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# Infective Endocarditis of the Aortic Valve with Anterior Mitral Valve Leaflet Aneurysm

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*Mitral valve leaflet aneurysm is a rare and potentially devastating complication of aortic valve endocarditis. We report the case of a 48-year-old man who had endocarditis of the native aortic valve and a concomitant aneurysm of the anterior mitral valve leaflet. Severe mitral regurgitation occurred after the aneurysm perforated. The patient showed no signs of heart failure and completed a 6-week regimen of antibiotic therapy before undergoing successful aortic and mitral valve replacement. In addition to the patient's case, we review the relevant medical literature. (Tex Heart Inst J 2016;43(4):345-9)*

**Key words:** Aneurysm, infected/etiology; endocarditis, bacterial/complications/diagnosis; heart aneurysm/microbiology/surgery; heart valve diseases/diagnosis/etiology; heart valve prosthesis implantation; mitral valve/microbiology/pathology/surgery; rare diseases; streptococcal infections/complications/diagnosis; treatment outcome

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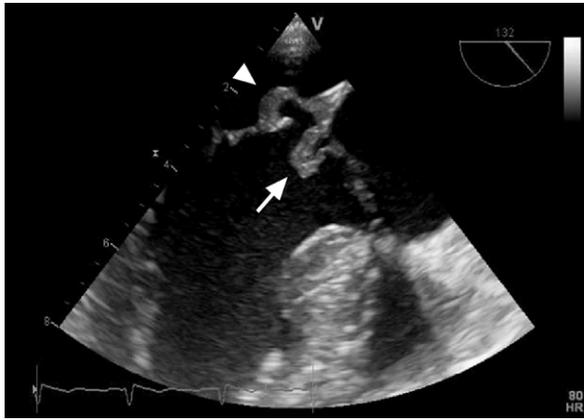
**M**itral valve (MV) aneurysms are rare and are most often associated with infective endocarditis (IE) of the aortic valve (AV). Possible mechanisms include regurgitant infectious flow from the AV, direct contact with AV vegetation, and direct spread across adjacent structures, such as the mitral–aortic intervalvular fibrous body.<sup>1,2</sup> Such an aneurysm poses a threat for septic embolization or aneurysm rupture. Acute, severe MV regurgitation and hemodynamic deterioration can follow, often necessitating urgent surgery.<sup>3</sup> Current guidelines on the optimal timing of surgery in IE suggest urgent treatment when signs of uncontrolled infection are present, including abscess formation, fistula formation, enlarging vegetation, and pseudoaneurysm formation.<sup>4</sup> However, there is no consensus about optimal treatment when MV-leaflet aneurysms form. To our knowledge, only 29 cases of MV-leaflet aneurysm associated with IE have been reported (Table 1<sup>3,5-12</sup>), including that of our patient. Of these patients, 75% underwent surgical treatment, usually because of severe MV regurgitation caused by perforation of the MV aneurysm.

We present here a case of native AV endocarditis complicated by anterior MV-leaflet (AMVL) aneurysm formation and subsequent severe MV regurgitation caused by aneurysm perforation. In addition, we review the relevant medical literature.

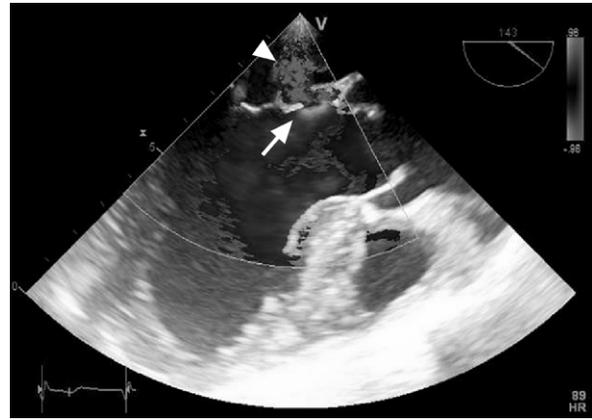
## Case Report

In August 2014, a 48-year-old man was referred to our center. He presented with a 2-month history of fever, fatigue, and dry cough. Blood analysis yielded a moderately elevated C-reactive protein (CRP) level and white blood cell (WBC) count. An electrocardiogram revealed a prolonged PR interval. A chest radiograph showed nothing unusual. The patient reported no obvious risk factors for IE. A transthoracic echocardiogram (TTE) revealed a bicuspid AV with a small vegetation (<1 cm) accompanied by severe aortic regurgitation. In addition, vegetations were observed on the AMVL, with minimal mitral regurgitation. The patient's left ventricular function was normal. *Streptococcus gordonii* species was isolated from blood cultures, and antibiotic therapy with intravenous gentamicin and benzylpenicillin was initiated. After 4 days of therapy, a transesophageal echocardiogram (TEE) showed an aneurysm of the noncoronary cusp of the AV, an AMVL aneurysm, and trace mitral insufficiency (Fig. 1). The patient showed no signs of heart failure and his CRP level and WBC count were decreasing, so we decided to continue the antibiotic therapy and to delay surgery. We closely monitored the patient by means of repeated blood analyses and TTE.

Despite weeks of antibiotic therapy, the patient experienced fever, pain in the left thigh, and a higher CRP level and WBC count. A TTE revealed a newly developed



**Fig. 1** Transesophageal echocardiogram shows an aneurysm of the noncoronary cusp of the aortic valve (arrow) and an aneurysm of the anterior mitral valve leaflet (arrowhead).



**Fig. 2** Transthoracic echocardiogram shows rupture of the anterior mitral valve leaflet aneurysm (arrow) with an eccentric regurgitant jet (arrowhead).

perforation of the AMVL aneurysm, accompanied by severe mitral regurgitation with an eccentric regurgitant jet (Fig. 2). No new vegetations were observed. The results of a positron emission tomographic-computed tomographic scan revealed a peripheral embolism in the deep femoral artery; the heart showed no signs of inflammation or failure. After a few days, the patient's CRP level and WBC count decreased, and the pain in his left thigh resolved. He underwent surgery after completing a 6-week regimen of antibiotic therapy.

Intraoperatively, a large, ruptured aneurysm was noticed on the AMVL, accompanied by signs of active inflammation (Fig. 3). Successful MV repair was unlikely, so we replaced the MV with a 29-mm mechanical prosthesis (St. Jude Medical, Inc.; St. Paul, Minn). The bicuspid AV was severely damaged, and swelling of the aortic annulus was noted without active involvement of the intervalvular fibrous body. We replaced the AV with a 21-mm mechanical prosthesis (St. Jude Medical). Perioperative TEE showed excellent prosthetic-valve function without paravalvular leakage. Intraoperative cultures were negative, and results of a pathologic examination suggested a resolving infection. The patient recovered uneventfully and was discharged to another institution to complete the postoperative antibiotic regimen (6 wk benzylpenicillin and 2 wk gentamicin). At his 6-month evaluation, the patient had no signs of recurrent infection.

## Discussion

Our patient had native AV endocarditis, accompanied by aneurysms of the AMVL and the noncoronary cusp of the AV. Although the AMVL aneurysm perforated after several weeks of therapy, no signs of heart failure were observed during the course of treatment. The patient underwent successful surgery after he had completed a full 6-week course of antibiotic therapy.



**Fig. 3** Intraoperative photograph shows the mitral valve and the aneurysm of the inflamed anterior mitral leaflet (arrow). Rupture of the aneurysm is seen (arrowhead).

Mitral valve aneurysms are rare, with an incidence of 0.2% to 0.3% on echocardiographic examinations in general.<sup>5,11</sup> Of the several causative mechanisms reported for MV aneurysm (among them connective-tissue disorders, pseudoxanthoma elasticum, and myxomatous valve degeneration), IE is the most prevalent.<sup>5,8,11</sup> To our knowledge, only 28 previous cases of MV aneurysms caused by IE have been reported (Table I).

Anterior MV-leaflet aneurysms in IE develop as infection progresses, involves the MV leaflet, forms an abscess, and causes local weakening of underlying tissue. This last is responsible for tissue-bulging and eventually aneurysm formation.<sup>5</sup> Further destruction of leaflet tissue often leads to perforation with accompanying regurgitation and possibly peripheral embolization.<sup>3</sup> Aneurysm perforation occurred in 72% of the reported cases. Guler and colleagues<sup>11</sup> affirmed that larger aneurysm size does not necessarily correlate with a higher risk of perforation. The moment of aneurysm perforation might be a crucial point for peripheral embolization, as in our patient when the timing of peripheral embolization correlated with echocardiographic evidence of aneurysm perforation. Peripheral embolization was seen in 18.2% (2/11) of the patients who had perforated aneurysms (Table I).

**TABLE I.** Reported Cases of Aortic Valve Infective Endocarditis with Mitral Leaflet Aneurysm

Reference	Pt. No.	Age (yr), Sex	Heart Failure	Embolism	Perforation	Infective Organism	Mitral Leaflet	AR	MR	Surgery
Vilacosta I, et al. <sup>5</sup> (1999)	1	24, M	Yes	No	Yes	Culture-negative	Anterior	Severe	Severe	MVR*
	2	22, M	No	Yes	No	<i>Staphylococcus aureus</i>	Anterior	Moderate	None	None
	3	22, M	Yes	No	Yes	<i>S. aureus</i>	Posterior	None	Moderate	None
	4	33, F	Yes	No	Yes	Culture-negative	Anterior	None	Severe	MVR*
	5	40, F	No	No	Yes	Culture-negative	Posterior	None	Severe	MVR*
	6	50, M	Yes	No	Yes	Q fever	Anterior	Severe	Severe	MVR*
	7	55, F	Yes	No	Yes	<i>Enterococcus</i>	Anterior	Severe	Severe	MVR*
	8	22, M	Yes	No	No	<i>S. aureus</i>	Anterior	Severe	None	None
	9	40, M	Yes	No	Yes	<i>S. aureus</i>	Anterior	Severe	Severe	MVR*
	10	55, F	Yes	Yes	Yes	<i>Enterococcus</i>	Anterior	Moderate	Severe	MVR*
	11	65, F	No	No	No	Culture-negative	Anterior	None	None	None
Marcos-Alberca P, et al. <sup>6</sup> (2000)	12	78, M	Yes	No	No	<i>Streptococcus sanguis</i>	Anterior	Severe	None	AVR, MVP
Gao C, et al. <sup>7</sup> (2004)	13	37, M	Yes	No	No	Culture-negative	Anterior	Severe	Moderate	AVR, MVR
Ruparelia N, et al. <sup>8</sup> (2011)	14	42, M	No	No	NR	Coagulase-negative <i>Staphylococcus</i>	Anterior	Severe	Mild	AVR, MVR
Stechert MM, et al. <sup>1</sup> (2012)	15	50, M	Yes	NR	No	<i>Streptococcus viridans</i>	Anterior	Severe	Moderate	AVR, MVP
Subban V, et al. <sup>9</sup> (2012)	16	28, M	Yes	NR	NR	Culture-negative	Posterior	NR	Severe	Died before operation

*Continues on next page*

The optimal timing of surgery in IE is a matter of debate. Three indications for urgent surgical intervention are large vegetations posing a threat of embolization, signs of heart failure, and signs of uncontrolled infection.<sup>4</sup> In MV aneurysm without the aforementioned observations, there is little consensus on a preferred course of therapy. In the reported cases of IE with MV aneurysms (Table I), most patients (75%) ultimately underwent surgical treatment, although the timing of surgery was usually unclear. Ruparelia and associates<sup>8</sup> suggested planning surgery as soon as the abnormality is observed, in order to prevent aneurysm rupture, the development of severe mitral regurgitation, and embolization. On the other hand, Vilacosta and co-authors<sup>5</sup> suggested the possibility of conservative management, with surgical intervention only in case of cardiac deterioration. Other authors have recommended a similar approach.<sup>7,10,12</sup>

Early surgery for IE has been advocated in general. The authors of several case series have reported that, in comparison with conventional treatment, early surgical treatment yields improved long-term outcomes and less risk of peripheral embolization.<sup>13-16</sup> This was verified in a small randomized clinical trial that included 76

patients who had left-sided IE and vegetations >10 mm in size.<sup>13</sup> No differences were found in 6-month mortality rates. However, early surgery (within 48 hr after randomization) was associated with a significantly lower embolic-risk rate (21% vs 3%).<sup>13</sup> Funakoshi and colleagues<sup>14</sup> retrospectively studied 212 patients with left-sided IE who had undergone surgery. The in-hospital mortality rate (5% vs 13%) was lower after early surgery versus late surgery, and the respective 7-year survival rate (94% vs 82%) was higher. However, the above studies chiefly included patients who had large vegetations—a known risk factor for repeated embolization. Furthermore, patients were usually divided into early-surgical and conventional-treatment groups; the conventional groups were heterogeneous, including patients who underwent late surgery and patients who were treated conservatively. Few studies have actually compared outcomes between early and late surgical intervention. Funakoshi and colleagues<sup>14</sup> did not find benefits in early surgical intervention when comparing only patients who underwent surgery (late surgery was defined as >2 wk after the initial diagnosis). Statistically significant decreases in aortic root surgery (1% vs 7%) and shorter aortic cross-clamp times (106 vs 132

**TABLE I Continued.** Reported Cases of Aortic Valve Infective Endocarditis with Mitral Leaflet Aneurysm

Reference	Pt. No.	Age (yr), Sex	Heart Failure	Embolism	Perforation	Infective Organism	Mitral Leaflet	AR	MR	Surgery
Jackson G, et al. <sup>3</sup> (2013)	17	35, M	Yes	Yes	NR	<i>Streptococcus sanguinis</i>	Anterior	Severe	Mild	Aortic root repair, AVR, MVP
Kharwar RB, et al. <sup>10</sup> (2014)	18	30, M	Yes	No	Yes	<i>S. aureus</i>	Anterior	Severe	Severe	AVR, MVP
Guler A, et al. <sup>11</sup> (2014)	19	48, M	NR	NR	Yes	<i>S. viridans</i>	Anterior	Moderate	Severe	AVR, MVR
	20	66, F	NR	NR	Yes	Culture-negative	Anterior	Severe	Severe	AVR, MVR
	21	26, M	NR	NR	Yes	<i>Enterococcus</i>	Anterior	None	Severe	None
	22	32, M	NR	NR	Yes	<i>S. aureus</i>	Anterior	Severe	Severe	AVR, MVR
	23	21, F	NR	NR	No	<i>S. aureus</i>	Anterior	Severe	Trace	AVR, MVR, TVP
	24	69, M	NR	NR	Yes	Culture-negative	Anterior	Mild	Moderate	None
	25	64, M	NR	NR	Yes	<i>S. aureus</i>	Posterior	None	Severe	MVR
	26	59, M	NR	NR	Yes	<i>S. aureus</i>	Anterior	Moderate	Severe	AVR, MVR
	27	57, M	NR	NR	Yes	Culture-negative	Anterior	Mild	Severe	AVR, MVR
Eiseman MS, et al. <sup>12</sup> (2014)	28	61, M	No	No	Yes	<i>S. viridans</i>	Anterior	Moderate	Severe	AVR, MVR
Current case	29	48, M	No	Yes	Yes	<i>Streptococcus gordonii</i>	Anterior	Severe	Severe	AVR, MVR

AR = aortic regurgitation; AVR = aortic valve replacement; F = female; M = male; MR = mitral regurgitation; MVP = mitral valve plasty; MVR = mitral valve replacement; NR = not reported; Pt = patient; TVP = tricuspid valve plasty

\*Vilacosta and colleagues<sup>5</sup> reported that 6 of 8 surgical patients (including one with no clinical history of infective endocarditis, not included in Table I) also needed AVR. The authors did not specify the patients to whom this applied.

min) were observed after late versus early surgery. This might indicate technical difficulties associated with weak and infected tissue when operating in the early phase of endocarditis. Furthermore, in a retrospective study of 129 patients who had left-sided IE, late surgery (>11 d after diagnosis) yielded a lower 6-month mortality rate.<sup>17</sup> The conclusions were not statistically significant; however, the hazard ratio was in the protective direction for late surgery. The lowest hazard ratio was reported for the patients who underwent surgery latest after diagnosis.

When planning surgery in complicated aortic valve IE, surgeons should consider possible extravalvular involvement, in particular the aortic root and the mitral–aortic intervalvular fibrous body. In our patient, this would have necessitated an extensive operation, including aortic root and MV replacement with reconstruction of the intervalvular fibrous body. This high-risk procedure has a reported intraoperative mortality rate of 10% to 16%.<sup>18,19</sup> Antibiotic therapy before surgery enabled our patient’s intervalvular fibrous body to be preserved. We think that simplifying operations is an important benefit of presurgical antibiotic therapy, be-

cause less extensive surgery is clearly associated with less operative risk. Given the extent of abnormalities associated with MV-leaflet aneurysm development, surgical MV replacement is often necessary; however, repair should be performed if possible, because of the lower risk of recurrent IE.<sup>14,20</sup>

The probability of peripheral embolism in AMVL aneurysm seems to be reasonably low, given its reported occurrence (Table I). The investigators of 1,456 cases of IE reported an embolization rate of 34.3%; most embolic events occurred before or during the first week of antibiotic therapy. After one week of therapy, surgery did not seem to provide sufficient benefit in preventing embolization.<sup>21</sup> In our patient, who had a good response to therapy, the risk of peripheral embolism was less than that of extensive surgery.

Conservative management before surgical intervention for IE with AMVL aneurysm, with or without perforation, can be both safe and beneficial, enabling healing and recovery of infected tissue and possibly avoiding unnecessarily extensive surgical procedures. However, when signs of heart failure are present, urgent surgery becomes advisable.

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