

# Mycotic Aneurysm Due to Non-typhi *Salmonella*: Report of 16 Cases

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From 1990 through 1994, we collected information on all cases of mycotic aneurysms due to non-typhi *Salmonella* that occurred at the Veterans General Hospital in Kaohsiung, Taiwan. All cases of salmonella bacteremia were reviewed to find any additional cases. A total of 16 cases of salmonella mycotic aneurysms occurred. The mortality rate was 100% among the three patients treated with medical therapy alone. Nine (70%) of the 13 patients who received surgical and medical therapy survived. Ten of the 16 cases were due to *Salmonella choleraesuis*. Diagnosis was established by computed tomography or aortography. Gallium scans were of no diagnostic utility. A culture of blood from a patient with underlying atherosclerosis that is positive for invasive *Salmonella* should prompt a search for a mycotic aneurysm. Treatment with a third-generation cephalosporin and resection of the infected vessel is usually successful.

In 1885, Osler [1] described a case of a mycotic aneurysm that originated from infective endocarditis. Subsequently, Crane [2] and Revell [3] reported that mycotic aneurysms of the aorta could arise from sources other than endocarditis. In a more-recent review, Brown et al. [4] found that endocarditis had been the important pathogenic factor in the preantibiotic era but accounted for only 10% of cases of mycotic aneurysms that were reported after 1965. Sower and Whelan [5] found that *Salmonella* was a common cause of mycotic aneurysms in patients with preexisting atherosclerosis, and they reported the first successful treatment of salmonella mycotic aneurysm. Since then, *Salmonella* species have been found to be associated with about 35% of all aortic infections [6]. In the past 20 years, there have been only sporadic case reports of salmonella mycotic aneurysms [7–10], and the general clinical picture is one of delayed diagnosis and high mortality.

In this article, we report our experience with aortic aneurysms. Most of these aneurysms were due to *Salmonella choleraesuis*, a particularly invasive serotype of *Salmonella* that is pathogenic for pigs [11].

## Materials and Methods

From January 1990 through December 1994, we collected information on all cases of salmonella mycotic aneurysms that occurred at the infectious diseases service of the Veterans General Hospital in Kaohsiung, Taiwan. This hospital has 900 beds and serves primarily veterans in a city of 2 million in the southwestern part of Taiwan. The families of veterans are also

eligible for care. About 75% of the patients admitted to Veterans General Hospital are men. All patients suspected of having an infectious disease are admitted to the 42-bed infectious diseases service.

The diagnosis of salmonella mycotic aneurysm was made if blood culture was positive for *Salmonella* and there was surgical or autopsy confirmation of a mycotic aneurysm or if a mycotic aneurysm was found at surgery or autopsy and a culture of an aortic specimen yielded *Salmonella*. Since we suspected that some patients with salmonella mycotic aneurysms may not have been admitted to our service, we reviewed the records of the microbiology laboratory to find all cases of salmonella bacteremia; we found 94 cases in adults and 20 cases in children younger than 14 years of age. We reviewed the charts of all these patients to find additional cases of mycotic aneurysms.

## Results

Sixteen cases fulfilled the definition of mycotic aneurysm. The rate of mycotic aneurysms was 17% among adults and 35% (15 of 43) among individuals older than 65 years of age. Data on all the cases of salmonella mycotic aneurysms are summarized in tables 1 and 2.

Of the 16 confirmed cases, 15 occurred in men. The mean age of the patients was 71 years (range, 64–79 years). Most patients presented with fever and either back or chest pain. Two patients had bloody stool. Histories or physical examinations did not reveal any pathognomonic characteristics for mycotic aneurysms. Therefore, it is not surprising that only two patients were suspected of having a mycotic aneurysm at the time of admission. Admitting diagnoses included fever of unknown origin, lung cancer, suspected dissecting aneurysm, relapsing salmonella bacteremia, and bloody stool of unknown cause. In most cases, the true diagnosis was not considered until the blood culture yielded *Salmonella*.

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**Table 1.** Summary of clinical features of patients with mycotic aneurysms due to *Salmonella*.

Case no.	Age (y)/sex	Symptom(s)	Initial diagnosis	Organism isolated	Culture specimen(s)	Aneurysm position	Surgical intervention	Underlying condition(s)
1	69/M	Chills, fever for 2 d	Recurrent salmonellosis	<i>Salmonella choleraesuis</i>	Aneurysm, blood	Abdominal aorta	In situ grafting	Atherosclerosis, diabetes mellitus
2	67/M	Fever, left flank pain for 14 d	Psoas muscle abscess	<i>S. choleraesuis</i>	Aneurysm, blood	Abdominal aorta	In situ grafting	None
3	72/M	Fever for 4 d	Fever, cause undetermined	<i>S. choleraesuis</i>	Aneurysm, blood	Thoracic aorta	None	Atherosclerosis, liver cirrhosis, hepatoma
4	69/M	Fever, chest pain for 20 d	Suspected dissecting aneurysm	<i>S. choleraesuis</i>	Aneurysm, blood	Thoracic aorta	In situ grafting	Atherosclerosis
5	79/M	Fever, abdominal pain for 14 d	Abdominal pain, cause unknown	<i>Salmonella enteritidis</i> group D	Aneurysm, blood	Abdominal aorta	In situ grafting	Atherosclerosis
6	75/M	Tarry stool for 14 d	Bloody stool, cause unknown	<i>Salmonella</i> species	Blood	Left iliac artery	None	Liver cirrhosis
7	64/M	Chest pain, hemoptysis for 21 d	Suspected lung cancer	<i>S. choleraesuis</i>	Aneurysm, blood	Aortic arch	In situ grafting	None
8	81/M	Chest pain, hoarseness for 3 mo	Suspected dissecting aneurysm	<i>S. choleraesuis</i>	Aneurysm, blood	Thoracic aorta	In situ grafting	None
9	72/M	Low-back pain for 30 d	Salmonellosis	<i>S. choleraesuis</i>	Aneurysm, blood	Superior mesenteric artery	In situ grafting	Diabetes mellitus
10	67/M	Fever, abdominal pain for 10 d	Suspected legionella pneumonia	<i>S. enteritidis</i> group B	Aneurysm, blood	Abdominal aorta	In situ grafting	None
11	69/M	Abdominal pain, fever for 14 d	Mycotic aneurysm	<i>S. enteritidis</i> group B	Aneurysm, blood	Abdominal aorta	In situ grafting	Atherosclerosis, diabetes mellitus
12	68/M	Abdominal pain, fever for 30 d	Mycotic aneurysm	<i>S. choleraesuis</i>	Aneurysm, blood	Abdominal aorta	In situ grafting	Liver cirrhosis
13	67/M	Abdominal pain, bloody stool for 2 w	Bloody stool, cause unknown	<i>S. enteritidis</i> group B	Ascites, blood	Abdominal aorta	None	Atherosclerosis
14	69/M	Abdominal pain for 10 d	Fever, cause undetermined	<i>S. enteritidis</i> group B	Aneurysm, blood	Abdominal aorta	Axillobifemoral bypass surgery	Diabetes mellitus
15	76/M	Fever for 30 d	Fever, cause undetermined	<i>S. choleraesuis</i>	Aneurysm, blood	Abdominal aorta	In situ grafting	None
16	70/F	Left-flank pain, fever for 4 mo	Salmonellosis	<i>S. choleraesuis</i>	Aneurysm, blood	Thoracic-abdominal aorta	In situ grafting	Atherosclerosis, liver cirrhosis

Cultures of blood from all the patients were positive. The most common *Salmonella* serotype isolated in this case series was *S. choleraesuis*, which was recovered from 10 patients. This organism was identified on the basis of typical biochemical reactions and serogrouping. Other *Salmonella* species were isolated from six patients; these six isolates were not serotyped, but five were grouped with use of commercial antisera. The abdominal aorta was infected in 10 of 16 cases; four patients had thoracic aneurysms, and two patients had large-artery infections. Predisposing conditions included diabetes mellitus in four patients and liver cirrhosis in four patients.

Most patients underwent gallium-67 scanning, but scans of only two patients suggested mycotic aneurysms. In contrast, in all definite cases, CT was positive, usually revealing sacculated or lobulated aneurysms that were often surrounded by an enhancing inflammatory mass. In some patients, the mass con-

tained gas. In two cases, aortography was done, and these films showed saccular aneurysms.

Thirteen of the patients underwent surgery, and nine of these patients survived. Three patients received only medical therapy because of their poor condition, and they all died. Surgery consisted of primary resection of the infected aorta and interposition of a knitted, gel seal graft in all cases but one (case 14). Surgery was delayed for  $\geq 1$  week after the diagnosis was made for patients whose conditions were medically stable because the surgeons found it easier to create a primary anastomosis after a course of antibiotic treatment. Twelve patients were treated with ceftriaxone; one, with ciprofloxacin; one, with ampicillin; one, with cotrimoxazole; and one, with cefazolin. All nine patients who received a graft and ceftriaxone therapy survived. After surgery, most patients received therapy with an oral antimicrobial agent for 3 months to 1 year. No relapses occurred in a 6- to 12-month

**Table 2.** Summary of clinical features of patients with mycotic aneurysms due to *Salmonella*.

Case no.	Preoperation diagnosis	Duration (d) of preoperation treatment	Diagnostic method	Antibiotic, duration of treatment after operation	Complication	Result	Duration of follow-up
1	Yes	2	CT	Ceftriaxone, 24 d	None	Survived	3 mo
2	Yes	2	CT	Ceftriaxone, 23 d	None	Survived	12 mo
3	Yes	<1	CT	Ceftriaxone, 11 d*	Rupture of aneurysm	Died	None
4	Yes	1	CT	Ceftriaxone, 30 d	Hypoxic encephalopathy	Died	None
5	Yes	1	CT	TMP-SMZ, 35 d	Intestinal obstruction	Survived	12 mo
6	Yes	<1	CT	Ampicillin, 18 d*	Rupture of aneurysm	Died	None
7	Yes	1	CT	Ceftriaxone, 30 d	Leakage of suture line	Died	None
8	Yes	7	CT	Ceftriaxone, 15 d	Leakage of graft	Died	None
9	Yes	1	CT, aortography	Ceftriaxone, 8 d	Death	Died	None
10	Yes	1	CT	Ceftriaxone, 30 d	None	Survived	12 mo
11	Yes	1	CT	Ceftriaxone, 30 d	Acute cholecystitis	Survived	12 mo
12	Yes	8	CT	Ceftriaxone, 30 d	Acute renal failure	Survived	12 mo
13	No	0	Exploratory laparotomy	Cefazolin, 13 d*	Gallbladder gangrene	Died	None
14	Yes	<1	CT	Ceftriaxone, 28 d	Ischemic myopathy	Survived	6 mo
15	Yes	7	CT	Ceftriaxone, 40 d	None	Survived	12 mo
16	Yes	8	CT, aortography	Ciprofloxacin, 30 d	Thoracic osteomyelitis	Survived	1 mo

NOTE. TMP-SMZ = trimethoprim-sulfamethoxazole.

\* These patients did not undergo surgical treatment.

follow-up. In seven of 13 cases, the pathologist confirmed the diagnosis of an infected atherosclerotic aneurysm.

## Discussion

While the number of typhoid infections in the world has dramatically decreased over the last 25 years, there has been a significant increase in the number of nontyphoidal infections and a parallel increase in the number of cases of salmonella aortitis [6]. *Salmonella* infection is still a major problem for public health. Gastroenteritis due to non-typhi *Salmonella* affects 30 people per 1 million population annually [12]. Transient bacteremia may be present in 10% of these patients [13]. It is presumably this bacteremia that results in localized extravascular infections such as osteomyelitis, septic arthritis, meningitis, and cardiovascular infections [14]. The sites of infection can be the carotid artery [15], heart valves [16], ventricular aneurysms [17, 18], vascular grafts, and thoracic and abdominal aortic aneurysms [7, 19–22].

What is the incidence of endovascular infection in patients with bacteremia? In 1978, Cohen et al. [23] found that endothelial infection occurred in 10 (9%) of 105 adults with salmonella bacteremia; this infection occurred in 25% of patients with salmonella bacteremia who were older than 50 years. In our study, 16 (17%) of 94 patients with salmonellosis had confirmed cases of mycotic aneurysms. If only patients older than 65 years were considered, the incidence rose to 35% (15 of 43).

The pathogenesis of mycotic aneurysms may include five different mechanisms [24]: septic embolization lodged in the vasa vasorum or vessel lumen; a contiguous inflammatory pro-

cess outside the vessel wall that extends to a nearby artery; inoculation of bacteria at the time of accidental arterial trauma; self-induced vascular manipulation or iatrogenic causes; and an intimal defect, such as an atherosclerotic plaque, that is seeded by concurrent bacteremia.

*Salmonella* organisms are particularly virulent pathogens that have a predilection for diseased arterial walls and may rarely infect healthy arterial intima, which is ordinarily highly resistant to bacterial encroachment [7]. We believe that our patients had preexisting atherosclerotic changes since pathological examination of a high percentage (seven of 13) of their resected aneurysms showed these changes. This belief is compatible with our postulation that salmonella bacteremia may preferentially infect atherosclerotic plaques.

When a patient has a preexisting arteriosclerotic aneurysm and *Salmonella* bacteremia, it should be kept in mind that an infected aortic aneurysm is highly possible. If CT does not provide a differential diagnosis, aortography is indicated [25, 26]. Most of our patients presented without distinctive clinical symptoms. If we would have reviewed the histories in detail, we could have found that most patients had back, abdominal, or chest pain (which is the most important clue for the diagnosis); however, these complaints are nonspecific. A detailed history should be obtained from patients with salmonella bacteremia who do not have concurrent diarrhea, and any symptoms of chest, abdominal, or back pain should be especially noted.

All of our patients but one were older than 65 years. Old age was a risk factor for an infected aortic aneurysm, especially an age of >65 years. Diabetes mellitus (25% of cases) and liver cirrhosis (25%) were the most frequently noted underlying

diseases, findings compatible with the recent report by Oskoui et al. [10], in which the rates of these conditions were 27% and 6%, respectively. When we analyzed these two underlying diseases as risk factors for patients with salmonella bacteremia, they were statistically insignificant ( $P = .57$ , diabetes mellitus;  $P = .79$ , liver cirrhosis). Although no conclusion could be made, both factors may accelerate the atherosclerotic changes of the major vessels.

*S. choleraesuis* was the most common pathogen (isolated in 62% of cases) in our series, which differs from the report by Oskoui et al. [10], in which 13% of the pathogens were *S. choleraesuis*. Pork is the major source of *S. choleraesuis* [11]. The distinguishing features of *S. choleraesuis* infection are the rarity of enteric disease but the high frequency of septicemia, metastatic manifestations, and repeated bouts of clinical disease due to survival of the organism outside the intestinal tract for several years [11, 22]. *S. choleraesuis* is one of a small number of non-typhi *Salmonella* species that have virulence plasmids [27]. These plasmids are highly associated with invasive infection in humans and animals [28, 29].

Most patients underwent gallium-67 scanning for detection of inflammatory lesions. It detected the presence of infected aortic aneurysms in only two patients who had a ruptured infected aneurysm and a massive inflammatory exudate over the periaortic area, respectively. There have been reports of successful use of gallium-67 scanning [30], but a mycotic aneurysm cannot be ruled out when a gallium scan is negative.

CT of the aorta was the chief diagnostic tool in this case series. The diagnostic features on CT included a periaortic soft-tissue density with rim enhancement; an eccentric, thickened wall with rapid growth; lack of calcium in the aneurysmal wall of the aorta; adjacent osteomyelitis of the vertebral spine; and gas in the perianeurysmal soft tissue [25, 26].

Aortography demonstrated saccular aneurysms arising eccentrically from the aortic wall. Differentiation from arteriosclerotic aneurysms depended on a nonfusiform appearance, an unusual location, and the rapidity of appearance [26]. Aortography is a crucial method for diagnosis of patients with an abdominal aneurysm and salmonella bacteremia.

The overall mortality rate among the patients with definite cases was 44% (seven of 16). Medical therapy alone was associated with a mortality rate of 100% (three of three patients). Surgical and medical therapy was associated with a success rate of 70% (nine of 13 patients). Most (12 of 13) of these patients underwent in situ grafting.

Some investigators [31, 32] recommend excision of the infective aneurysm, ligation of the aorta, drainage of the retroperitoneum, and remote bypass grafting as treatments of choice. In situ reconstruction of an aortic graft with aneurysmal resection has been reported [33, 34]. In our case series, 10 of 12 in situ graft reconstructions had good results, and the two deaths were suspected to be due to leakage of the graft. The good results could have been due to early diagnosis and prompt treatment with an effective antimicrobial agent. Most investiga-

tors favor immediate surgical intervention. We treated four patients for >1 week with appropriate antibiotic treatment after the diagnosis. After longer treatment before surgery, we found fewer adhesions, and debridement was easier. Therefore, longer treatment before surgical intervention could increase the success rate associated with in situ graft reconstruction.

The emergence of antibiotic-resistant *Salmonella* strains continues to increase worldwide [35]. Ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole have been the standard treatments of systemic salmonella infection. In our case series, the *Salmonella* organisms causing mycotic aneurysms were resistant to ampicillin (75%), chloramphenicol (75%), and trimethoprim-sulfamethoxazole (50%). It was therefore necessary to use new antimicrobial agents for the treatment of extraintestinal salmonella infections, such as third-generation cephalosporins or the new quinolones [36]. Thirteen of our patients received ceftriaxone treatment. In one case (case 16), ceftriaxone therapy was replaced by 4 weeks of ciprofloxacin therapy. There were no relapses after treatment. We conclude that third-generation cephalosporins and the new quinolones are new alternative drugs for the treatment of salmonella mycotic aneurysms.

The duration of antibiotic treatment after surgery was 21–40 days. Although there is no consensus on the exact duration of postoperative antibiotic therapy, most investigators still recommend at least 6 weeks [16, 37]. Most patients received therapy with an oral antimicrobial agent for 3–12 months. None of the patients relapsed, although longer or lifelong therapy is recommended for immunocompromised patients [38]. Although we did not recommend that our patients receive antibiotic treatment alone, the three patients who were treated only with antibiotics (ceftriaxone, ampicillin, and cefazolin, respectively) died. Therefore, we conclude that surgical resection of the infected aneurysm plus medical therapy is required for successful treatment.

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