group. However, beta-lactamase producing organisms in this group are occurring more frequently, prompting a change in treatment strategy which would include a beta-lactamase stable cephalosporin in place of ampicillin.

References


