CASE REPORT

Peripheral Artery Embolism as a Complication of Infective Endocarditis in Mitral Insufficiency

by

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Abstract

Infective endocarditis in a 10 years old boy complicated by left brachial artery emboly in a case of rheumatic mitral insufficiency has been reported. The etiologic micro-organism was coagulase positive Staphylococci. Though clinical cure was achieved by a 4 weeks long high dose of antibiotic (Ceftriaxone), peripheral artery emboly, had complicated the disease. Since adequate collateral circulation has already occurred, no specific treatment has been given. A further follow-up and infective endocarditis prophylaxis are still needed.

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Introduction

Infective endocarditis is an inflammatory process resulting from infection of the endocardial surface of the heart [1,2,3]. Although the heart valves are most commonly affected, the disease may also occur on septal defects or on the mural endocardium [2,3]. The clinical manifestations of infective endocarditis differ greatly [1]. Four processes contribute to the clinical picture [3] : 1. the infectious process on the valve including the local intracardiac complications; 2. bland or septic embolization to virtually any organ; 3. constant bacteremia, often with metastatic foci of infection; and 4. circulating immune complexes and other immunopathologic factors.

Peripheral embolization is one of the common findings in infective endocarditis involving the left heart and specific clinical findings depend upon the localization of the emboli [1]. Prior to the 1950's, rheumatic heart disease was the major underlying condition, but at present, the majority of children with infective endocarditis have complex congenital heart defect [2,4]. However, in Indonesia like in other developing countries, rheumatic heart disease is still an important underlying condition until now. Streptococci (espicially viridans) are the most common etiologic agents, while the staphylococci (aureus and epidermidis) are usually the second largest group [1,2,4,5]. In the preantibiotic era, infective endocarditis was a uniformly fatal disease. At the present time, the mortality rate is between 20-30% due to improved methods of diagnosis and appropriate antibiotic therapy [2,4,5]. There is a general agreement that parenteral administration of high doses antibiotic with specific activity against the causative organism should be given for the treatment of infective endocarditis [1,2,3,4]. In some cases, surgery has become a valuable adjunct to medical therapy [2]. The purpose of this paper is to report a case of left brachial artery emboly caused by infective endocarditis is a child who suffered from rheumatic heart disease.

Case Report

T.R., a 10 year-old Indonesian boy was referred from Gresik General Hospital to the Department of Child Health of Dr. Soetomo Hospital on March 31, 1992 with the diagnosis of suspected septicemia.

The patient suffered from high fever, sore throat and joint pain at the left elbow and wrist and the right knee since 4 days before being admitted to the Gresik Hospital. One day before admission he experienced epistaxis and gum bleeding. Palpitation, chest pain, cyanosis and dyspnea on exertion were denied, but since 8 year of age, he had occasionally experienced joint pain when he suffered from fever. He was treated with Ampicillin and Gentamycin. As there was no improvement, after 18 days of hospitalization, the patient was referred to the Department of Child Health of Dr. Soetomo Hospital. Physical examination on admission at Dr. Soetomo Hospital revealed an apathetic boy with a body weight of 23 kg, the blood pressure was 110/70 mmHg, the pulse rate 108/minute, the respiration rate 32/minute and the body temperature 37.6^{O}C. He appeared pale but there was no jaundice, cyanosis or dyspnea. The lungs were normal. The examination of the heart revealed a quiet precordium. On percussion, the heart was slightly enlarged. The first and second heart sounds were normal. There was a grade III/VI pansystolic murmur with maximal intensity at the apex transmitted to the axilla. The liver and the spleen were not palpable. There were painful swellings of the left elbow and wrist and the right knee causing limitation of motion. Tender subcutaneous erythematous papules on the distal phalanx of the left thumb and second toe of the right foor were found. Laboratory examinations showed the following : Hb 9.9 g/dl, RBC 3,220,000/cmm, WBC 11,800/cmm with 80% PMN cells, 19% Lymphocytes and 1% Monocytes. Platelets were sufficient in number, ESR was 118/hour. The peripheral blood film showed anisocytosis and hypochromia. Urinalysis was normal. The liver and renal function tests were within normal limits. The ASO titer was 64 Todd Units, the C - reactive protein was positive qualitatively. The chect X-Ray showed an enlarged heart (CTR about 58%), and the apex pointed down wards suggesting left ventricle enlargement. The lungs were normal. The ECG examination showed sinus rhythm with a heart rate of 136/minute, the frontal axis was about 45^{O}, the PR interval was 0.12 sec and there was a borderline left ventricle hypertrophy pattern. The echocardiographic examination showed that the mitral valve was slightly thickened and there was vegetation on the atrial surface of the mitral valve (Fig. 1a + 1b). The left ventricle dimension was slightly enlarged and mitral regurgitation pattern was shown on Doppler.

These findings confirmed the diagnosis of infective endocarditis associated with rheumatic mitral insufficiency. The patient was then treated with ampicillin 4 x 1 g/day and cloxacillin 4 x 500 mg/day I.V., gentamycin 2 x 60 mg/day I.V., acetyl salicylic acid 3 x 500 mg/day orally. Liquid food with high calorie and high protein was given and total bedrest instituted. The blood culture drawn at day 2 of hospitalization yielded negative result. As the patient still had intermittent fever, repeated blood cultures for 3 consecutive days were done. Because of disuse atrophy of the extremities, the Department of Medical Rehabilitation was consulted, and the patient was planned for passive ROM (range of motion) with strengthening and stretching exercises. After more than 2 weeks treatment with parenteral. ampicillin, cloxacillin and gentamycin showing no satisfactory improvement, the antibiotics were changed to ceftriaxone 2 x 1 g/day intravenously on day 18. Five days after ceftriaxone was given, the patient's condition improved significantly, the fever subsided and the painful limitation of motion of the left elbow and wrist were minimal. The body temperature was 36.4^{O}C. Repeated echocardiographic examination on day 30 showed that the vegetation on the atrial surface of the mitral valve has disappeared. The blood culture yielded coagulase positive staphylococci, susceptible to the antibiotic that was given, so ceftriaxone was continued for 28 days. After 37 days of hospitalization the patient's condition was good, but the left upper extremity was clammy compared to the right upper and the lower extremities. Further examination showed that the left upper extremity was pulseless, and the blood pressure was O, while the other extremities had normal pulses and blood pressure. Obstruction of the left subclavian artery or brachial artery caused by peripheral embolism was suspected. Repeated routine blood examination showed Hb 11.3 g/dl, WBC 6,600/ul with 4% eosinophils, 29% neutrophils and 67% lymphocytes. Platelets were sufficient in number and ESR was 72/hour. Urinalysis was normal. The liver and renal function tests were within normal limits. The hemostatic function test was also normal. Ceftriaxone and acetyl salicylic acid were discontinued. Benzathine penicillin G 1,2 million units was given once a month for secondary prophylaxis. Thoracic aortography was performed in May 22, 1992 which showed an obstruction of the left brachial artery (Fig. 2a). On selective arteriography, there was an obstruction along the left brachial artery, with adequate collateral system (Fig. 2b). Based on these findings, the dignosis of total obstruction of the left brachial artery caused by peripheral embolism of vegetation was established. No specific treatment was given the strengthening and stretching exercises were continued. The patient was discharged in a good condition after 65 days of hospitalization,

although the left arm was still pulseless and the muscle strength was slightly decreased. The last routine blood examination showed that Hb 10.5 g/dl, WBC : 5,600/ul with 2% eosinophils, 52% neutrophils, 37% lymphocytes and 9% Monocytes, the ESR 47/hour.

The echocardiography examination revealed that the vegetation had disappeared, the left ventricle function was normal but there was still mild mitral regurgitation. The ECG examination was normal. The patient was asked to come regularly for follow up in the Pediatric Cardiology Section and the Department of Medical Rehabilitation.

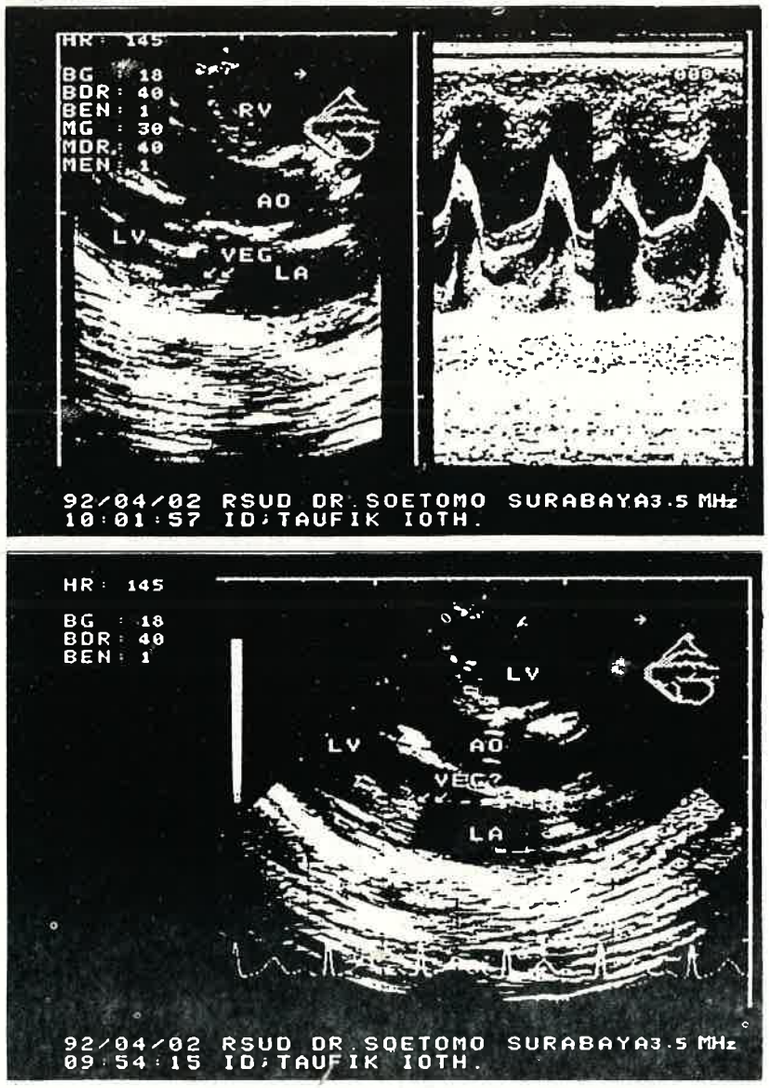

Figure 1a + 1b. *The echocardiographic examination showed that the mitral valve was slightly thickened and there was vegetation on the atrial surface of the mitral valve.*

Fig. 2a. *Thoracic aortography showed an obstruction of the left brachial artery*

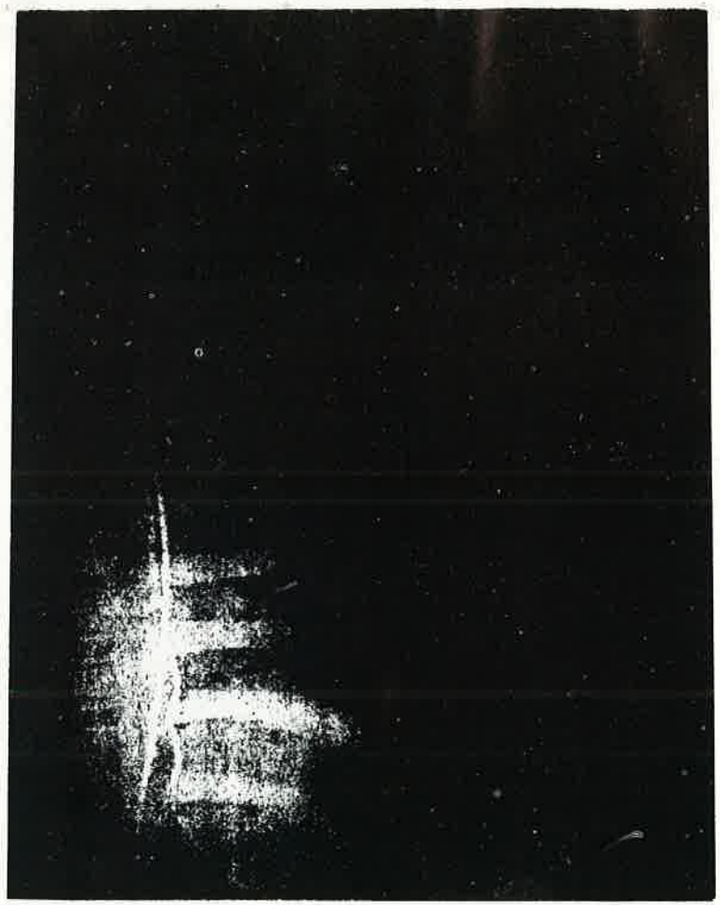

Fig. 2b. *On selective arteriography, there was an obstruction along the left brachial artery, with adequate collateral system*

Table I. *Most frequent clinical and laboratory findings associated with endocarditis*

Clinical findings	
Fever	++++*
Heart murmur (new or changing)	++++
Non specific symptoms (myalgia arthralgia, headache, malaise etc.) Heart failure	+++/++++
	++/+++
Petechiae	+++
Embolic phenomena	++/+++
Splenomegaly	++/+++
Osler nodes, Janeway lesion	+/++
Laboratory findings	
Positive blood culture (off antibiotics)	++++
Positive active phase reactans	++++
Anemia	+++
Hematuria	+++
Presence of rheumatoid factor	++
Leukocytosis	++

* ++++ Very common; +++ in a majority of instances; ++ infrequent; + rare.

Discussion

Infective endocarditis is one of the most feared complication of structural heart diseases [1,6]. It is still a significant cause of morbidity and mortality among children and adolescents, despite advances in the management of the disease with antimicrobial agents and the widespread advocacy of prohylactic measures [7]. The development of infective endocarditis most likely requires the occurence of two preexisting conditions. The first is the presence of the infective agent in the blood stream, the second is the presence of an acquired or congenital lesion in the heart or great vessels [1,3,8]. The valve surface must first be altered to produce a suitable site for bacterial attachment and colonization. These alterations result in the deposition of platelets and fibrin and in the formation of so called non bacterial thrombotic endocarditis (NBTE). Bacteria must then reach this site and adhere to the NBTE to produce colonization. After colonization, the surface is rapidly covered with a protective sheath of fibrin and platelets to produce an environment conductive to bacterial multiplication and vegetation growth [3]. The underlying heart disease in our case was mitral insufficiency. The diagnosis was based on the presence of a pansystolic murmur with maximal intensity at the apex, a left ventricular hypertrophy pattern on ECG examination, an enlargement of the left ventricle on chest X-Ray and confirmed by the mitral regurgitation pattern detected by Doppler Echocardiography which is characteristic for mitral insufficiency [1,5,9,10]. Mitral insufficiency is the commonest lesion found in children and adolescents with rheumatic heart disease in developing countries where rheumatic fever and its reccurences are common [1,9,10], while congenital mitral insufficiency is an extremely rare isolated defect [1]. So it was likely that mitral insufficiency in our case was a rheumatic heart disease, although the history of rheumatic fever was denied except for the experience of joint pain

since the age of 8 years when the patient suffered from fever. The signs and symptoms of infective endocarditis are frequently non specitic and may simulate a wide variety of diseases [1,2,3,4,6]. Fever is the most common symptom of infective endocarditis. It is usually low grade and has no specific pattern [1,2,3,4] and may often be the only medical history which can be elicited [7]. Except for positive blood culture, other laboratory tests are not specific for confirming a diagnosis of endocarditis [1]. The common clinical and laboratory findings associated with infective endocarditis are listed in Table I [1].

In our case, infective endocarditis was suspected because of unexplained fever for more than 2 weeks with an underlying structural heart disease eg. mitral insufficiency. Besides that, the presence of tender subcutaneous erythematous papules on the distal phalanx which resemble Osler node, the elevation of ESR and positive C-reactive protein supported the diagnosis, and the result of echocardiographic examination confirmed the it.

Echocardiography has become a valuable adjunct to the diagnosis of endocarditis in children [1,2,6,7,11]. The sensitivity and specificity of this technique are still being defined with positive results in 36-100% of children in various series of pediatric patients [2] and echocardiography can be of value in helping to establish the diagnosis of endocarditis in culture negative cases [2,11]. However, absence of vegetations does not exclude endocarditis [1,2,6]. The most important diagnostic procedure is the blood culture [1,2,3,6,7]. It is recommended to obtain 3 separate blood culture sets in the first 24 hours [3,6,7]. More cultures may be necessary if the patient has received antibiotics in the preceeding 2 weeks [3]. In our case, the blood culture which was taken once at the second day of hospitalization was negative on day 14, but the repeated blood cultures for 3 consecutive days on day 15, 16 and 17 yielded coagulase positive Staphylococci. It is possible that coagulase positive Staphylococci was the etiologic agent, because the in vitro sensitivity test showed that this microorganism was resistant to Ampicillin and Gentamycin but sensitive to Cephalosporin, so when the therapy was changed to Ceftriaxone, the patient's condition improved. Besides that, the bacteremia in infective endocarditis is usually low grade and continuous [2,3,4,12], so the bacteremia could persist in our case, because the microorganism was resistant to the previous antibiotics that had been given for about 4 weeks. The most common organism as the etiology of infective endocarditis are streptococci and staphylococci [1,2,3,5]. They account for 90% of the cases in which the organism was isolated [2]. The frequency in which staphylococci have been isolated from patients with infective endocarditis are 20-30% [2,3,7] and 80-90% of these due to coagulase positive Staphylococci like Staphylococcus aureus, which is the etiologic agent in most cases of acute endocarditis [2,3,12]. Several general principles provide the framework for the current recommendation for the treatment of endocarditis, [2] such as (1) parenteral administration is preferred because the erractic absorption of oral antibiotics can lead to therapeutic failure; (2) prolonged treatment, usually 4 to 6 weeks or longer, is necessary to sterilize the vegetations and prevent relapse; (3) bacteriostatic antibiotics are not effective, leading to frequent relapses and/or failure to eradicate the infection. The choice of antibiotic should be based on the sensitivity of the organism cultured from the blood [1,2,3,5]. But if the results of the initial examination are strongly indicative of the diagnosis and the child is very ill, treatment should be started as soon as the blood cultures are drawn [2,5,12]. Initial empirical therapy depends upon the clinical setting in which a tentative diagnosis is made. If the presentation is subacute, a combination of penicillin G and aminoglycoside is usually recommended. If Staphylococcus aureus endocarditis is a strong consideration, a penicillinase resistant penicillin should be added to the regimen [2]. In some cases, surgery has become a valuable adjunct to medical therapy in the management of infective endocarditis [2]. The generally accepted indications for surgical intervention during active endocarditis are as follows [1,2,3,12]. (1) refractory congestive heart failure; (2) uncontrolled infection; (3) more than one serious embolic episode; (4) fungal endocarditis; (5) most cases of prosthetic valve endocarditis; (6) local suppurative complications including perivalvular or myocardial abcess with conduction system abnormalities.

Initially, our patient had been treated by the physician at Gresik Hospital with ampicillin and gentamycin for 2 weeks.

When the patient was referred to our department, the same regimen was continued with cloxacillin was added. This treatment was given on the assumption that staphylococci or streptococci as the presumptive etiologic agents are penicilin resistant although the first blood culture was negative. As the fever did not subside and a repeated routine blood examination showed features of systemic infection, the therapy was changed to ceftriaxone. This antibiotic is considered as more potent that would also cover streptococci and staphylococci infections. On this treatment, the patient's condition improved and a repeat blood culture yielded coagulase positive staphylococci sensitive to ceftriaxone. An important characteristic of infective endocarditis is its tendency for embolization [2,13]. In our case, left brachial artery emboli occurred during the course of the infective endocarditis. It has been stated that in leftsided infective endocarditis, the potential embolic effects are more disseminated since any organ or tissue supplied by the systemic arterial circulation may be affected, but most commonly affect the brain, kidney, spleen and skin [2]. In some cases, embolization to the major vessels may occur [13,14].

According to Thompson et al (as quoted from 14), about 6% of the peripheral artery emboli cases occur in the axillary and brachial arteries. Generally, the clinical manifestation of sudden peripheral artery occlusion may include any or all of the 5 Ps - pain, pallor, paresthesia, pulselessness and paralysis - in varying degrees [15]. In 25% of cases, pain is entirely absent and the only symptom may be numbness and coldness [14], and if the collateral circulation is adequate, the emboli may be silent [13]. The most important physical sign is the absence of pulsation in arteries that were known to have had palpable pulses [14]. No significant symptoms were observed in our case except that the affected areas were cold to the thouch and on physical examination, the left upper extremity was pulseless. Arteriography is the only diagnostic procedure that can demonstrate the location of occlusive arterial disease and its extent and the character of the arterial circulation proximally and distally [15]. In our case, on selective arteriography we know that there was an obstruction along the left brachial artery with an adequate collateral system. Regardless of the etiology of occlusive peripheral arterial disease, conservative measures are a basic part of proper management [15].

In infective endocarditis, it consists of eradication of the source of emboli and in increasing the collateral circulation of the affected area [13]. The use of thrombolytic agents such as heparin, streptokinase may be useful in selected cases, but the usual side effects and complications of the thrombolytics are limiting factors [14, 15]. Surgical therapy such as embolectomy may be indicated in specific instances [13, 14]. In our case, no specific treatment was given and physiotherapy was continued to maintain adequate collateral circulation.

REFERENCES

01. Kaplan EL and Shulman ST. Endocarditis. In : Adams FH and Emmanoullides GC, eds. Moss Heart Disease in Infants. Children, and Adolescents 3rd Ed. Baltimore, Williams & Wilkins Co.1983; 565 - 76.
02. Strake JR. Infective Endocarditis. In ; Feigin RD and Cherry JD, eds. Textbook of Pediatric Infectious Diseases 2nd Ed.Philadelphia,WB Saunders Co, 1987; 359 - 76.
03. Scheld WM and Sande MA. Endocarditis and Intravascular Infection. In ; Mandell GL, Douglas RG JR and Bennett JE, eds. Principle and Practice of Infectious Disease.2nd Ed. New York, Churchill Livingstone, 1985; 504 - 30.
04. Friedman RA and Starke JR. Infective Endocarditis. In Oski FA, ed.Principle and Practice of Pediatrics, Philadelphia, JB Lippincott Co, 1991; 1475 - 85.
05. Jordan SC and Scott D. Heart Disease in Pediatrics 3rd Ed. London, Butterworth & Co,1989; 265 - 71.
06. Yip WCL. Infective Endocarditis. In Yip WCL and Tay JSH, eds. A practical manual of Acute Paediatrics. Singapore. p.g. Publishing Pte Ltd, 1989; 134 - 53.
07. Gersony WM and Hordof AJ. Infective Endocarditis and Disease of the Pericardium. Pediatr.Clin.N.Am. 1978; 25: 831 - 46.
08. Blumenthal S, Griffiths SP and Morgan BC. Bacterial Endocarditis in Children with Heart Disease. A review based on the Literature and Experience with 58 cases. Pediatrics, 1960; 26 : 993 - 1017.
09. Kaplan S. Rheumatic Endocarditis. In : Vaughan VC, Mc Kay RJ and Behrman RE eds. Nelson Text Book of Pediatrics, 11th Ed, Tokyo, Igaku shoin Ltd, 1979; 1337 - 41.
10. El Said GM. Rheumatic Heart Disease. In : Oski FA ed. Principle and Practice of Pediatric. Philadelphia, J.B. Lippinchott Co, 1991; 1491 - 98.
11. O' Brien JT and Geiser EA. Infective endocarditis and echocardiography. Am. Heart J. 1984; 108 : 386 - 94.
12. Cleary TG and Kohl S. Anti Infective therapy of Infec-tious Endocarditis. Pediatr. Clin.N.Am 1983; 30: 349 - 64.
13. Kaplan S. Diseases of the blood vessels. In : Vaughan VC, Mc Kay RJ and Behrman RE eds. Nelson Textbook of Pedi-atrics, 11th ed, Tokyo, Igaku Shoin ltd 1979; 1351 - 3.
14. Young JR. Diseases of the peripheral arteries. In : Hurst WJ ed. The Heart 6th ed, New York, Mc Graw Hill Book Co 1986; 1339 - 54.
15. Spittell JA JR and Spittell PC. Diseases of the Aorta and Peripheral Arteries. In : Chatterjee K, Cheitlen MD et al eds. Cardiology, an illustrated text/reference, Volume 2, Philadelphia, Lippincott Co, 1991; 1227 - 45.