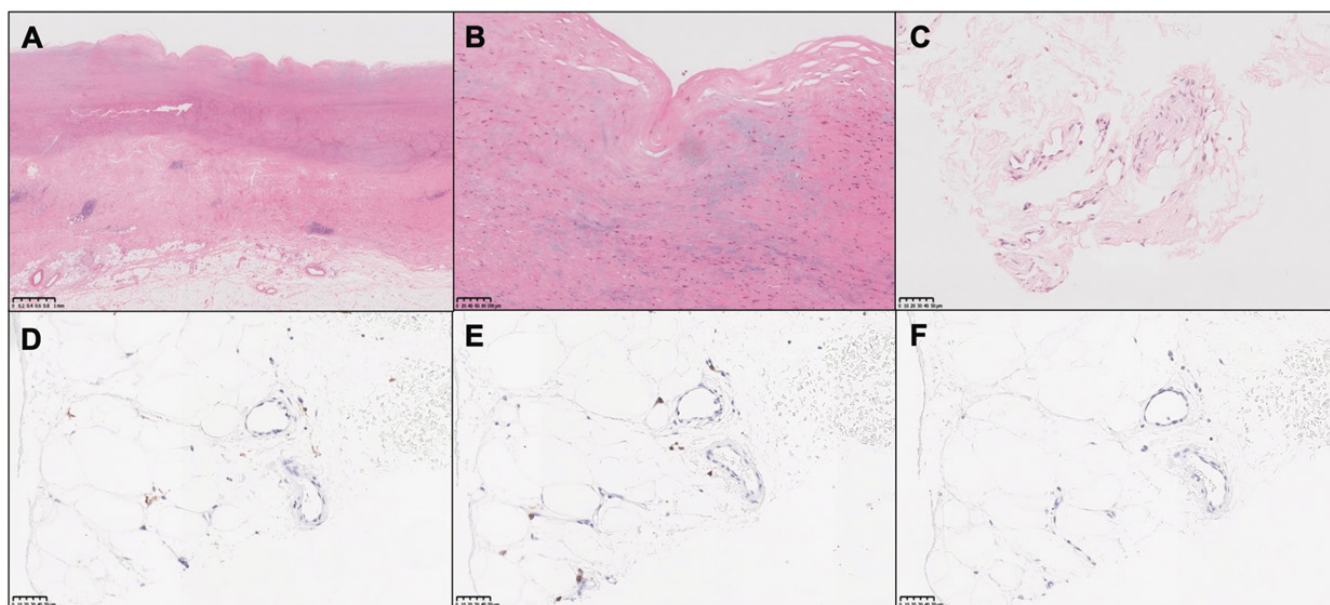
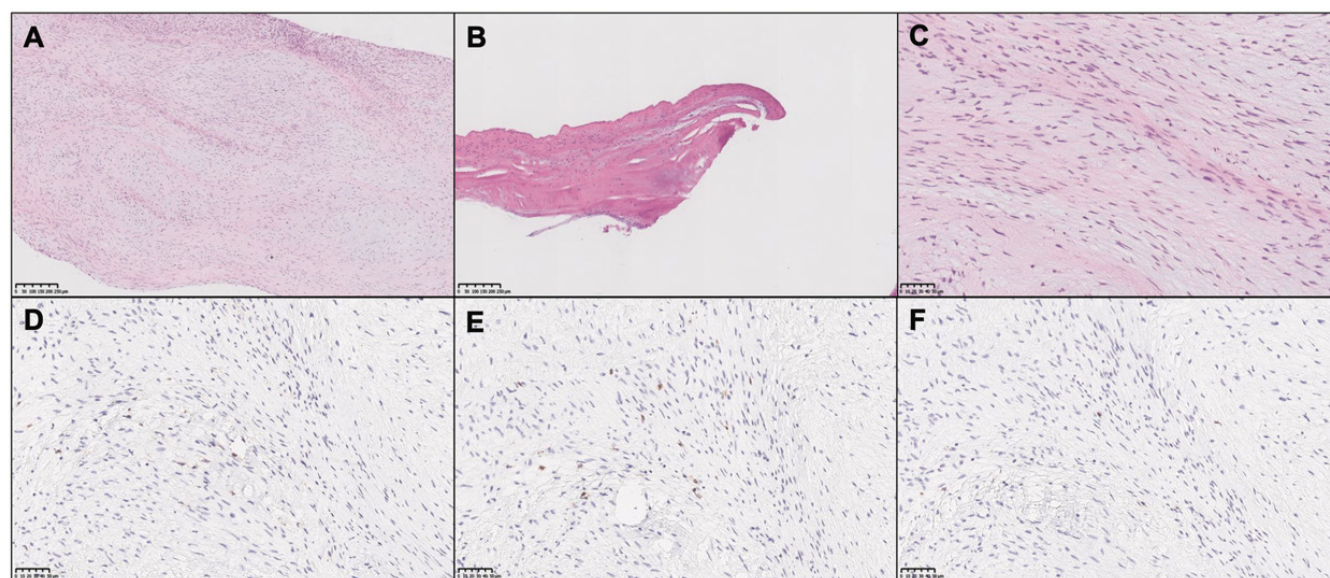




Supplementary Fig. S1. Representative images of the aortic wall in remission patients with severe AR caused by BS.

A) Low power shows lymphocytes focally aggregate in the severely fibrous adventitia (HE); **B)** High power shows mild degeneration in the fibrous intima (HE); **C-F)** High power shows a few lymphocytes scattered in the adventitia; **C)** HE; **D)** CD4⁺; **E)** CD8⁺ and **F)** CD20⁺, at the corresponding location in the serial sections.



Supplementary Fig. S2. Representative images of the aortic valve in remission patients with severe AR caused by BS.

A) Low power shows mild mucoid degeneration (HE); **B)** Fibrous with mild-to-moderate mucoid degeneration (HE); **C-F)** Lymphocytes imperceptibly scattered in the mild mucoid degeneration background; **C)** HE; **D)** CD4⁺; **E)** CD8⁺ and **F)** CD20⁺ at the corresponding location in the serial sections.

Supplementary Table S1. Pathological parameter of the aortic valve in patients with severe AR caused by BS.

Pathological parameter of aortic valve			Active BS	Remission BS
Inflammatory cell infiltration			5/5 (100%)	13/13 (100%)
HE assessment	Cell type	Neutrophils	3/5 (60%)*	1/13 (7.7%)*
		Eosinophils	1/5 (20%)	1/13 (7.7%)
		Lymphocytes	5/5 (100%)	13/13 (100%)
		Plasma cells	0/5 (0%)	2/13 (15.4%)
		Distribution	Diffuse	4/13 (30.8%)
IHC assessment	CD4+ T cell infiltration	Scattered/Focal	1/5 (20%)	9/13 (69.2%)
			5/5 (100%)	5/5 (100%)
		Distribution	Diffuse	1/5 (20%)
	CD8+ T cell infiltration	Scattered/Focal	2/5 (40%)	4/5 (80%)
			4/5 (80%)	4/5 (80%)
		Distribution	Diffuse	3/4 (75%)
	CD20+ B cell infiltration	Scattered/Focal	1/4 (25%)	3/4 (75%)
			4/5 (80%)	2/5 (40%)
		Distribution	Diffuse	0/4 (0%)
	CD68+ macrophage infiltration	Scattered/Focal	4/4 (100%)	2/2 (100%)
			4/5 (80%)	3/5 (60%)
		Distribution	Diffuse	0/3 (0%)
	Scattered/Focal	1/4 (25%)	3/3 (100%)	
Mucoïd degeneration			2/5 (40%)	8/13 (61.5%)
Neovascularisation			4/5 (80%)	7/13 (53.9%)
Fibrous tissue proliferation			5/5 (100%)	13/13 (100%)
Calcification			1/5 (20%)	2/13 (15.4%)
Necrosis			4/5 (80%)	6/13 (46.2%)

HE: haematoxylin and eosin; IHC: immunohistochemistry. *indicates a statistically significant difference between active BS and remission BS, with $p < 0.05$.

Supplementary Table S2. Pathological parameter of the aortic wall in BS patients with or without preoperatively biologics.

Pathological parameter of aortic wall			Intima		Media		Adventitia	
			GCs ± Immunosuppr.	GCs+ Immunosuppr. + Biologics	GCs ± Immunosuppr.	GCs+ Immunosuppr. + Biologics	GCs ± Immunosuppr. ressan	GCs+ Immunosuppr. + Biologics
Inflammatory cell infiltration			12/14 (85.7%)	5/5 (100%)	14/14 (100%)	5/5 (100%)	13/14 (92.9%)	5/5 (100%)
HE assessment	Cell type	Neutrophils	0/12 (0%)	0/5 (0%)	1/14 (7.1%)	0/5 (0%)	8/13 (61.6%)	1/5 (20%)
		Eosinophils	0/12 (0%)	0/5 (0%)	0/14 (0%)	0/5 (0%)	9/13 (69.2%)	2/5 (40%)
		Lymphocytes	12/12 (100%)	5/5 (100%)	14/14 (100%)	5/5 (100%)	13/13 (100%)	5/5 (100%)
		Plasma cells	0/12 (0%)	0/5 (0%)	0/14 (0%)	0/5 (0%)	13/13 (100%)	5/5 (100%)
		Distribution	Diffuse	3/12 (25%)	0/5 (0%)	1/14 (7.1%)	0/5 (0%)	4/13 (30.8%)
	Scattered/Focal	9/12 (75%)	5/5 (100%)	13/14 (92.9%)	5/5 (100%)	9/13 (69.2%)	5/5 (100%)	
	IHC assessment	CD4+ T cell infiltration		8/14 (57.2%)	2/5 (40%)	6/14 (42.9%)	1/5 (20%)	14/14 (100%)
Distribution		Diffuse	2/8 (25%)	1/2 (50%)	2/6 (33.3%)	0/1 (0%)	8/14 (57.1%)*	0/5 (0%)*
		Scattered/Focal	6/8 (75%)	1/2 (50%)	4/6 (66.7%)	1/1 (100%)	6/14 (42.9%)	5/5 (100%)
CD8+ T cell infiltration		12/14 (85.7%)	4/5 (80%)	10/14 (71.4%)	3/5 (60%)	12/14 (85.7%)	5/5 (100%)	
Distribution		Diffuse	1/12 (8.3%)	1/4 (25%)	1/10 (10%)	0/5 (0%)	6/12 (50%)	1/5 (20%)
		Scattered/Focal	11/12 (91.7%)	3/4 (75%)	9/10 (90%)	3/3 (100%)	6/12 (50%)	4/5 (80%)
CD20+ B cell infiltration		1/14 (7.1%)	0/5 (0%)	3/14 (21.4%)	0/5 (0%)	12/14 (85.7%)	4/5 (80%)	
Distribution		Diffuse	0/1 (0%)	/ 0/3 (0%)	/	0/12 (0%)	0/4 (0%)	/
		Scattered/Focal	1/1 (100%)	/ 3/3 (100%)	/	12/12 (100%)	4/4 (100%)	/
CD68+ macrophage infiltration		5/14 (35.7%)	2/5 (40%)	4/14 (28.6%)	1/5 (20%)	8/14 (57.2%)*	0/5 (0%)*	
Distribution		Diffuse	0/5 (0%)	0/2 (0%)	0/4 (0%)	0/1 (0%)	2/8 (25%)	/
		Scattered/Focal	5/5 (100%)	2/2 (100%)	4/4 (100%)	1/1 (100%)	6/8 (75%)	/
Muroid degeneration			9/14 (64.3%)	5/5 (100%)	7/14 (50%)	4/5 (80%)	1/14 (7.1%)	1/5 (20%)
Fibrous tissue proliferation			12/14 (85.7%)	5/5 (100%)	14/14 (100%)	5/5 (100%)	12/14 (85.7%)	5/5 (100%)
Vasa vasorum muroid degeneration			/	/	/	/	12/14 (85.7%)*	1/5 (20%)*
Neurofibril thickening			/	/	/	/	10/14 (71.4%)	1/5 (20%)
Granulation tissue			/	/	/	/	6/14 (42.9%)	0/5 (0%)

HE: haematoxylin and eosin; IHC: immunohistochemistry; /: not applicable. *indicates a statistically significant difference between active BS and remission BS, with $p < 0.05$.

Supplementary Table S3. Pathological parameter of the aortic valve in BS patients with or without preoperatively biologics.

Pathological parameter of aortic valve			GCs ± immunosuppressant	GCs + immunosuppressant + biologics
Inflammatory cell infiltration			14/14 (100%)	4/4 (100%)
HE assessment	Cell type	Neutrophils	4/14 (28.6%)	0/4 (0%)
		Eosinophils	2/14 (14.3%)	0/4 (0%)
		Lymphocytes	14/14 (100%)	4/4 (100%)
		Plasma cells	2/14 (14.3%)	0/4 (0%)
		Diffuse	7/14 (50%)	1/4 (25%)
	Distribution	Scattered/Focal	7/14 (50%)	3/4 (75%)
		IHC assessment		
CD4+ T cell infiltration		8/8 (100%)	2/2 (100%)	
	Distribution	Diffuse	4/8 (50%)	0/2 (0%)
		Scattered/Focal	4/8 (50%)	2/2 (100%)
CD8+ T cell infiltration		7/8 (87.5%)	1/2 (50%)	
	Distribution	Diffuse	4/7 (57.1%)	0/1 (0%)
		Scattered/Focal	3/7 (42.9%)	1/1 (100%)
CD20+ B cell infiltration		6/8 (75%)	0/4 (0%)	
	Distribution	Diffuse	0/6 (0%)	/
		Scattered/Focal	6/6 (100%)	/
CD68+ macrophage infiltration		6/8 (75%)	1/2 (50%)	
	Distribution	Diffuse	3/6 (50%)	0/1 (0%)
		Scattered/Focal	3/6 (50%)	1/1 (100%)
Mucoïd degeneration			6/14 (42.9%)	4/4 (100%)
Fibrous tissue proliferation			14/14 (100%)	4/4 (100%)
Calcification			3/14 (21.4%)	0/4 (0%)
Necrosis			10/14 (71.4%)*	0/4 (0%)*

HE: haematoxylin and eosin; IHC: immunohistochemistry; /: not applicable. *indicates a statistically significant difference between active BS and remission BS, with $p < 0.05$.