

Clinical and microbiological characteristics of mycotic aneurysms in a medical center in southern Taiwan

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Background and Purpose: Mycotic aneurysm poses a high risk of mortality. This study evaluated the demographic and clinical characteristics and outcomes of hospitalized patients with mycotic aneurysm.

Methods: Patients with mycotic aneurysm hospitalized between March 1996 and May 2006 at a medical center in southern Taiwan were retrospectively analyzed.

Results: Fifty two patients (38 men and 14 women; mean age, 64.5 ± 15.6 years) were included. The leading underlying diseases were diabetes mellitus (40.4%), hypertension (21.2%), and renal disease and heart disease (19.2% each). The most common pathogens isolated from blood and/or resected tissue were *Salmonella* spp. (34.6%), *Klebsiella pneumoniae* (11.5%) and *Staphylococcus aureus* (11.5%). Mycotic aneurysms caused by Gram-negative bacilli were significantly more likely to occur in older patients ($p=0.018$) and at infrarenal sites ($p=0.021$). There were trends suggesting that mycotic aneurysms were more likely to be caused by Gram-negative bacilli in patients receiving steroid treatment and in those with underlying diabetes mellitus. Mycotic aneurysms caused by Gram-positive cocci were significantly more likely to occur in suprarenal arteries ($p=0.048$), especially intracranially ($p=0.002$), in younger patients ($p=0.018$) and in patients with concurrent endocarditis ($p=0.008$). The overall in-hospital mortality rate was 30.6%, and there was no significant difference in in-hospital mortality between mycotic aneurysms caused by Gram-negative bacilli and those due to Gram-positive cocci.

Conclusions: The relationship between the anatomic site of mycotic aneurysm and the spectrum of culprit bacteria may help clinicians promptly choose appropriate antibiotic regimens on an empirical basis. Further study is required to understand better the role of *K. pneumoniae* in mycotic aneurysm in Taiwan.

Key words: Aneurysm, infected; Gram-positive cocci; *Klebsiella pneumoniae*; *Salmonella*

Introduction

Mycotic aneurysm poses a high risk to affected patients, especially those with complications such as aneurysm rupture, intractable sepsis and extensive periaortic infection [1,2]. The commonly encountered pathogens for mycotic aneurysm include *Salmonella* spp., *Staphylococcus* spp. and *Streptococcus* spp. [1-10]. The outcome of mycotic aneurysm depends on appropriate antibiotic therapy and timely aggressive

surgical intervention [1-3]. Unfortunately, the diverse clinical features of mycotic aneurysm due to a variety of pathogens reported in the literature offer little specific information regarding clinical management of this disease entity. In order to understand better the clinical and microbiological characteristics of mycotic aneurysms and to improve management of this infection, we performed a retrospective study of patients with a diagnosis of mycotic aneurysm.

Methods

All patients hospitalized between March 1996 and May 2006 with a discharge diagnosis of mycotic aneurysm retrieved from the records were included in a compiled

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list of patients, and were subject to medical chart review. Patients eventually included in this study were those in whom the diagnosis of mycotic aneurysm was made based on at least one of the following criteria: 1) pus was found macroscopically in the aneurysm during operation; 2) aspirate or dissected tissue specimen from arterial wall or periaortic soft tissue histopathologically indicated purulent inflammation; and 3) presence of compatible clinical manifestations and computed tomography or magnetic resonance imaging of mycotic aneurysm [11-13] in patients who were clinically improved under medical treatment if surgical intervention was not carried out.

Demographic, clinical and laboratory data were collected for analyses. End-stage renal disease referred to chronic renal failure in patients who underwent long-term hemodialysis. Renal diseases referred to impaired kidney function reflected by serum creatinine level >1.5 mg/dL in patients who did not receive regular hemodialysis. Liver diseases were diagnosed in patients with elevated aminotransferases indicating abnormal liver function or in those with abnormal hepatic sonography (e.g., uneven liver surface). Heart diseases referred to valvular heart disease, coronary artery disease or hypertensive cardiomyopathy, which had been diagnosed by a cardiologist. Antibiotic treatment was regarded as appropriate if the pathogen isolated from the resected tissue or blood was susceptible *in vitro* to the prescribed antibiotic(s). Susceptibility testing on the pathogens was performed on a clinical-service-basis using the Kirby-Bauer diffusion method, in accordance with National Committee for Clinical Laboratory Standards at the time of tests [14]. Aneurysms involving aorta were specifically categorized in terms of location into suprarenal (thoracic, abdominal, intracranial and brachial) and infrarenal (abdominal, femoral, iliac and popliteal) for further analyses. Emergency surgery was defined as urgent non-elective operation for rapid clinical deterioration of a mycotic aneurysm (e.g., persistent fever or septic shock under medical treatment, and impending aneurysm rupture). The endpoint for outcome of evaluation was in-hospital mortality of the patients, regardless of whether the cause was directly or indirectly related to mycotic aneurysms.

Patients were classified based on the pathogens responsible for the mycotic aneurysm as Gram-negative bacilli and Gram-positive cocci. Fisher's exact test was used in comparisons of discontinuous variables, while Mann-Whitney *U* test was used to compare

continuous variables. A *p* value <0.05 was considered statistically significant.

Results

A total of 52 patients comprising 26 cases of suprarenal and 27 infrarenal mycotic aneurysms (one patient had mycotic aneurysms involving both sites) were identified during the study period and were included in analyses. Demographics, underlying diseases, clinical manifestations and laboratory data of these patients are summarized in Table 1. There were 38 men (73.1%) and 14 women (26.9%), with a mean age of 64.5 ± 15.6 years. Forty five patients (86.5%) were found to have underlying diseases, and among the 52 patients, the leading underlying diseases were

Table 1. Demographic, clinical and laboratory data of patients with mycotic aneurysm

Variable	Number of patients (n = 52) [%]
Male gender	38 (73.1)
Age (years; mean ± SD)	64.5 ± 15.6
Underlying disease/condition	
Diabetes mellitus	21 (40.4)
Hypertension	11 (21.2)
Heart disease	10 (19.2)
Immunosuppressive treatment	8 (15.4)
Renal disease	7 (13.5)
Liver disease	6 (11.5)
End-stage renal disease	3 (5.8)
Malignancy	
Small cell lung cancer	1 (1.9)
Uterus choriocarcinoma	1 (1.9)
Pulmonary tuberculosis	2 (3.8)
Intravenous drug user	1 (1.9)
Clinical manifestation	
Localized pain	39 (75.0)
Fever	33 (63.5)
Shock	4 (7.7)
Heart failure	1 (1.9)
Pulsatile mass	1 (1.9)
Laboratory data	
White blood cell count (/mm ³ ; mean ± SD)	11,378 ± 2067
Primary infection focus	
Endocarditis	6 (11.5)
Retroperitoneal abscess	5 (9.6)
Infectious spondylitis	4 (7.7)
Sternum osteomyelitis and mediastinal abscess	3 (5.8)
Small bowel perforation	1 (1.9)

Abbreviation: SD = standard deviation

diabetes mellitus (40.4%), hypertension (21.2%), and renal diseases and heart diseases (19.2% each). Only one patient was an intravenous drug user. A variety of symptoms/signs were found in these patients, and the two leading ones were localized pain in the vicinity of the mycotic aneurysms (75.0%) and fever (63.5%). Primary foci of infection were found in 19 patients, the 2 most common being endocarditis (6/52 patients [11.5%]) and retroperitoneal abscess (5/52 patients [9.6%]).

Three of the 52 patients were transferred to other hospitals shortly after admission. As a result, 49 patients were available for detailed assessments; among them, morbidities were found in 19 patients (38.8%), which included aneurysm rupture in 7, intractable sepsis in 4, nosocomial pneumonia in 2, and internal bleeding, graft infection, chyloperitoneum, surgical site infection, ventricular arrhythmia, and seizure in one patient each.

A number of infectious etiologies were identified in this series. The mycotic aneurysm in each individual patient was caused by a single pathogen, and in cases where both blood and resected tissue were culture-positive, the identical bacteria were isolated. Bacteria isolated from blood (49 cases) and resected tissues (32 cases) are summarized in Table 2. Of the 52 patients, 29 (55.8%) were infected with a Gram-negative bacillus and 14 (26.9%) with a Gram-positive coccus. Thirteen of the 43 patients (30.2%) with infectious etiologies identified had positive bacterial growth in blood and tissue cultures. The three most commonly found pathogens were *Salmonella* spp. (18 [34.6%]), *Klebsiella pneumoniae* (6 [11.5%]) and *Staphylococcus aureus*

(6 [11.5%]). None of the *K. pneumoniae* isolates was an extended-spectrum beta-lactamase-producing strain. Among the 6 *S. aureus* isolates, 1 was a methicillin-resistant strain that grew from the resected tissue from the mycotic aneurysm of a patient who had undergone aortic valve replacement for severe aortic stenosis 5 months earlier.

With the exception of one patient with concurrent thoracic and infrarenal abdominal mycotic aneurysms both caused by *Salmonella enteritidis*, all patients suffered from a single mycotic aneurysm. Among the 51 patients with available descriptions of the morphology of the mycotic aneurysm, saccular aneurysms were found in 21 (41.2%) and fusiform aneurysms in 30 (58.8%); aneurysms were found to be larger than 5 cm in diameter in 30 patients (58.8%) upon diagnosis. Of the 26 suprarenal aneurysms, 10 (38.5%) developed in the abdominal aorta, 8 (30.8%) in the intracranial artery, 7 (26.9%) in the thoracic aorta, and 1 (1.9%) in the brachial artery. Of the 27 infrarenal aneurysms, 21 (77.8%) developed in the abdominal aorta, 4 (14.8%) developed in the iliac artery, and one each (3.7%) developed in the popliteal artery and the femoral artery.

All patients received empirical parenteral antibiotic treatment immediately on the diagnosis of mycotic aneurysm. Inappropriate empirical antibiotic therapy in the first three days was found in 14 of 49 patients (28.6%) with available information for evaluation of their antibiotic treatments. Of the 52 patients, 31 (59.6%) underwent surgery (elective operations were performed in 17 and emergency surgery in 14). Among the 31 patients receiving operations, in situ graft reconstruction was carried out in 23 patients,

Table 2. Infectious etiologies for mycotic aneurysms (n = 52)

Pathogen	Blood culture (n = 49)	Tissue culture (n = 32)	Either or both (n = 52)
	No. (%)	No. (%)	No. (%)
Gram-negative bacilli	20 (40.8)	19 (59.4)	29 (55.8)
<i>Salmonella</i> spp.	14 (28.6)	9 (28.1)	18 (34.6)
<i>Klebsiella pneumoniae</i>	3 (6.1)	5 (15.6)	6 (11.5)
<i>Escherichia coli</i>	1 (2.0)	2 (6.3)	2 (3.8)
<i>Enterobacter</i> spp.	1 (2.0)	1 (3.1)	1 (1.9)
<i>Burkholderia pseudomallei</i>	1 (2.0)	1 (3.1)	1 (1.9)
<i>Propionibacterium</i> spp.	0 (0.0)	1 (3.1)	1 (1.9)
Gram-positive cocci	11 (22.4)	6 (18.8)	14 (26.9)
<i>Staphylococcus aureus</i>	5 (10.2)	2 (6.3)	6 (11.5)
<i>Staphylococcus saprophyticus</i>	0 (0.0)	1 (3.1)	1 (1.9)
Streptococcus group D	1 (2.0)	0 (0.0)	1 (1.9)
Streptococcus group non-A,B,D	1 (2.0)	0 (0.0)	1 (1.9)
Viridans streptococci	4 (8.1)	3 (9.4)	5 (9.6)
Negative culture	18 (36.7)	7 (21.9)	9 (17.3)

extra-anatomic bypass in 4 (for intra-abdominal aneurysms), and aneurysmectomy coupled with hematoma removal in the other 4 (for intracranial aneurysms). Surgical interventions were not performed in the remaining 19 patients because of clinically unstable condition or because surgery was not feasible due to the complexity of the mycotic aneurysm. In-hospital mortality occurred in 15 patients (15/49 [30.6%]). No significant difference in in-hospital mortality was found between patients who received operation (33.3%)

and those who did not (26.3%) [$p=0.754$]. The mean interval between admission and in-hospital mortality was 11.4 ± 9.5 days.

Demographic and clinical characteristics and outcomes of patients with mycotic aneurysms caused by a Gram-negative bacillus or a Gram-positive coccus are summarized in Table 3. Mycotic aneurysms due to Gram-negative bacilli were found to develop in significantly older patients ($p=0.018$) and were more common in infrarenal sites ($p=0.021$). There were

Table 3. Differences in demographic, clinical and laboratory data between patients with mycotic aneurysms caused by Gram-negative bacilli and Gram-positive cocci

Variable	Gram-negative bacilli (n = 29) No. (%)	Gram-positive cocci (n = 14) No. (%)	<i>p</i>
Age (years; mean \pm SD)	69.9 \pm 8.7	58.6 \pm 16.1	0.018
Male gender	22 (75.9)	10 (71.4)	1.000
Clinical manifestation			
Fever	20 (69.0)	9 (64.3)	1.000
Localized pain	24 (82.8)	8 (57.1)	0.133
Heart failure	1 (3.4)	0 (0.0)	1.000
Shock	2 (6.9)	0 (0.0)	1.000
Pulsatile mass	0 (0.0)	1 (7.1)	0.326
Underlying disease/condition			
Renal disease	6 (20.7)	1 (7.1)	0.396
Steroid use	7 (24.1)	0 (0.0)	0.076
Hypertension	7 (24.1)	4 (28.6)	1.000
Diabetes mellitus	18 (62.1)	4 (28.6)	0.055
Liver disease	3 (10.3)	1 (7.1)	1.000
Solid tumor ^a	2 (6.9)	0 (0.0)	1.000
Heart disease	1 (3.4)	7 (50.0)	0.001
Infective endocarditis	0 (0.0)	4 (28.6)	0.008
Intravenous drug user	0 (0.0)	1 (7.1)	0.326
Location of mycotic aneurysm			
Suprarenal	10 (34.5)	10 (71.4)	0.048
Thoracic	5 (17.2)	2 (14.3)	1.000
Abdominal	5 (17.2)	3 (21.4)	1.000
Intracranial	0 (0.0)	5 (35.7)	0.002
Infrarenal	20 (69.0)	4 (28.6)	0.021
Abdominal	16 (55.2)	3 (21.4)	0.052
Femoral	1 (3.4)	0 (0.0)	1.000
Iliac	3 (10.3)	0 (0.0)	0.539
Popliteal	0 (0.0)	1 (7.1)	0.326
Initial size of mycotic aneurysm			
>5 cm	20 (69.0)	7 (50.0)	0.316
<5 cm	8 (27.6)	6 (42.9)	0.488
Characteristics of mycotic aneurysm			
Saccular	9 (31.0)	5 (35.7)	1.000
Fusiform	19 (65.5)	8 (57.1)	0.739
White blood cell count (/mm ³ ; mean \pm SD)	10,606 \pm 5387	12,878 \pm 6369	0.190
In-hospital mortality	8 (27.6)	5 (35.7)	0.726
Inappropriate empirical antibiotic therapies	9 (31.0)	3 (21.4)	0.720

Abbreviation: SD = standard deviation

^aSolid tumor (small cell lung cancer and uterus choriocarcinoma in one patient each).

trends suggesting that mycotic aneurysms caused by Gram-negative bacilli were more likely to occur in patients with steroid use ($p=0.076$) or with underlying diabetes mellitus ($p=0.055$). Mycotic aneurysms due to Gram-positive cocci tended to develop in arteries located suprarenally ($p=0.048$), especially intracranially ($p=0.002$), were associated with a higher frequency of a concomitant infective endocarditis ($p=0.008$), and developed in younger patients ($p=0.018$). No significant difference in in-hospital mortality was found between patients with mycotic aneurysms caused by Gram-negative bacilli and Gram-positive cocci (27.6% vs 35.7%, $p=0.726$).

Because *Salmonella* spp. and *K. pneumoniae* were the 2 most common Gram-negative bacilli responsible for mycotic aneurysms in this series (Table 2), patients with mycotic aneurysm caused by *Salmonella* spp. and those with mycotic aneurysm due to *K. pneumoniae* were further analyzed. Only the male:female ratio (16:2 for *Salmonella* spp. vs 1:5 for *K. pneumoniae*) was found to be significantly different between the pathogens ($p=0.030$). Two of the six patients with mycotic aneurysms caused by *K. pneumoniae* in this series are noteworthy; one suffered from endogenous endophthalmitis due to *K. pneumoniae* of the presumably identical strain 2 months earlier, and another had concurrent *K. pneumoniae* liver and splenic abscess.

Discussion

In spite of the high morbidity and mortality [1-7], the clinical nonspecificity of mycotic aneurysm makes the early diagnosis in affected patients challenging [15]. Fever, localized pain and pulsatile mass, which have been regarded as the classic triad of mycotic aneurysm [2], were found in only one patient in this series. With regard to imaging, saccular aneurysm (lobulated saccular aneurysm in particular), rapid enlarging of the original aneurysm, and perianeurysm soft tissue mass with or without localized stranded fluid were reported to be typical radiographic manifestations of mycotic aneurysms [11-13]. Unfortunately, this imaging is often found in the later course of the disease, and upon the detection of such imaging presentations, the mycotic aneurysm is enlarged to the extent of impending rupture with an uncontrolled sepsis [2].

The 30.6% in-hospital mortality in the present study was similar to previously reported rates, ranging from 16% to 44% [5]. Successful management of mycotic aneurysm includes early diagnosis, prolonged

appropriate antibiotic therapy and effective surgical intervention [1,4-6,16-18]. With respect to surgery, in situ reconstruction instead of extra-anatomic bypass was increasingly recommended for patients with mycotic aneurysm [2,4-7,16]. Consistent with other series [2], a substantial number of our patients were immunocompromised and typically had at least one chronic comorbidity, and were thus at high risk for fatality [2].

The pathogenesis of mycotic aneurysm includes: 1) septic arterial emboli lodged in the vasa vasorum or vessel lumen; 2) contiguous spreading of infection to the nearby artery wall; 3) inoculation of pathogens at the time of artery trauma; 4) iatrogenic causes; and 5) an intimal defect (e.g., disintegrated atherosclerotic plaque) seeded by the culprit microbe from the bloodstream in a bacteremic patient [19]. Evolution from either bacteria lodging in vessel lumens or seeding the injured vessel intima is the most frequently encountered mechanism for mycotic aneurysm [19]. In agreement with a previous report, intracranial aneurysms in our study tended to be caused by Gram-positive cocci as a result of metastasis from a remote infection site (e.g., endocarditis) [20], while intra-abdominal aneurysms were more likely to be caused by Gram-negative bacilli, especially by *Salmonella* spp. [1,3]. It is very important to start effective antibiotic therapy immediately upon diagnosis of mycotic aneurysm. Our study and those previously reported suggest that empirically prescribed antibiotic regimens may be based on the location of the aneurysm, and then adjusted later, if necessary, based on the results of culture and susceptibility testing.

Non-typhoid *Salmonella* spp., are a well-known cause of mycotic aneurysm [1-10]. When the aortic wall is heavily atherosclerotic, the intima is vulnerable to invasion by non-typhoid *Salmonella* spp., leading to the development of a mycotic aneurysm [21,22]. In the present study, the incidence of mycotic aneurysms caused by *S. aureus* was relatively low, which might be explained by the comparatively low prevalence of intravenous drug use in Taiwan during the study period [23]. Surprisingly, *K. pneumoniae* was the second leading infectious etiology in this series, accounting for 11.5% of mycotic aneurysms. An extensive review of reports on mycotic aneurysm published from 1962 to 2000 by Cinà et al found that only 2% of mycotic aneurysms were caused by *K. pneumoniae* [24]. *K. pneumoniae* has the potential to cause a wide variety of community-acquired infections, such as pneumonia, urinary tract infection, acute cholangitis, and skin and soft tissue infection [25]. Taiwan is unique

in that *K. pneumoniae* is most frequently responsible for community-acquired liver abscess and endophthalmitis [25-28] and also not uncommon as a cause of splenic abscess [29], especially in diabetic patients. The present study suggests that *K. pneumoniae* is also a common pathogen for mycotic aneurysm in Taiwan, which has long been ignored because of the rarity of mycotic aneurysm. Our data show that clinical characteristics and outcomes of patients with mycotic aneurysms caused by *Salmonella* spp. and *K. pneumoniae* were not significantly different, although there was a trend suggesting that *K. pneumoniae* was prone to cause mycotic aneurysm in patients with underlying diabetes mellitus. Further study with larger sample size is needed to clarify whether diabetic patients in Taiwan are more susceptible to *K. pneumoniae* in the infectious etiology of mycotic aneurysm.

The limitations of our study are that being a retrospective investigation, it was not standardized with regard to evaluation of the clinical severity of mycotic aneurysm, in the decision to perform surgery or not, and in determining the timing of any surgery. As a result, it is not possible to evaluate the impact of surgery on the outcome of mycotic aneurysms, not to mention the impact of different surgical modalities.

In summary, mycotic aneurysm with inherent high morbidity and mortality often develops in immunocompromised patients or in patients with predisposing factors such as heart diseases and atherosclerotic vessels. Mycotic aneurysms due to Gram-negative bacilli tended to develop in infrarenal locations in elderly patients, while those caused by Gram-positive cocci tended to develop intracranially, in younger patients and in those with concurrent infective endocarditis. The relationship between the anatomic site of mycotic aneurysm and the spectrum of culprit bacteria may help clinicians in the choice of appropriate antibiotic(s) for empirical treatment of mycotic aneurysm, which can be adjusted later, if indicated, based on the results of culture. It is a unique finding in this series that *K. pneumoniae* was the second most frequent pathogen in mycotic aneurysm. Further study is warranted to allow better understanding of the role of *K. pneumoniae* in mycotic aneurysm in Taiwan, where *K. pneumoniae* is well known as a cause of liver abscess, endophthalmitis and splenic abscess.

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