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Fatal Staphylococcal Endocarditis Complicated with Systemic Septic Emboli

– Report of an Autopsy Case With Review of Literature –

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전신성 혈전증이 합병된 포도구균 심내막염의 부검 1예

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포도구균은 용연균 다음으로 흔하게 심내막염을 일으키는 원인균으로 자연판막 심내막염 원인미생물의 15~26%를 차지하고 있다. 심내막염은 여러 종류의 내과적 치료와 외과적 치료에도 불구하고, 치명률이 20%를 상회하는 실정이다. 우리나라에서도 외국에 못지않게 포도구균 심내막염이 자주 연구 보고되었지만, 부검예는 많지 않다. 저자들은 최근 포도구균 심내막염에 다발성 전신적 혈전증이 합병된 부검 1예를 경험하여 문헌고찰과 함께 보고하는 바이다.

INTRODUCTION

Infective endocarditis is a relatively uncommon infectious disease which produces vegetations on the endocardium, and is always fatal if untreated. The clinical features of endocarditis are from the vegetations and an immune reaction to the infection[1~4]. Between 60 to 80% of patients have an identifiable predisposing heart disease[5].

Arterial embolization is diagnosed in up to two thirds of patients with acute endocarditis. In order of frequency arteries supplying the brain, lung, myocardium, spleen, and extremities are involved[4].

Neurologic manifestation was detected in 29% in Mayo study and in 60% of those with neurologic involvement it was either chief complaint or one of the major presenting symptoms[6,7]. Neurologic manifestations can be caused by thrombosis, embolization, intracerebral hemorrhage. And the mortality of endocarditis with cerebrovascular manifestations was approximately 60%.

There are not a few reports on staphylococcal endocarditis in Korea[1~3], however, pathologic finding including autopsy has not been precisely depicted, herein clinical manifestation and postmortem

findings are described.

CASE REPORT

A 34-year-old tall Korean female was admitted because of abruptly developed fever, weakness of both lower extremities for 4 days.

She had a past history of arthritis on both knee joints for several years, and was managed frequently with acupuncture and Korean herb medicine. Thereafter she had been relatively well until 4 days before admission. At the time of admission, she complained of fever, generalized ache, and weakness of both lower extremities, hematuria and watery diarrhea.

On physical examination the patient appeared emaciated, acutely ill-looking, and dull. The blood pressure was 100/60 mmHg, heart rate was 72/min, respiration rate was 22/min, and body temperature fluctuated up to 39.2°C. Subconjunctival hemorrhage was noticed and erythematous papules were seen on both palms, soles, left wrist and right knee joint. Fine crackles with coarse breath sounds were heard in right lower lung. The heart was normal except regularly rapid heart beats. The abdomen was tense and diffusely painful on palpation; no palpable organs. The decreased bowel sounds were with a tenderness on bilateral costovertebral areas. Right and left knee joints were swollen and painful on palpation.

Neurologic examination revealed motor weakness of both upper and lower extremities. The deep tendon reflexes were + in the biceps, triceps, knee and ankle jerks bilaterally.

The hemoglobin level was 12.8 mg/dl, the hematocrit was 39.2%, the white-cell count was 11,800 with 60% neutrophils, 32% band forms, 5% lymphocytes, 3% monocytes. The platelet count was 20,000, and the erythrocyte sedimentation rate 48 mm/hr. The urine gave a $^{+++}$ test for protein, the sediment contained 25 to 35 red cells and 10 to 15 white cells per cubic millimeter. The urea nitrogen was 16 mg per 100 ml, the creatinine 1.1 mg per 100 ml, the protein 4.6 gm per 100 ml, the albumin 2.3 gm per 100 ml, the total bilirubin 1.4 mg per 100 ml, the conjugated bilirubin 0.8 mg per 100 ml. A test for fibrin-split products was positive in a titer of 1:20, and fibrinogen 563 mg per 100 ml.

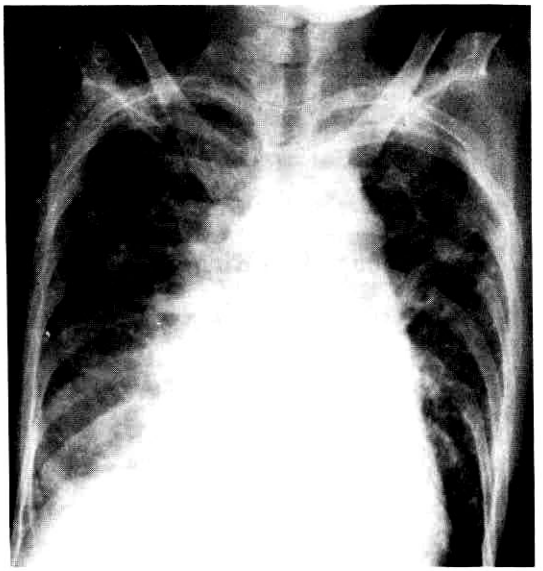

Fig. 1. Chest roentgenogram disclosed an increased patch, parenchymal infiltration in left upper lung.

The sodium was 132 mEq, the potassium 2.7 mEq, the chloride 107 mEq. The serum aspartate aminotransferase (ASAT, SGOT) 30 U, the serum alanine aminotransferase (ALAT, SGPT) 42 U. A lumber puncture yielded clear colorless cerebrospinal fluid under an initial pressure of 190 mm of water, the CSF contained 14 red cells and 2 white cells per cubic millimeter, the protein 60 mg per 100 ml. The CSF culture did not yield any microorganism. The electrocardiography revealed the incomplete right boundle branch block. Echocardiography showed moderate mitral regurgitation.

She was treated with penicillin and tobramycin under the diagnosis of infective endocarditis with Marfan syndrome. On the third hospital day, her clinical signs progressively worsened and grade 2

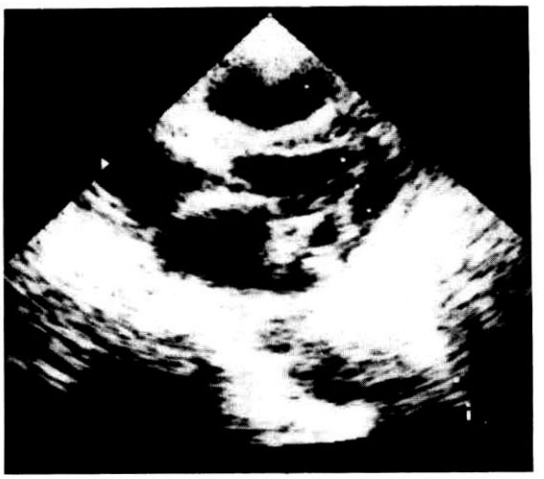

Fig. 2. The two dimensional echocardiography revealed a large mitral valve vegetation with mitral regurgitation.

early systolic murmur was audible on the left lower sternal border. An X-ray film of the chest disclosed a parenchymal abnormality predominantly in left upper lung (Fig. 1).

On the 7th hospital day examination of the heart revealed a grade 3 systolic murmur at the apex and the left sternal border. The echocardiography disclosed large mitral valve vegetation (Fig. 2) with mitral regurgitation. Blood culture yielded methicillin resistant Staphylococcus aureus and she was managed with vancomycin and amikacin but her condition deteriorated. And the patient did not respond to treatment and expired on the fifteenth hospital day.

AUTOPSY FINDINGS

1. General Apperance

She was tall and slender. Her height was 186 cm. Extremities looked relatively long with spider-like fingers, measuring 11.5 cm in the longest one. Hairs were black and the skin showed small brownish papules on both soles and palms. There was no palpable mass in the abdomen.

2. Internal Organs

The heart weighed 280 gm and the wall of left ventricle measured 2.2 cm in thickness. There was no evidence of myocardial infarction. In the mitral valve we found multiple variable sized soft friable vegetations on the surface of leaflets at the downward margin of jet stream (Fig. 3).

The largest one was bulky, measuring 2.2×1.6×1.2 cm and its underlying cardiac wall showed erosion. Posterior surface of the valve leaflet was free of vegetation. Other valves were grossly unremarkable. Right and left lungs weighed 750 gm and 650 gm respectively. They were edematous and congested. A small grayish white tubercle, measuring 0.1 cm, was identified in the left upper lobe. A few atheromatous plaques were found on the abdominal aorta.

The liver weighed 1,780 gm. Its outer surface was smooth and congested and its edge was sharp. The external surface showed alternating whitish infarcted and congested areas resulting in nutmeg-like appearance. The gallbladder and gastrointestinal tracts were grossly unremarkable. The spleen weighed 300 gm and revealed marked congestion. Right and left kindneys weighed 300 gm and 250 gm and their outer surfaces were grayish discolorated and coarsely granular. The right ureter was doubled (Fig. 4A). The cortex revealed a few foci of small infarction in cut section. Corticomedullary junction and some pyramidal structures were blunted (Fig. 4B).

3. Brain

The brain weighed 1,250 gm. The meninges was moderately turbid (Fig. 5C). Multiple serial coronal sections revealed a few foci of embolism in white matter of the temporal and parietal lobes (Fig. 5A) and cerebellar hemisphere (Fig. 5B), measuring 0.3 cm in dimension. Ventricular system was not dilated. Two golden yellowish nodules, measuring 0.4 cm in size, were found in the choroid plexus of the lateral

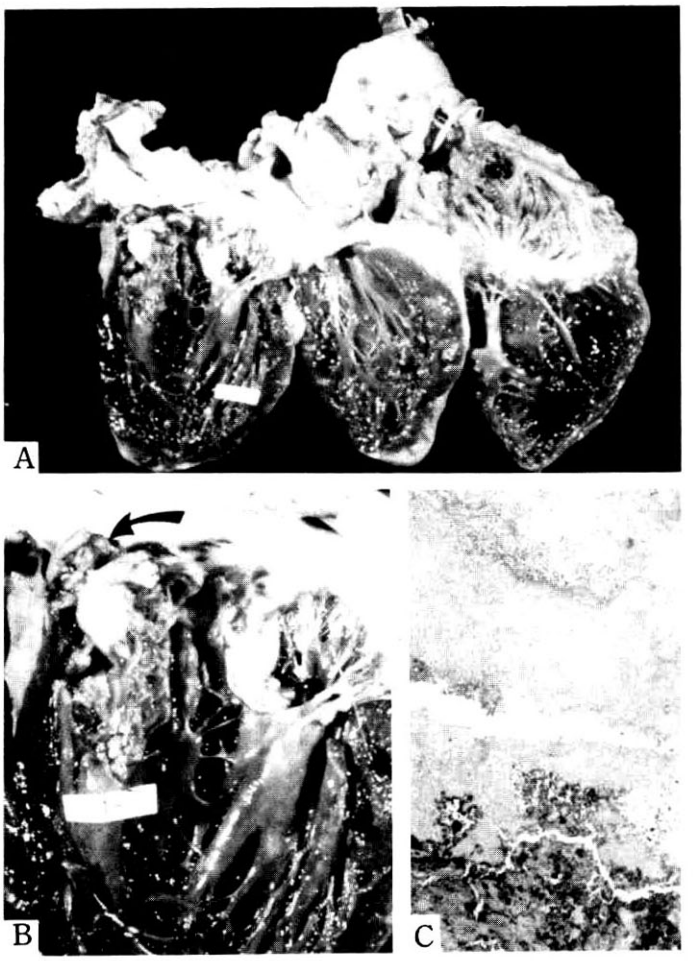

Fig. 3. Multiple variable sized friable vegetations are noted on the leaflets of mitral valve(A). Close-up view shows a bulky vegetation, 2.2×1.6×1.2 cm in size, (arrow) on the downward margin of jet stream(B). Vegetation consists of fibrin, platelets, neutrophils, and bacterial colonies (C:H-E, ×100).

ventricle.

4. Microscopic Findings

Secctions of the heart revealed bulky bacteria -laden vegetation on the endocardial site of mitral valves, which eroded into the underlying myocardium. Endomyocardium was necrotic and ulcerated by marked suppurative inflammation. Vegetation consisted of fibrin, platelets, bacterial colonies and acute inflammatory cells (Fig. 3C). Lungs showed diffuse edema and congestion.

There was a focus of old tubercle in the apex of the left upper lobe. Sections of the liver showed generalized zonal necrosis of aciner zone III and sinusoidal congestion. Kidneys showed interstitial edema, congestion, multifocal infarctions and microabscesses (Fig. 4A). A few vessels were obliterated by septic emboli containing bacterial colonies and surrounding parenchyme was infarcted. Tubular lumens were filled with numerous casts, some of which contained

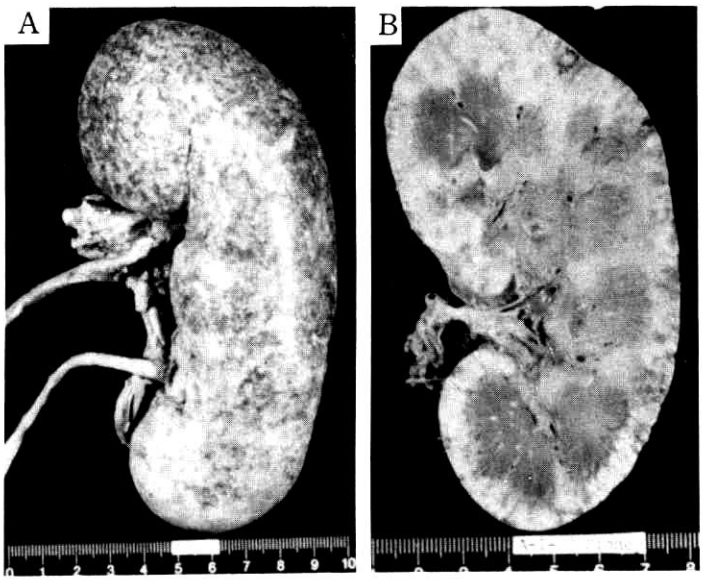

Fig. 4. Cortical surface of the kindey is coarsely granular and dark brownish discolorated, double ureters are found(A). Cut surface reveals a few foci or embolic infarction and blunting of corticomedullary outline, particlarly at the midpole(B).

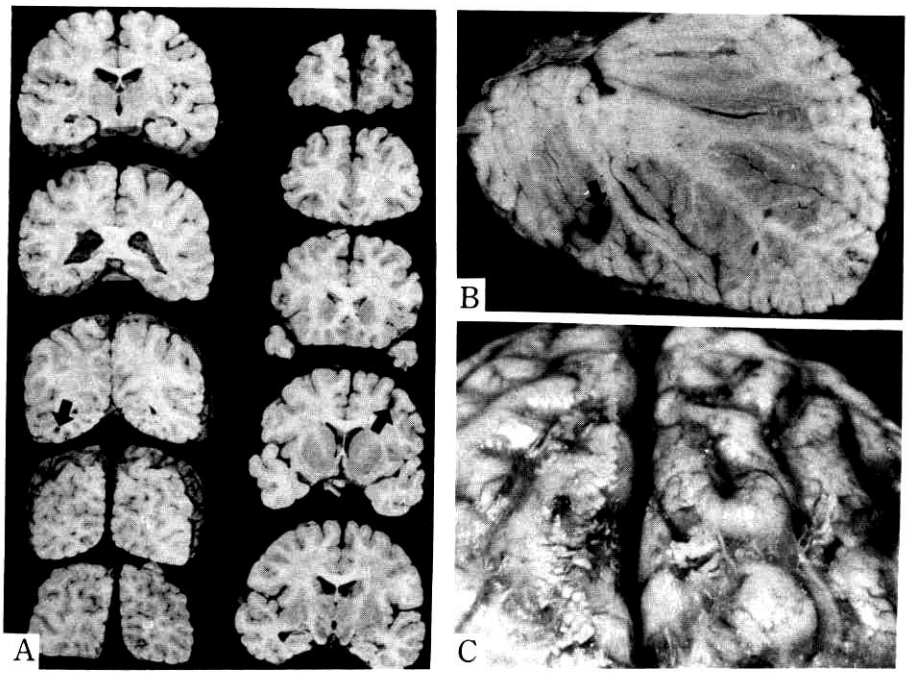

Fig. 5. Multiple serial coronal sections of the brain demonstrate a few septic embolic foci in the white matter of right parietal and left temporal lobes (A:arrows) and cerebellar hemisphere (B:arrow). Meninges are thick and turbid (C).

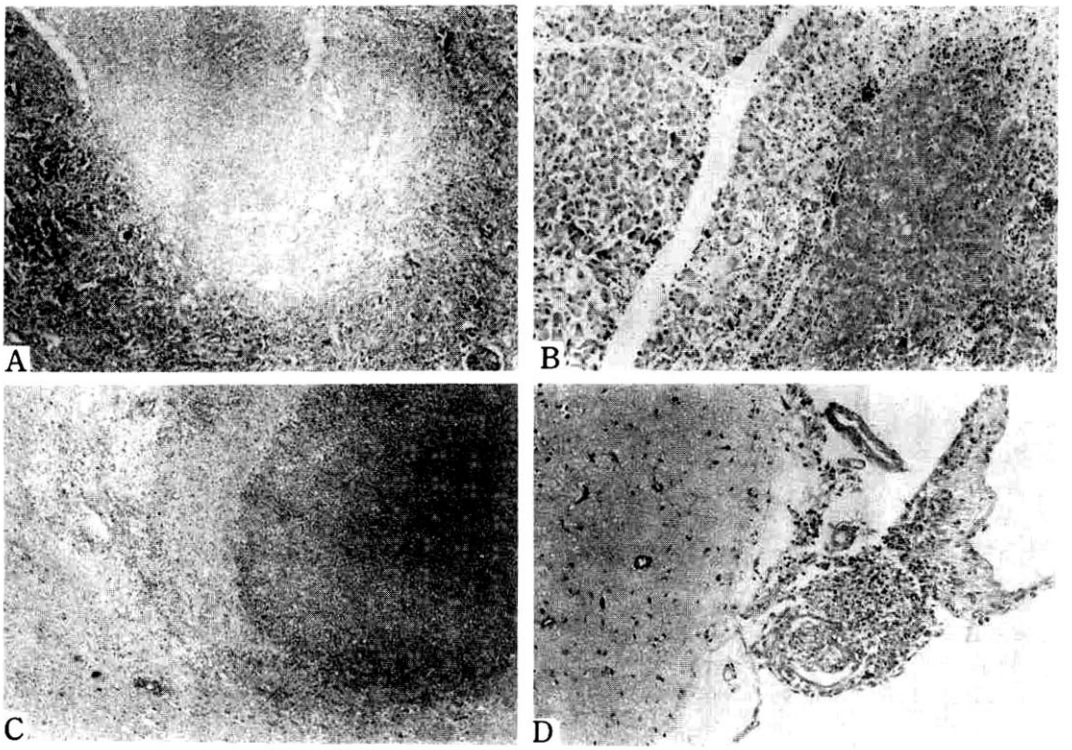

Fig. 6. Systemic septic emboli were found in the kidneys (A), pancreas (B), brain (C), and meninges (D).

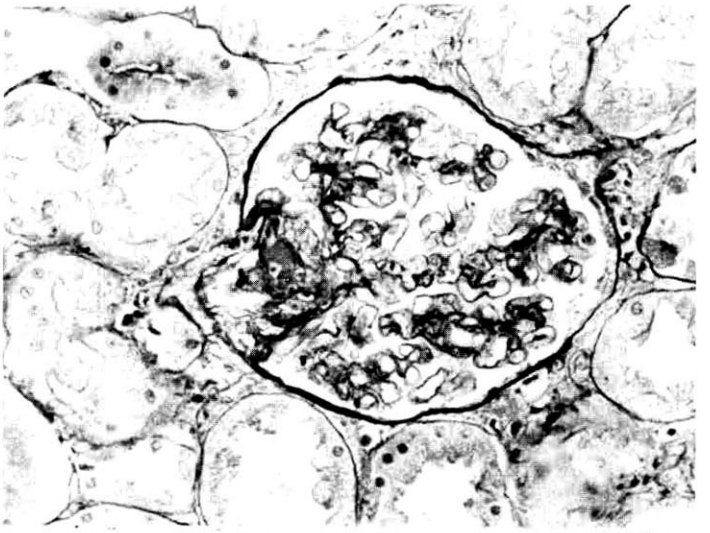

Fig. 7. Sections of renal glomerulus with fresh embolus at the hilum. (periodic acid Schiff, ×200).

bacterial colonies. Glomeruli were focally affected by embolic glomerulonephritis: there were microemboli within the hilar vessels without cellular proliferation (Fig. 7). In the spleen red pulp was expanded

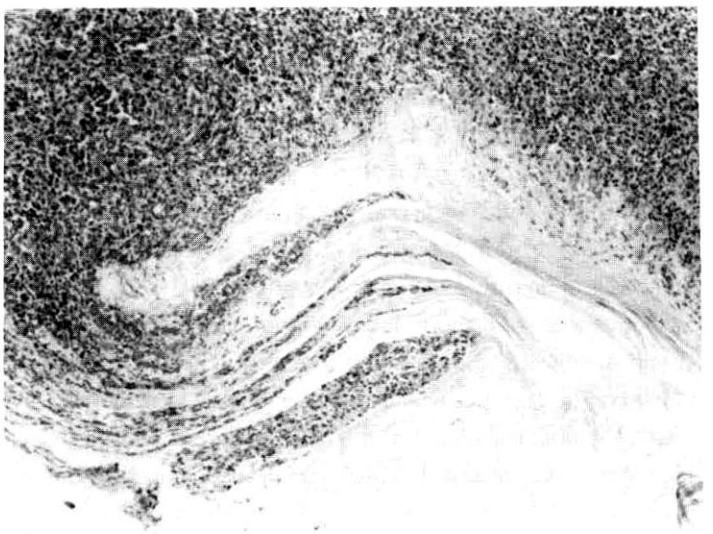

Fig. 8. Section of skin lesion reveals collection of neutrophils in the horny layer (H-E, ×100).

and congested, while white pulp was atrophic. Sections of the pancreas showed multifocal infarction (Fig. 4B). Meninges at the cerebral convexity was infiltrated by neutrophils and plasma cells, and meningeal vessels contained septic emboli (Fig. 6D). Foci of brownish embolisms in temporal and parietal lobes and cerebellar hemisphere revealed microabscesses (Fig. 6C). Two small round yellowish nodules in the choroid plexus revealed collection of foamy histiocytes, which had abundant, pale staining fat -laden cytoplasm. Sections obtained from the papules of palm showed intracorneal pustule (Fig. 8). There was no morphological evidence of Marfan syndrome.

Postmortem microbiologic examination from the vegetation in mitral valve demonstrated Staphylococcus aureus and from blood of the right atrium Pseudomonas aeruginosa.

DISCUSSION

During the hundred or so years since Alexander Ogstons original discription of Staphylococcus aureus, this microbe has shown itself to be a remarkably versatile pathogen capable of causing a range of infection more diverse than most other bacterial genera[8]. Acute bacterial endocarditis is one of the most dramatic syndromes produced by Staphylococcus aureus. An otherwise healthy person, often with a previously asymptomatic, benign, left sided, valvular abnormality may have a flu-like syndrome that proceeds within hours to the overt syndrome of acute endocarditis[9,10]. The course is frequently fulminant with widespread metastatic infection as in the case of our patient[6,11,12].

Staphylococci cause 20~30% of the cases of infective endocarditis, and myocardial abscess (with conduction disturbance), purulent pericarditis, and valve ring abscess are common. Peripheral foci of suppuration (brain, lung, spleen, kidney, and so forth) are common afflict over 40% of these patients[6,11~13]. Emboli are more common in patients with mitral valve infection and in those infected with more virulent organisms such as S. aureus.

It is well known that embolic phenomena may occur weeks to months after the infectious process on ther valve has been eradicated. Most likely this is related to the fact as long as six months may be

required before the vegetations on the affected valve become completely covered by endothelium.

Cerebral embolism is the most common and the most important occurring in as many as 30% of all patients, most of whom ultimately die. Emboli that are infected also account for mycotic aneurysm, meningitis, or meningoencephalitis, brain abscess.

The management of a cerebral mycotic aneurysm depends on the presence or absence of hemorrhage, its anatomic location and the clinical course. The indication for surgical intervention must be evaluated on an indivdual basis[14]. Cerebral emboli occur in at least one third of infective endocarditis[10]. The CSF tends to reflect the nature of infecting organism rather than nature of the neurologic complication, except when hemorrhage is present.

Staphylococcal endocarditis is usually associated with a purulent CSF formula, where as nonvirulent organisms usually have aseptic or normal CSF formulas. Cerebral infarction, arteritis, abscess, mycotic aneurysms, intracerebral or subarachnoid hemorrhage, encephalomalacia, cerebritis, and meningitis have all been reported[11].

The identification of a vegetation is a hallmark manifestation of infective endocarditis by echocardiography[15,16]. Over 55% of patients with S. aureus endocarditis have embolism to the kidneys in severe progressive renal failure[4]. Septic emboli in the kidneys were also found in our patient. However, in recent report the presence of vegetations on echocardiography was not associated with a significantly higher risk for embolus in patients with left -sided native valve infective endocarditis[17]. Presumably, S. aureus enters the blood stream from a peripheral site asymptomatically and seed to the abnormal valve. The affected person becomes highly febrile and progressively toxic and confused, and may have cerebral emboli and the syndrome of septic shock[9,10].

An important determinant of the eventual outcome of this disease is a failure to institute treatment early in the course of the disease; a delay of as little as 4 to 5 days may increase the risk of a fatal outcome. Even large doses of the most active antimicrobial drugs fail to cure the infection in patients in whom a large number of abscesses develop either before or after therapy has been initiated.

Through autopsy of this case, multiple systemic septic emboli were conspicuous in multiple organs (brain, heart, spleen, both kidneys) associated with acute staphylococcal endocarditis and mitral valve vegetations were noticed. We guess the source for the S. aureus may be infected knee joints due to frequent acupuncture and S. aureus enters the blood stream and disseminated in multiple organs. Mortality rate are age dependent and range from 20% in younger patients to more than 50% in the elderly[11].

Operative intervention during active staphylococcal endocarditis has also been suggested for patients with recurrent emboli, uncontrolled septicemia, endocardial abscess, and pericarditis. The clinical condition of this patient was too poor to tolerate the operative risk. Although the mortality is higher among patients who undergo cardiac valve replacement during active infection than among patients who undergo valve replacement after completion of antimicrobial therapy, the increased risk associated with a surgical procedure is justified in patients with cardiac failure, and operation may offer the only hope for survival.

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