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Case Report

Mycotic aneurysms: case reports in China and a review of the most current literature

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Abstract: Mycotic aneurysm, a rare but severely life-threatening disorder, is a type of aneurysms that appear in the wall of certain arteries suffering from bacterial infections. It is estimated that the mortality rate remains at approximately 40% despite the best surgical care provided. Here, we reported the major clinical manifestations, location of mycotic aneurysms, underlying diseases, etiology, treatment and prognosis of 8 cases with mycotic aneurysms diagnosed in a single center during the period from January 2007 to June 2015, and illustrated the clinical characteristics, etiology, treatment and prognosis of the disease, with a summary of the most recent literature captured from PubMed and Web of Knowledge between January 2007 through July 2016. The present study may add to the understanding of clinical characteristic, diagnosis and treatment of mycotic aneurysms. Multi-center randomized controlled trials are encouraged to evaluate the treatment options for mycotic aneurysms.

Keywords: Mycotic aneurysm, case report, literature review

Introduction

Mycotic aneurysms, which were firstly described in 1885 [1], are a type of aneurysms that appear in the wall of certain arteries suffering from bacterial infections and account for approximately 2.5% of all aortic aneurysms [2]. Only 40% of the patients with mycotic aneurysms develop classic clinical manifestations of fever, pain and pulsatile mass, making the early diagnosis, the cornerstone of effective treatment, difficult [3]. In addition, it is easy for the mycotic aneurysms to rupture and the rate of successful management of such condition is low, resulting in the extremely high mortality rate of the disorder [4]. It is estimated that the mortality rate remains at approximately 40% despite the best surgical care provided [5]. In this study, we presented 8 cases of mycotic aneurysms to illustrate the clinical characteristics, etiology, treatment and prognosis of the disease, with a summary of the most recent literature.

Case presentation

In the period from January 2007 to June 2015, a total of 8 patients were diagnosed with mycotic aneurysms at our hospital. All the diagnoses were made based by a combination of clinical evidence of infection (fever and elevated white blood cell count) and imaging evidence (CT or MRI) of infected aorta and/or pathological evidence, while iatrogenic or traumatic aneurysms were excluded. This study was approved by the Ethical Review Committee of Nanjing First Hospital (Nanjing, China). Written informed consent was obtained from all subjects described in this study, and all the participants consented to the publication of their medical data.

The 8 patients discussed were all men with median age of 53 years old (range: 25 to 67 years old). The underlying diseases included intravenous drug abuse in 4 cases; type II diabetes mellitus in 2 cases; intravenous drug abuse complicated by type II diabetes mellitus,

Table 1. Demographic, clinical, etiologic characteristics and treatment and prognosis of the 8 cases with mycotic aneurysm

Case number	Underlying diseases	Age (years)	Sex	Site	Fever	Pulsatile mass	WBC ($\times 10^9$/L)	Etiology	Surgical option	Anti-infective agents	12-month prognosis
1	Intravenous drug addiction, hypertension, T2DM, nephropathy and artificial arteriovenous fistula on the left forearm	62	Men	Left brachial artery	Yes	Yes	15.81	MRSA	Pseudoaneurysm resection + bypass grafting	Vancomycin	Survival
2	T2DM	67	Men	Left internal iliac artery	Yes	No	15.33	*Salmonella enteritidis*	Endovascular exclusion of left internal iliac artery	Piperacillin-sulbactam	Death 3 months post-therapy (septic shock)
3	None	62	Men	Abdominal aorta	Yes	No	19.04	*Salmonella* spp.	Pseudoaneurysm resection + bypass grafting of right axillary artery-bilateral femoral artery	Meropenem	Survival
4	Intravenous drug addiction	43	Men	Right femoral artery	Yes	Yes	18.26	Negative	Right femoral artery ligation	Piperacillin-sulbactam	Survival
5	Marfan syndrome, Bentall surgery, infective endocarditis and aortic dissection	25	Men	Aorta + right brachial artery	Yes	Yes	16.52	MSSA	Pseudoaneurysm resection + autologous vascular grafting	Vancomycin	Survival
6	Intravenous drug addiction	53	Men	Right femoral artery	No	Yes	9.05	Negative	Pseudoaneurysm resection + autologous vascular grafting	Penicillin	Survival
7	Intravenous drug addiction	41	Men	Left femoral artery	Yes	Yes	12.78	MSSA	Pseudoaneurysm resection + autologous vascular grafting	Linezolid	Survival
8	T2DM	54	Men	Thoracic aorta	Yes	No	12.25	MSSA	Endovascular exclusion	Ceftriaxone + moxifloxacin	Death 2 months post-therapy (hemoptysis)

MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.

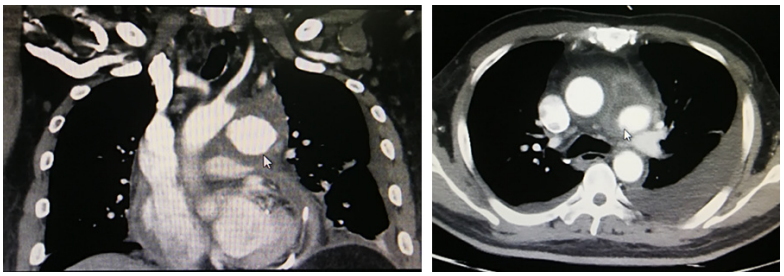

Figure 1. Computed tomography angiography (CTA) displays pseudoaneurysm of the aortic arch. Cystic bulge is seen in the local aortic arch. Contrast agent is found in the cystic bulge, and annular low-density shadows are observed surrounding the cystic bulge.

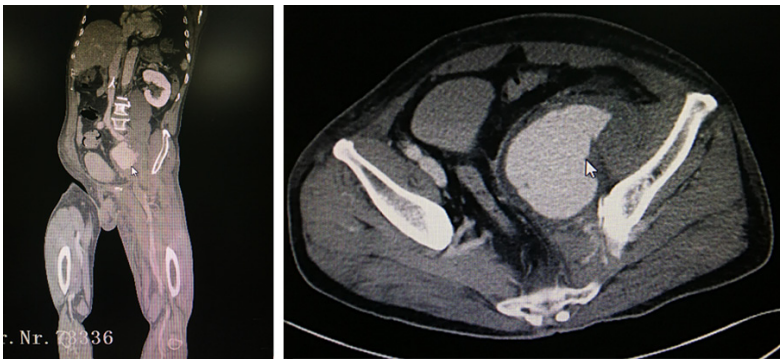

Figure 2. Computed tomography angiography (CTA) shows pseudoaneurysm of the left internal iliac artery. Soft-tissue mass shadows are seen anterior to the left ilium, which is filled with the contrast agent. There is no clear boundary between the soft tissue mass and internal iliac artery, and the soft tissue mass causes compression on left external iliac artery and common iliac artery.

diabetic nephropathy and artificial arteriovenous fistula on the left forearm in one case; Marfan syndrome, infective endocarditis, Bentall surgery and aortic dissection in one case, and one case of no obvious underlying disease (**Table 1**).

Of the 8 cases, 2 cases involved a mycotic aneurysm of the aorta (**Figure 1**), one case involved the internal iliac artery (**Figure 2**), one case involved the brachial artery, three cases involved the femoral artery (**Figure 3**), and in the case with Marfan syndrome, both the aorta and brachial artery were involved. The cases with intravenous drug abuse had mycotic aneurysms predominantly located in the injured peripheral vessels on the left forearm and right lower limbs (due to right handedness), where local pain, pulsatile sensation, suppuration and even bleeding were observed (**Table 1**).

Seven out of the 8 cases developed a fever, and a remarkable rise in peripheral white blood cell count was seen in those 7 cases. Blood culture was positive in 5 cases and pus culture was positive in 2 cases, including one case positive for both blood and pus cultures. Bacterial culture showed *Staphylococcus aureus* infection in 4 cases and *Salmonella* spp. infection in 2 cases and all the cases with intravenous drug abuse had a blood culture positive for *S. aureus* (**Table 1**).

All the patients underwent empirical therapy with broad-spectrum antibiotics in the early course of the disease and some cases had their therapeutics adjusted based on the culture results. 6 cases underwent surgical therapy and 2 cases were treated by digital subtraction angiography (DSA)-guided endovascular stent-graft exclusion. During the surgical treatment, one case received femoral artery ligation and the remaining 5 cases received aneurysm excision + arterial reconstruction. Death was observed in the 2 cases with endovascular exclusion, and the other 6 cases survived for the one-year follow-up period (**Table 1**).

Literature review

We researched the studies pertaining to mycotic aneurysms in PubMed and Web of Knowledge using the MeSH term “mycotic aneurysm”, and the time limit was assigned from January 2007 through July 2016. Publications meeting the following criteria were excluded from the study: (1) non-English publications; (2) publications in which less than 10 cases of mycotic aneurysms were included; and (3) publications where the full-text file was not available. The patients’ age, gender, location of mycotic aneurysms, underlying diseases, major clinical manifesta-

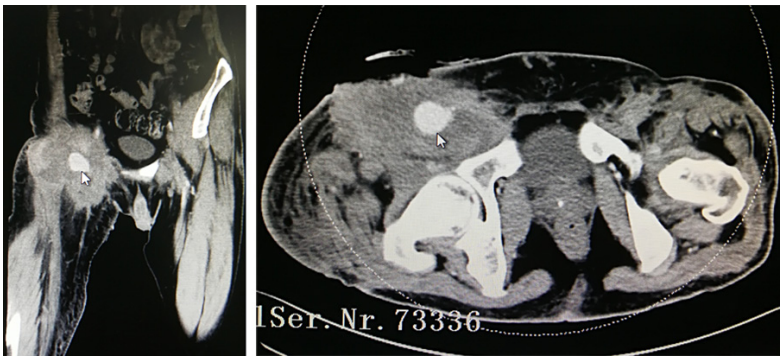

Figure 3. Computed tomography angiography (CTA) reveals pseudoaneurysm of the right femoral artery. The structure of the groin area is not clear, and mass shadows with uneven density and unclear boundary are displayed in the groin area. In addition, the interruption of right external iliac artery continuity is found.

tions, etiology, treatment and mortality were obtained from the researched publications.

A total of 2465 publications were retrieved from PubMed and Web of Knowledge using "mycotic aneurysm" as a MeSH term, and 2429 publications were excluded according to the exclusion criteria. Finally, a total of 36 publications were enrolled in the final analysis, which involved 1093 cases of mycotic aneurysms.

The 1093 cases of mycotic aneurysms included 823 men (75.3%) and 270 women (24.7%) with age ranging from 2.5 to 93 years old. The mycotic aneurysms were predominantly located in the aorta, including 231 cases (21.1%) with a mycotic aneurysm of the thoracic aorta, and 172 cases (15.7%) with a mycotic aneurysm of the abdominal aorta. There were 192 cases with a mycotic aneurysm of the femoral artery. Most cases with mycotic aneurysms were complicated by underlying conditions including hypertension (34.9%), diabetes (26.1%), smoking (14.4%), and coronary heart disease (10%). The most common clinical symptoms included pain (71.6%), fever (57.8%), a pulsatile mass (14.5%) and hemoptysis (10.0%), and 4.4% of the patients had shock. *Salmonella* spp. was the most frequent causative organism (39.1%), followed by *Staphylococcus* and *Enterobacter* spp. Currently, surgery remains the primary option for the treatment of mycotic aneurysms (845 cases, 77.3%); however, endovascular stent grafting was reported to achieve comparable outcomes for the treatment of mycotic aneurysms in relation to surgical therapy, and may be used as an alternative in patients with poor systemic conditions who would not tolerate open surgery [7]. The patients with a mycotic aneurysm of the femoral artery were found to achieve a satisfactory prognosis, with a low mortality rate (2.2%), and the mortality rate estimated from all merged data was 32.4% (312/964) among all the patients who showed up on the follow-up (**Table 2**).

Discussion

A mycotic aneurysm is an uncommon, but dreaded disorder that occurs more frequently in men than in women [8]. During the 9.5 year period from January 2007 to June 2015, all 8 patients who were diagnosed with mycotic aneurysms in our hospital were men, which is in accordance with the epidemiological data [8]. Based upon the origin of infection and the cause, a mycotic aneurysm is classified into mycotic emboli, arteritic aneurysm, secondary aneurysm infection and post-traumatic secondary pseudoaneurysm infection [8].

Prior to the widespread use of antibiotics, approximately 90% of the cases with mycotic aneurysms were estimated to be associated with infective endocarditis [9-11]. However, the incidence of trauma-associated mycotic aneurysms and arteritic aneurysms gradually increased with the raise in number of invasive endovascular procedures, intravenous drug abuse, and atherosclerosis incidence, as well as ageing population [12-15]. In the current study, out data showed mycotic aneurysms in relation to infective endocarditis in one case, and the other 7 cases developed mycotic aneurysms after intravenous drug use, invasive endovascular procedures and atherosclerosis, which is consistent with the current status of mycotic aneurysms worldwide. In addition, data captured from the most recent publications revealed that most cases with mycotic aneurysms had underlying diseases with chronic vascular injury, such as diabetes, hypertension, coronary heart disease, peripheral vascular diseases and smoking.

Table 2. Demographic, clinical, etiologic characteristics and treatment of the cases with mycotic aneurysm captured from literatures published between January 2007 and July 2016

Characteristic		Positive/total patients
Male		823/1093
Age (range)		2.5 to 93 years
Location	Thoracic aorta	231/1093
	Thoraco-abdominal aorta	44/1093
	Abdominal aorta	172/1093
	Suprarenal abdominal aortic aneurysm	60/1093
	infrarenal abdominal aorta	291/1093
	Iliac arteries	18/1093
	Visceral segment of the arota	192/1093
	Renal segment of the aorta	20/1093
	Femoral artery	32/1093
	Axillary artery	15/1093
	Intracranial/juxtarenal/paravisceral aorta	13/1093
Underlying diseases	Hypertension	303/869
	Chronic obstructive pulmonary disease	56/869
	Diabetes	227/869
	Peripheral arterial disease	31/869
	Chronic respiratory disease	60/869
	End-stage renal disease	30/869
	Coronary artery disease	84/869
	Concurrent systemic infection	35/869
	Cancer	34/869
	Immunodeficiency	76/869
	Ahistory of tobacco use	125/869
Clinical manifestation	Pulsatile mass	146/1005
	Fever	581/1005
	Hemoptysis	100/1005
	Pain	720/1005
	Shock	44/1005
	Bacteremia	25/1005
	Swelling	42/1005
Etiology	*Salmonella* species	366/936
	Staphylococcus aureus	34/936
	Staphylococcus epidermidi	24/936
	Klebsiella pneumoniae	26/936
	Brucellosis	33/936
	Escherichia faecalis	44/936
	Streptococci species	23/936
	Aspergillus species	9/936
	Serratial fonticola	17/936
Treatment	Surgery	845/1082
	Endovascular stent grafting	139/1082
	Surgery + endovascular stent grafting	3/1082
	Medication	88/1082
	Embolization	1/1082
	Untreated	6/1082
Death		312/964

Currently, the diagnosis of mycotic aneurysms manly depends on clinical symptoms, laboratory examinations together with imaging techniques [16], and a definitive diagnosis can be made only after a positive culture of the mycotic aneurysm specimens is obtained or pathological examinations display typical characteristics of pyogenic infections surrounding the affected artery [17]. Early diagnosis and prompt intervention are of great importance for the prognosis of mycotic aneurysms; however, the low incidence and lack of specific clinical manifestations make missed diagnosis frequent, which thereby increases the mortality rate [18]. Therefore, a high suspicion of mycotic aneurysms is required in the patients with infective endocarditis, use of endovascular agents, invasive endovascular procedures or immunosuppression [12-15]. The clinical features of mycotic aneurysms include pain, pulsatile mass, fever, elevated white blood cell count and even life-threatening shock [6, 19]. In this study, elevated white blood cell count was seen in 7 out of the 8 cases with mycotic aneurysms, which is similar to the findings reporting a high incidence of elevated white blood cell count seen in patients with mycotic aneurysms [20]. Our literature review revealed pain as

the most common symptom of mycotic aneurysms (71.64% incidence), followed by fever (57.8% incidence), while only 14.53% of the patients had a pulsatile mass, which confirms that pain and fever are the two most common symptoms of mycotic aneurysms.

Like infective endocarditis, group A beta-hemolytic streptococci, *Streptococcus pneumonia* and *Haemophilus influenzae* are the predominant causative organisms of mycotic aneurysms before the extensive use of antibiotics [21]. Currently, *S. aureus* and Salmonella spp. are the most common causative organisms leading to mycotic aneurysms, and *Salmonella* infections are predominantly detected in atherosclerotic lesions, while *S. aureus* infections mainly occur in intravenous drug abusers [20]. Among the causative organisms, gram-negative bacilli exhibit a high invasive and destructive ability, which is more likely to cause rupture of mycotic aneurysm [22, 23]. In the present study, bacterial culture revealed *S. aureus* and *Salmonella* spp. infections in 6 of the 8 cases with mycotic aneurysms, which is consistent with the current causative organisms of mycotic aneurysms [20].

Previous studies have demonstrated that mycotic aneurysms are mainly located in the aorta, followed by the femoral arteries, visceral arteries (superior mesenteric artery, splenic artery and hepatic artery) and cerebral arteries [24-27]. Similar to the previous reports, our literature review also showed that the mycotic aneurysms are predominantly located in the aorta (36.8%) and femoral artery (17.6%). In our case report, however, only two cases had a mycotic aneurysm of the aorta, while 3 cases had a mycotic aneurysm of the femoral artery and one case had a mycotic aneurysm of the brachia artery, secondary to intravenous drug use. In addition, in one case, the patient had a mycotic aneurysm of the aorta and brachial artery, which was considered to be attributed to the congenital mesodermal dysplasia in Marfan syndrome [27]. That patient recently suffered from infective endocarditis which increased his likelihood of developing a mycotic aneurysm.

The most common imaging sign of a mycotic aneurysm is a local vascular expansion, followed by perivascular inflammation and aneurysm enlargement, while vascular rupture and gas shadow surrounding the vascular wall is rare [20]. To date, the rapid imaging changes associated with infective inflammation have been considered as the specific features of mycotic aneurysms [20]. Ultrasonography is easily affected by the gas in the body, especially when detecting mycotic aneurysms in a deep body cavity, and the detection is greatly influenced by subjective factors, resulting in an unsatisfactory accuracy [28]. Currently, computed tomography angiography (CTA) is the first choice imaging tool to identify mycotic aneurysms, with 92% to 96% sensitivity and 93% to 100% specificity, and such technique has been widely employed for screening mycotic aneurysms since three-dimensional reconstruction can be readily performed [29]. In our case series, all the patients were subjected to CTA evaluation. The great advances in enhanced-MRI techniques facilitate the application of MR tools in detecting vascular diseases. Magnetic resonance angiography (MRA), a tool based on MRI to obtain images of blood vessels, is able to clearly display T2-weighted high-intensity signals at periarterial edema, which is effective in the monitoring the inflammatory changes in the vascular wall [30]. In addition, ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET-CT) imaging, which is able to display active inflammation in blood vessels through the monitoring of tissue metabolism [31], has been proved to be an effective approach for the diagnosis of mycotic aneurysms, and a higher 18-fluorodeoxyglucose uptake (4.5 SUV or greater) is measured in mycotic aneurysms as compared to non-infected aneurysms [32]. In addition to the identification of mycotic aneurysms, ^{18}F-FDG PET-CT imaging may be used to evaluate the efficacy of anti-infective therapy through the dynamic examinations [33].

Until now, there have been no randomized clinical trials to standardize the treatment of mycotic aneurysms. Empirical therapy mainly includes the control of infections and reconstruction of arterial circulation [34]. Anti-infective intervention is an important treatment, and the course of anti-infective therapy depends on the site of infection and causative agent, which ranges from 6 weeks to 6 months; however, lifetime low-dose anti-infective therapy may be required for recurrence of the infections or graft infec-

tions [35]. Since mycotic aneurysm rupture is easy to occur, surgical treatment is encouraged in the absence of absolute contraindications, in order to completely remove the infected necrotic tissues and perform vascular reconstruction [36]. In patients with mycotic aneurysms of the aorta, the primary vascular reconstruction includes extra-anatomic bypass reconstruction, in situ revascularization and endovascular revascularization [37]. Extra-anatomic reconstruction may avoid the direct contact between artificial blood vessels and infected foci, and reduce the occurrence of recurrent infections and graft infections; however, the long-term patency rate is not satisfactory [38], while *in situ* revascularization has the problem of high incidence of graft infections [39]. Some researchers consider that extra-anatomic bypass reconstruction is the first choice for vascular reconstruction [40, 41], while endovascular repair is recognized as a safer approach [42-44]. However, a systematic review revealed no significant differences in the early and late diagnosis between extra-anatomic reconstruction and endovascular treatment [7]. With the continuous development of endovascular equipment and updates on endovascular procedures, endovascular aneurysm repair (EVAR), a simple, easy-to-perform and low risk endovascular approach, was developed, which is more applicable to patients with critical diseases, intolerant to open surgery, mild infections or controlled infection following antibiotic therapy [45]. In the presence of mycotic aneurysm ruptures and fever, EVAR may be used as a temporary measure, and a subsequent surgical therapy may be performed after the condition improves [46]. In addition, endovascular treatment alone is reported to achieve a satisfactory clinical prognosis for the treatment of patients with mycotic aneurysm ruptures; however, long-term antibiotic therapy is required [47]. In patients with mycotic aneurysms of the peripheral artery, proximal ligation or aneurysm excision may be done [48]. For mycotic aneurysms secondary to intravenous drug use, the body may tolerate the chronic ischemia since arterial collateral circulation has been established prior to aneurysm rupture and bleeding; therefore, arterial ligation alone is considered and recommenced [49]. However, this approach can easily cause intermittent claudication and even amputation, and aneurysm excision and vascular reconstruction are therefore encouraged [50]. Additionally, vascular reconstruction with internal iliac artery was reported to achieve a satisfactory clinical prognosis in the treatment of mycotic aneurysms of the femoral artery [51].

Following active therapy, mycotic aneurysms still have a high mortality, with a 5-year survival rate of 35% to 55% [6, 25, 52]. In the current study, the one-year mortality was 25% (2/8) in the case series, and the literature review showed 32.4% mortality, estimated from the merged data. In addition, the patients with mycotic aneurysms of the femoral artery were found to have a good prognosis, with only 2.2% mortality, which may be attributable to the low incidence of underlying diseases and relatively simple management of local foci. In our case reports, both of the dead cases received endovascular treatment; however, endovascular exclusion was reported to achieve a 94% one-year survival rate in treatment of the patients with mycotic aneurysms of the aorta, which showed a better clinical prognosis than traditional surgeries [36]. It is considered that endovascular exclusion is notably suitable for the patients with mycotic aneurysms that cannot tolerate surgeries or require emergency management of bleeding [53]. In addition, open surgery is considered as the first choice treatment for mycotic aneurysms, since non-open surgery has a high incidence of long-term fatal infections [54].

In conclusion, mycotic aneurysm is a rare, but severely life-threatening disorder that greatly affects the quality of life. Since its first description in 1885 [1], a large number of studies have been conducted to explore its etiology, diagnosis and treatment; however, there is no consensus on the standard treatment, since there are no large-scale randomized controlled clinical trials to compare the available treatment options. In this report, only 8 cases of mycotic aneurysms were presented, with only one-year follow-up. However, we illustrated the clinical characteristics, etiology, treatment and prognosis with a summary of the most current literature based on the literature search on PubMed and Web of Knowledge. The present study may add to the understanding of clinical characteristic, diagnosis and treatment of mycotic aneurysms. Multi-center randomized controlled tri-

als to evaluate the treatment options for mycotic aneurysms are encouraged.

Disclosure of conflict of interest

None.

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