The Phantom Menace

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EVERY SAGA HAS A BEGINNING
STAR WARS
EPISODE I
THE PHANTOM MENACE

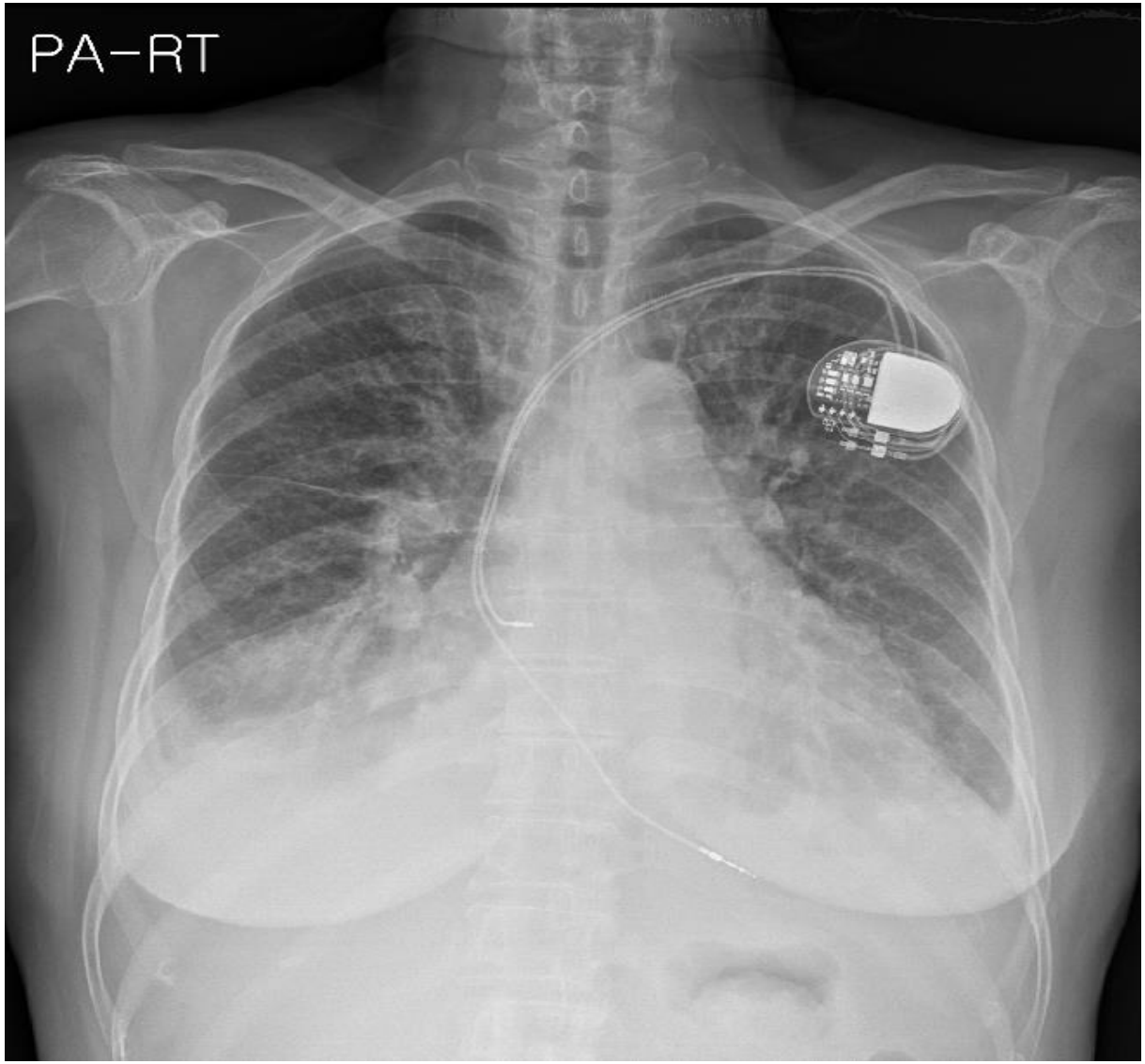
F/59

- **Chief complaint**
  - **Dyspnea (NYHA III)**
  - **Orthopnea**
  - **Dizziness**
- **Vital sign**
  - **BP 99/70mmHg, HR 95/min, RR 20/min**
- **Physical exam**
  - **Both leg edema G II/IV**

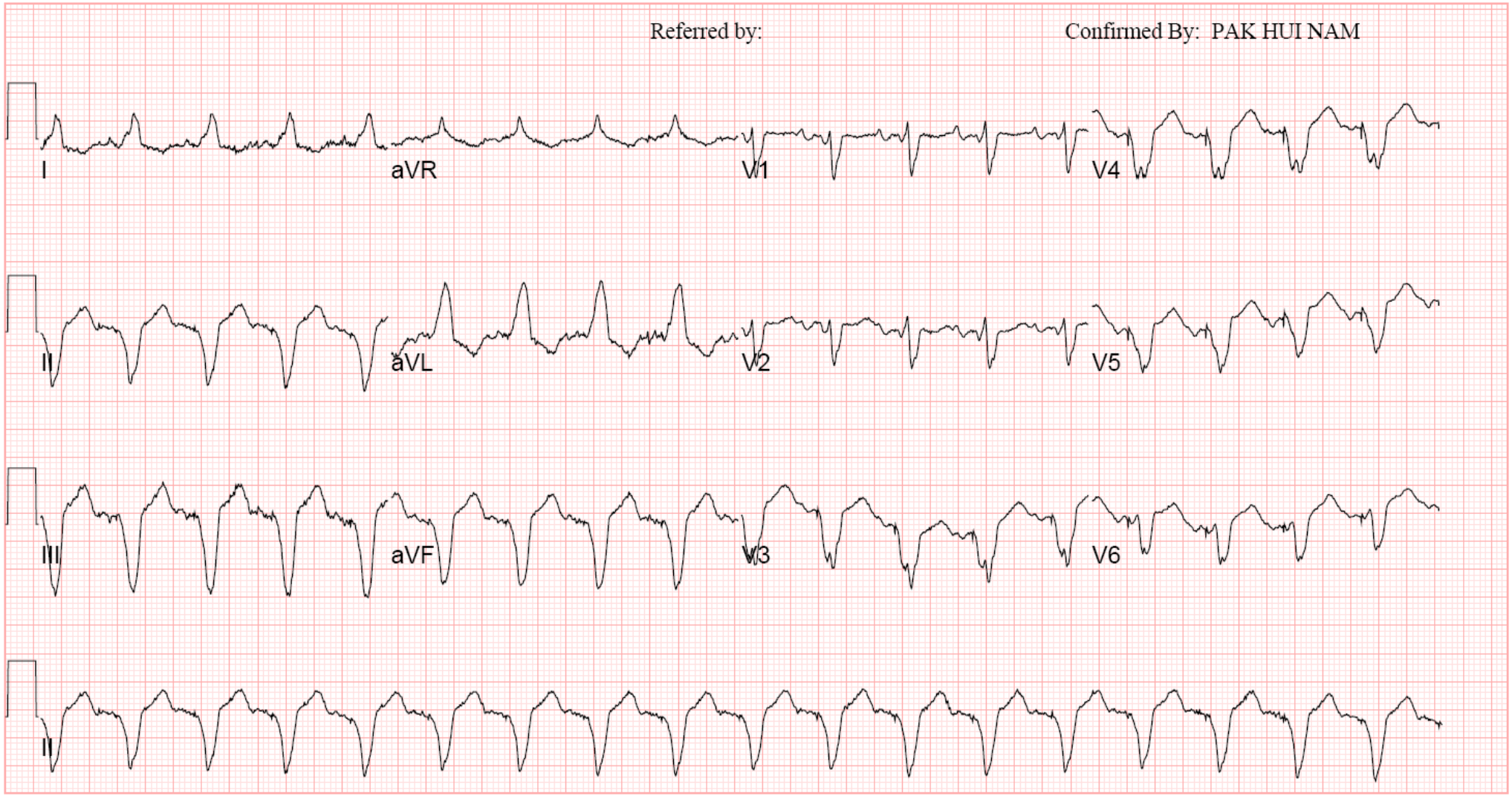
Past History

- HFrEF
- Complete AV block
  - s/p pacemaker insertion (DDD, 2010/8)
- HTN
- DM, type II

Chest X-ray (HOD#1)



EKG (HOD#1)


Referred by:
Confirmed By: PAK HUI NAM
I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II

Present Illness

- Complete AV block s/p DDD PM insertion (2010/8)
  - TTE, no RWMA, LVEF 76%
  - C-angio, normal coronary

- 1st Heart failure (2015/12)
  - LVEF 34%, LVEDD/ESD 64/53mm, LAVI 35ml/m2
  - Mild MR(I), mild TR(t)

- 1st admission for ADHF (2016/11)
  - LVEF 17%, LVEDD/ESD 73/68mm, LAVI 79ml/m2
  - Severe MR (IV), severe TR (III)

Laboratory Parameters

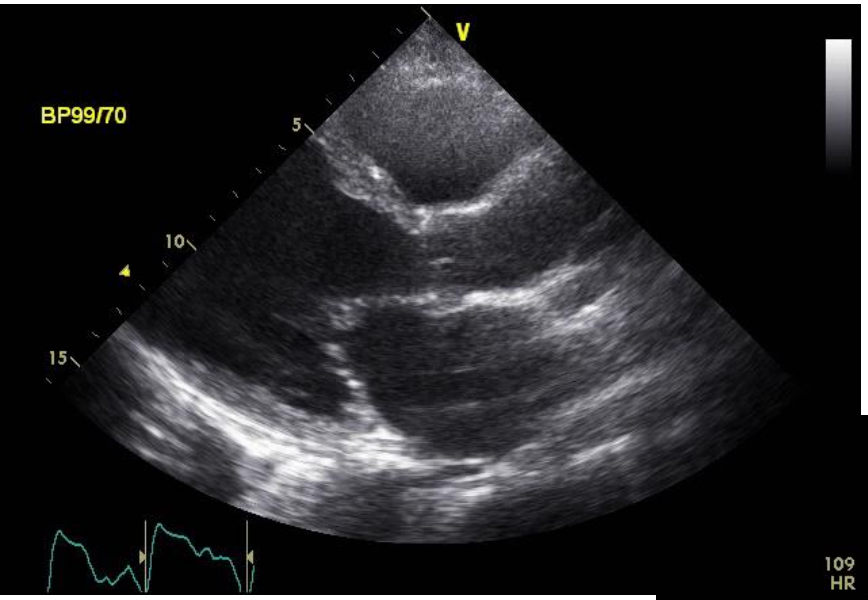
- CBC 5910(69.3%)/11.8/236k
- Bun / Cr 21.4/0.93 mg/dL
- Na/K/Cl/tCO2 140/4.0/102/20 mmol/L
- OT/PT/T bil 26/16/0.9 IU/L
- PT(INR)/aPTT 1.10/32.1

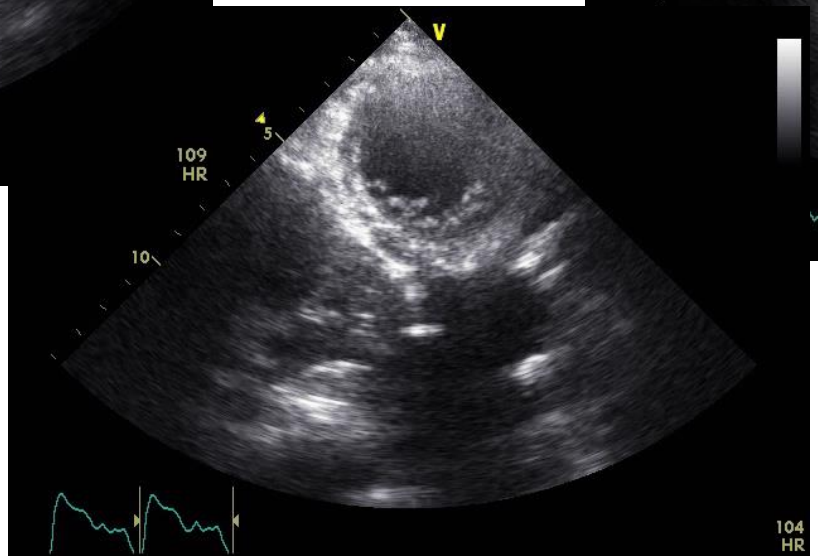
- HbA1c 5.8%
- CK/CK-MB/Troponin-T 52/2.3/28 pg/ml
- NT-proBNP 5144 pg/ml

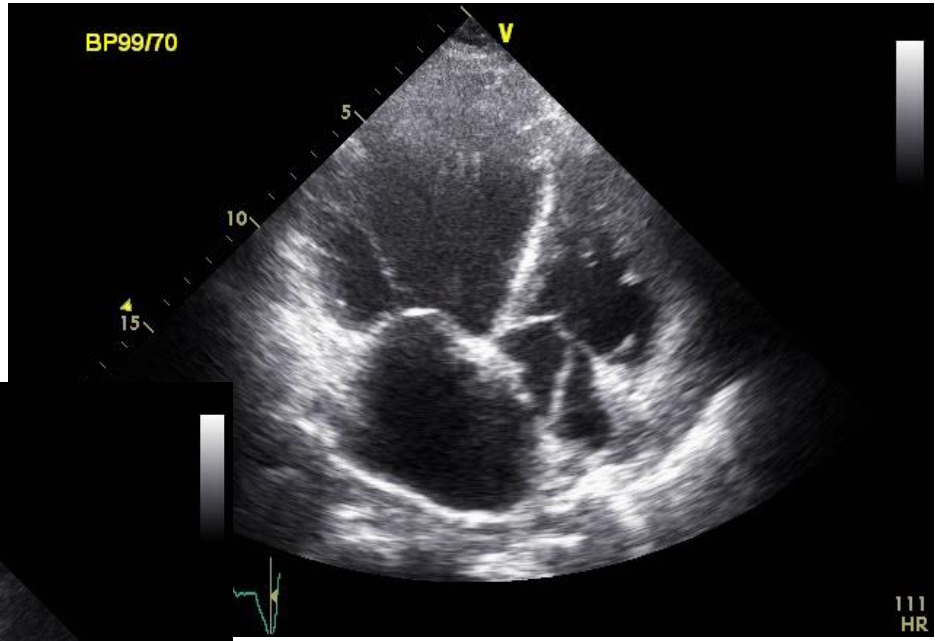
Medications

- **Pre-admission medications (2015/12~)**
  - Furosemide 40mg BID
  - Spironolactone 25mg BID
  - Losartan 80mg QD
  - Carvedilol 12.5mg BID
- -> dizziness related to low blood pressure
- **Latest medications**
  - Furosemide 40mg BID
  - Spironolactone 25mg BID
  - Aspirin 100mg QD
  - Rosuvastatin 10mg QD

TTE (HOD#1)

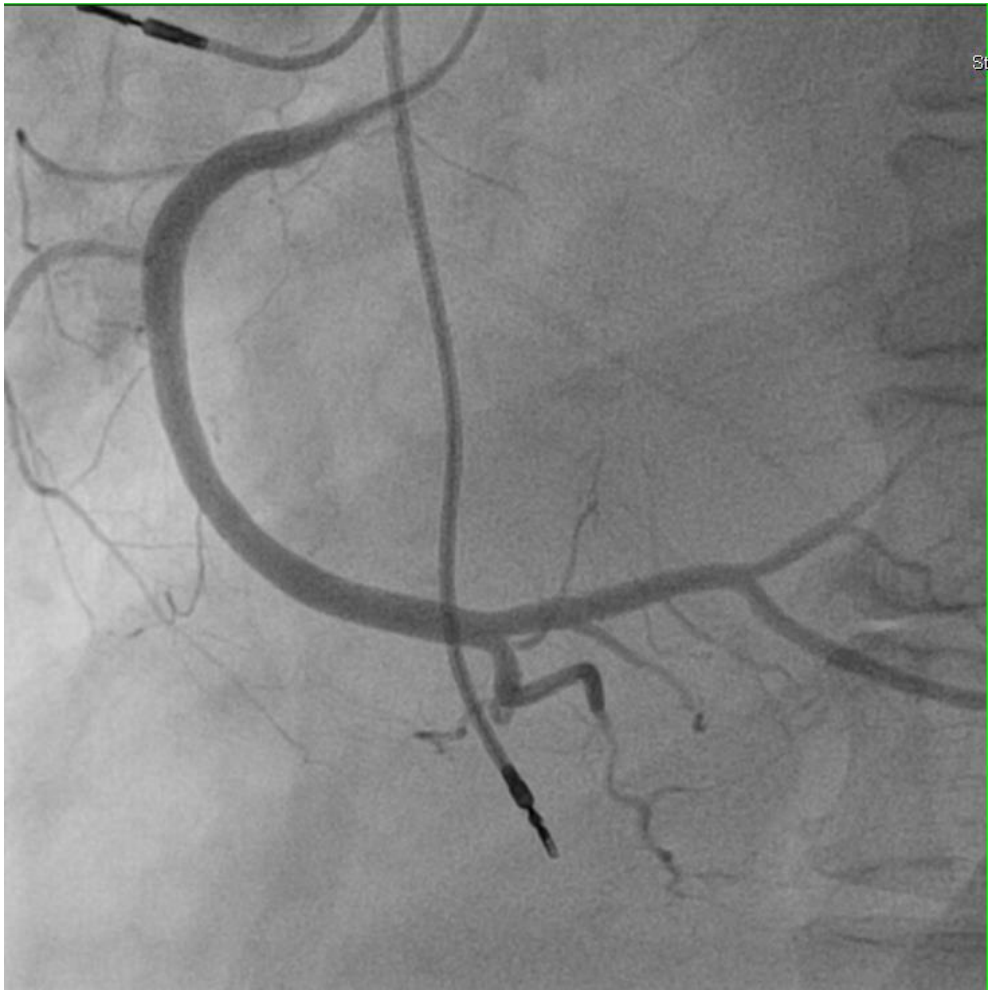


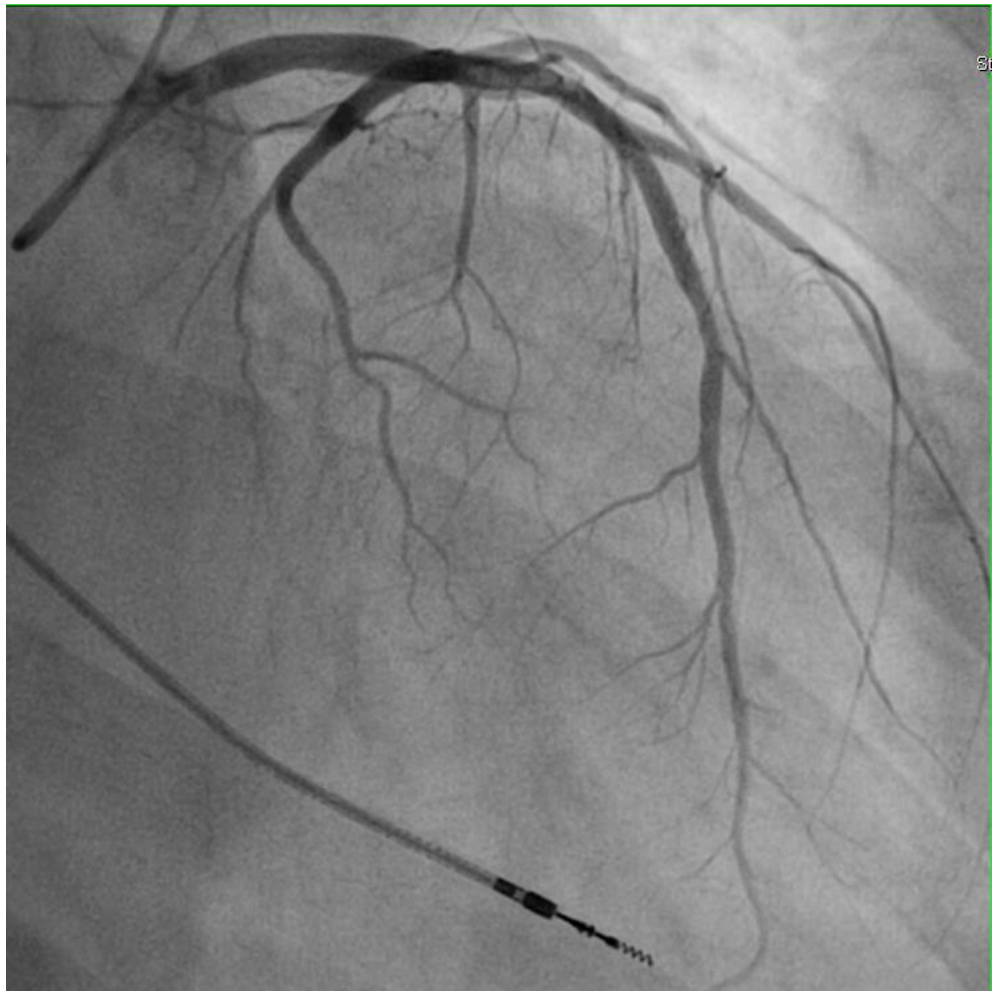




- LVEDD/ESD 73/68mm LAVI 79ml/m2 LVEF 17%
- TV TDI S' 8cm/s, TAPSE 15mm
- Severe MR severe TR RVSP 89mmHg

C-Angio (pre-admission)





What's Your Impression?

- 1. Ischemic CMP
- 2. Dilated CMP
- 3. Pacing-induced CMP
- 4. Any others

What's Your Next Plan?

- 1. Resume ARB/BB
- 2. Add ARNI
- 3. ICD upgrade
- 4. CRT-P upgrade
- 5. CRT-D upgrade

8.2 Cardiac resynchronization therapy

Recommendations for cardiac resynchronization therapy implantation in patients with heart failure

Recommendations	Class[a]	Level[b]	Ref[c]
CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration ≥150 msec and LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	I	A	261–272
CRT should be considered for symptomatic patients with HF in sinus rhythm with a QRS duration ≥150 msec and non-LBBB			
CRT rather than RV pacing is recommended for patients with HFrEF regardless of NYHA class who have an indication for ventricular pacing and high degree AV block in order to reduce morbidity. This includes patients with AF (see Section 10.1).	I	A	
CRT should be considered for patients with LVEF ≤35% in NYHA Class III–IV[d] despite OMT in order to improve symptoms and reduce morbidity and mortality, if they are in AF and have a QRS duration ≥130 msec provided a strategy to ensure bi-ventricular capture is in place or the patient is expected to return to sinus rhythm.	IIa	B	275, 278–281
Patients with HFrEF who have received a conventional pacemaker or an ICD and subsequently develop worsening HF despite OMT and who have a high proportion of RV pacing may be considered for upgrade to CRT. This does not apply to patients with stable HF.	IIb	B	282
CRT is contra-indicated in patients with a QRS duration < 130 msec.	III	A	266, 283–285

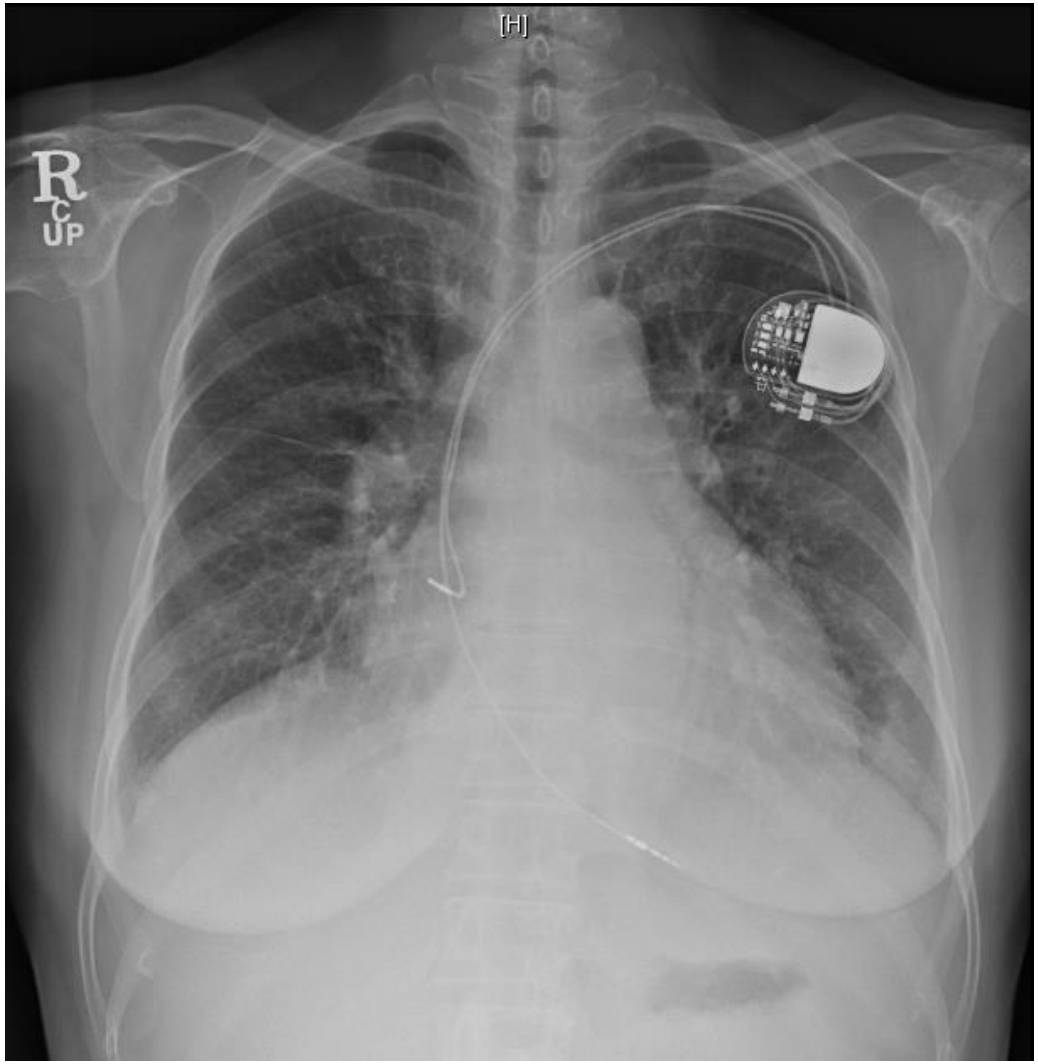
What We Did

- **<u>Decongestion then CRT-D upgrade</u>**

- **↑ Furosemide 60/40mg BID with IV shooting**
- **Spironolactone 25mg BID**
- **Captopril titration**
- **IV dobutamine infusion (2mcg/kg/min) on HOD#3**

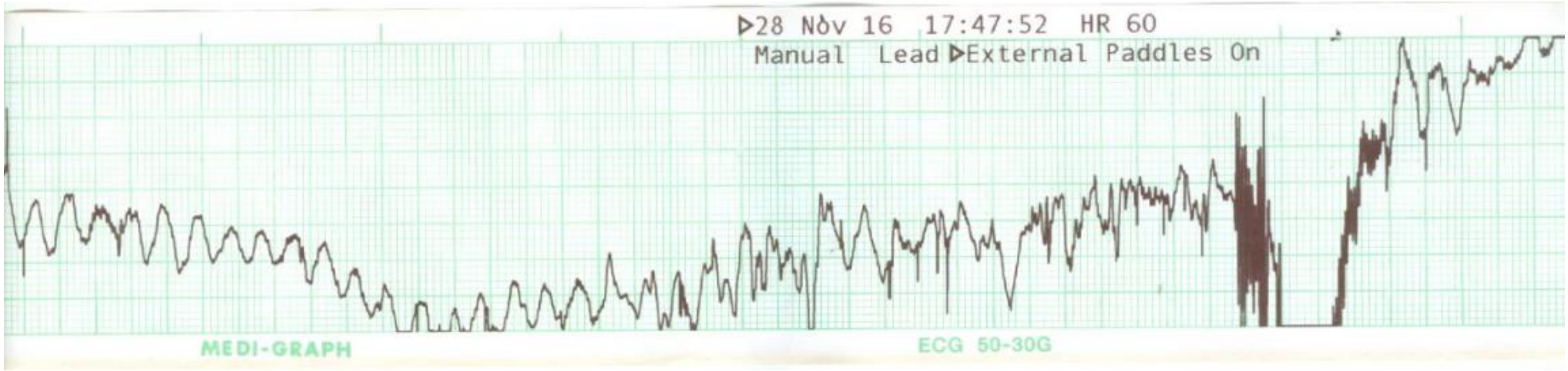
Hospital Course

- **NYHA II-III**
- **↑ IV Dobutamine (5mcg/kg/min)**
- **Dobutamine dependency**



HOD#20

- Sudden collapse in general ward
- Loss of consciousness, grasping for breath

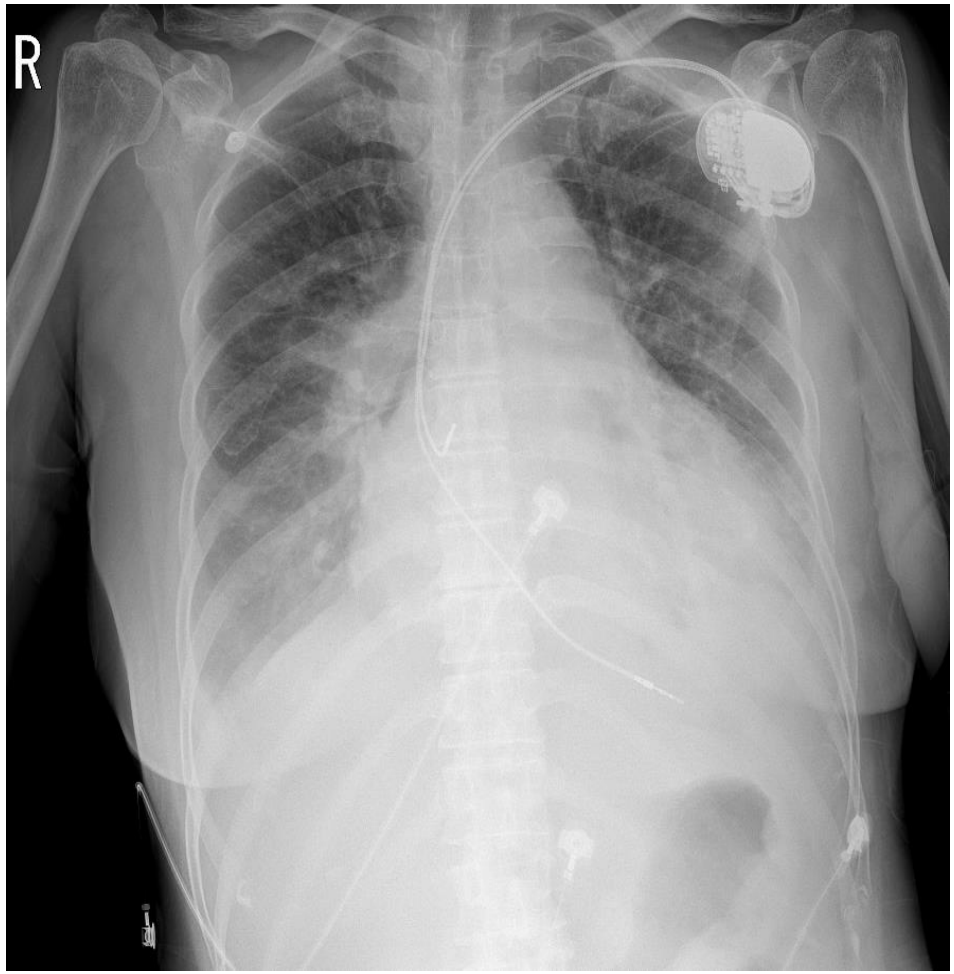


- CPR with 150J Defibrillation (3 minutes)
- Transfer to CCU again
- CRT hold & consult for heart transplant

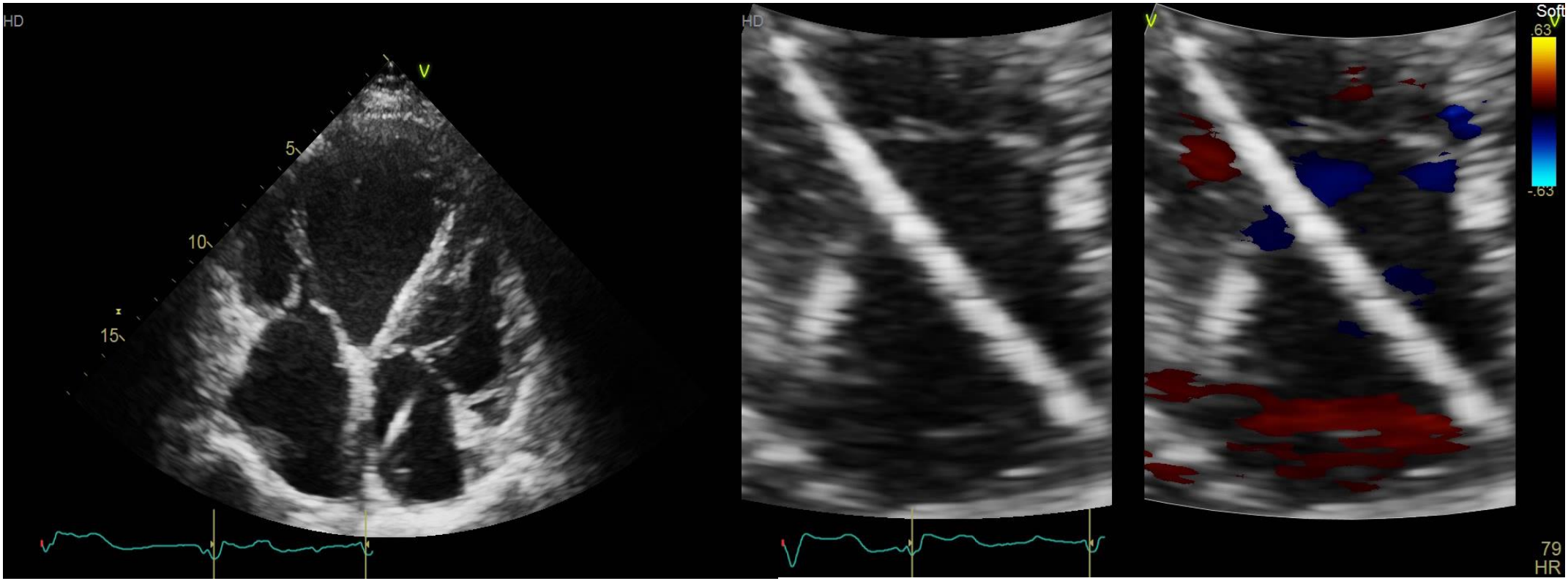
HOD#21-24

- Fever (38.4C) HOD#21
- Piperacillin/tazobactam

- Spiking fever (39.4C) HOD#22
- Empirical teicoplanin add

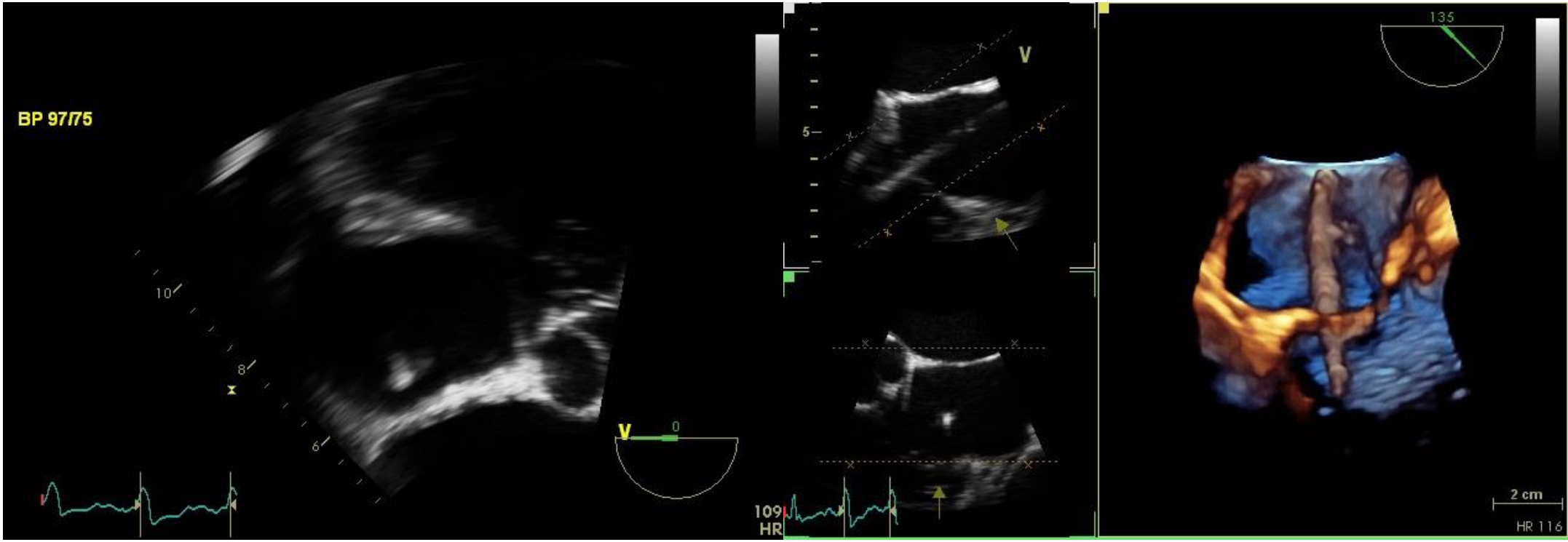


TTE (HOD#25)



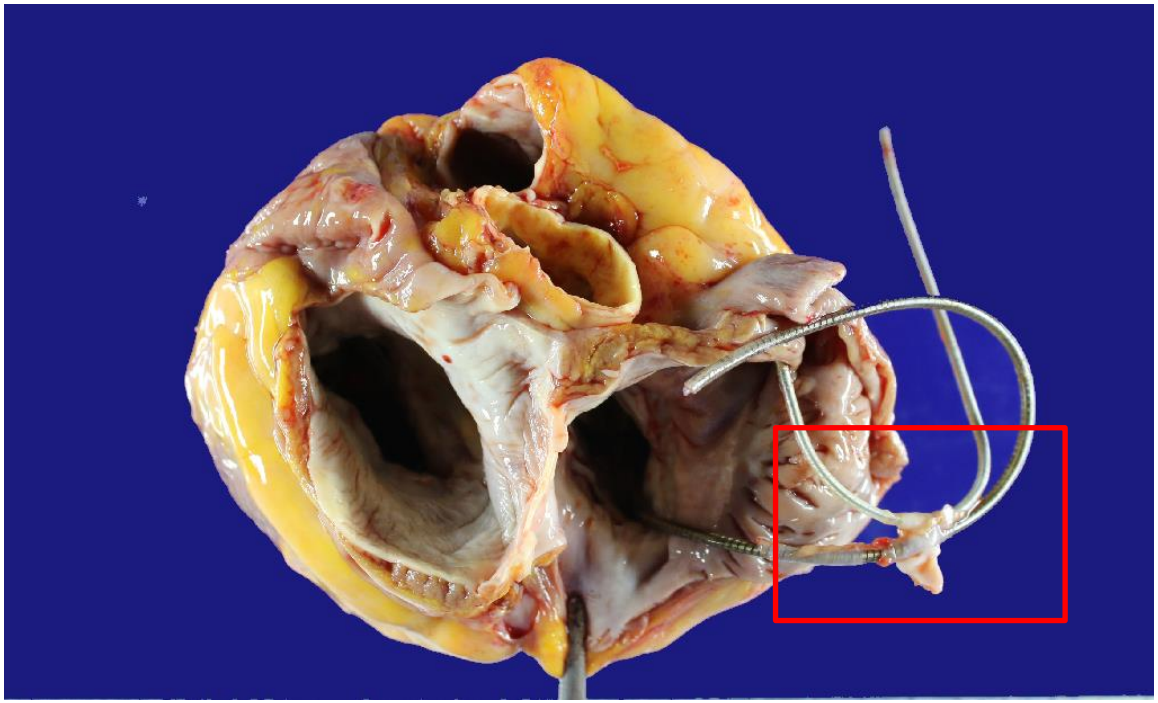
- R/O infective endocarditis in PM lead
- Gentamycin + Vancomycin -> no more spiking fever

TEE (HOD#27)



HOD#33

- Orthotropic heart transplantation
- Removal of pacemaker
- Thrombus in PM lead tip -> culture (negative)
- Blood culture (negative)



Now, What's Your Impression?

- 1. Ischemic CMP
- 2. Dilated CMP
- 3. Pacing-induced CMP
- 4. PM lead infection, r/o IE

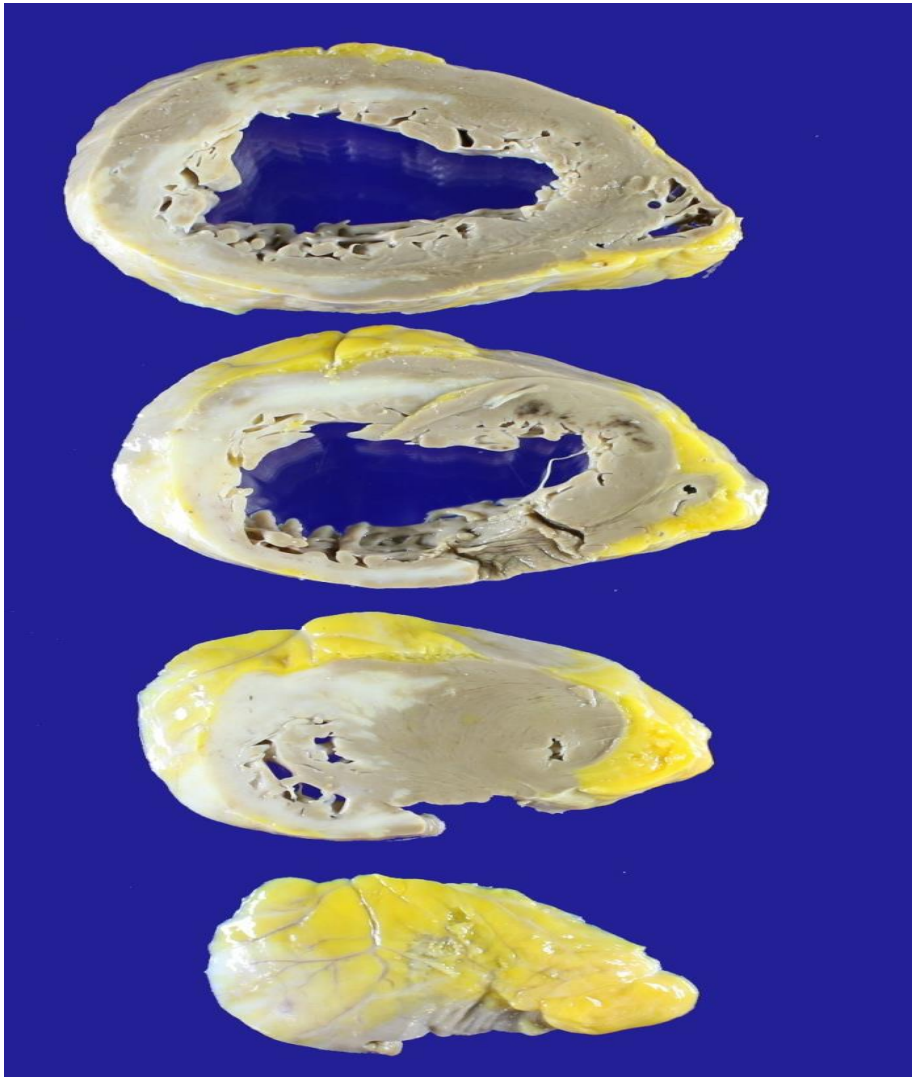
From Pathologist !!!

Explanted Heart

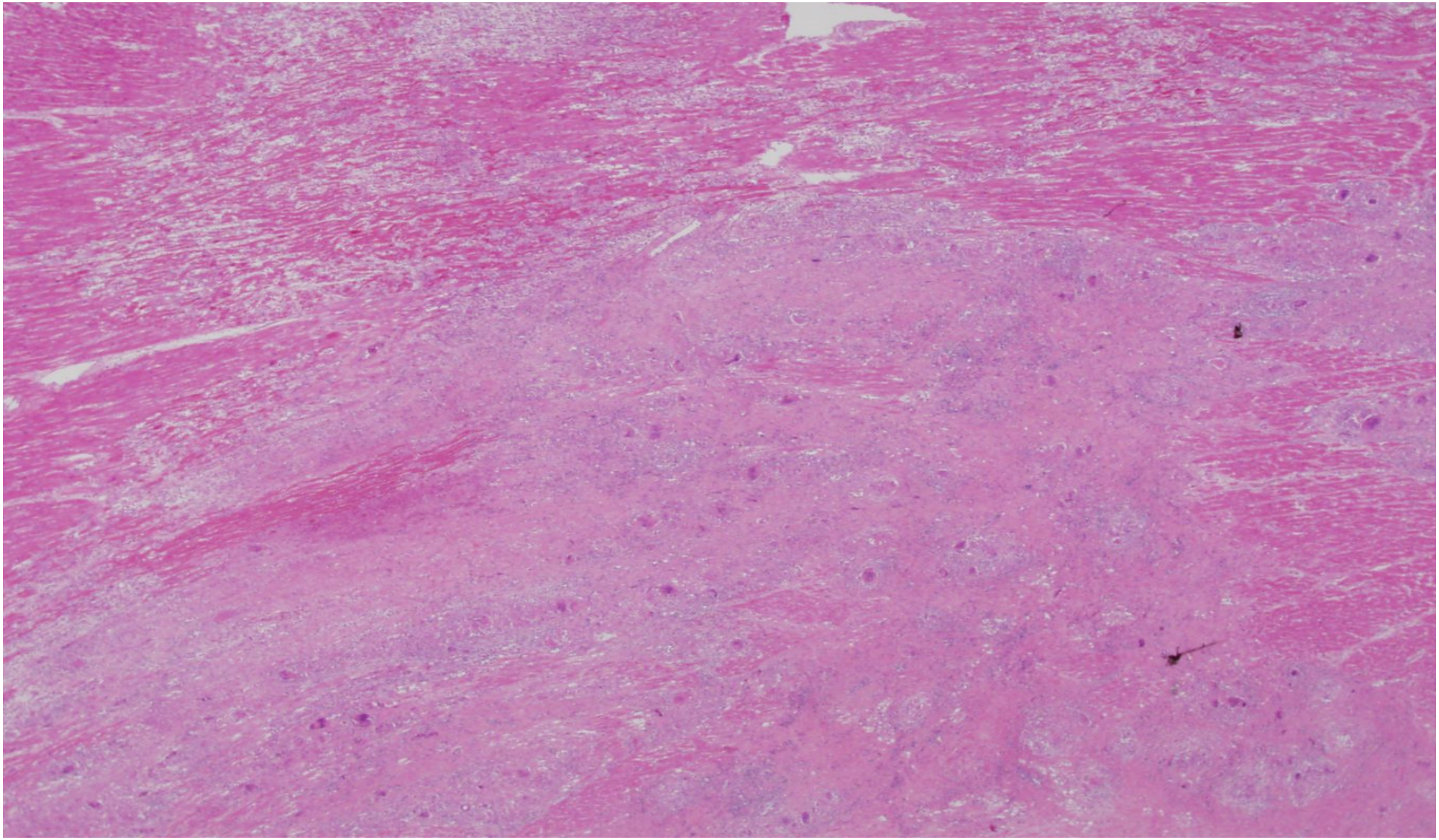
- **Multi-nucleated giant cell infiltration with chronic inflammatory cells in left ventricle, right atrium, atrial septum, suggestive of giant cell myocarditis**

- **Ziehl-Neelsen stain reveals no acid-fast bacilli.**
- **D-PAS stain reveals no fungal hyphae.**
- **Tb-PCR(Nested PCR): Negative**

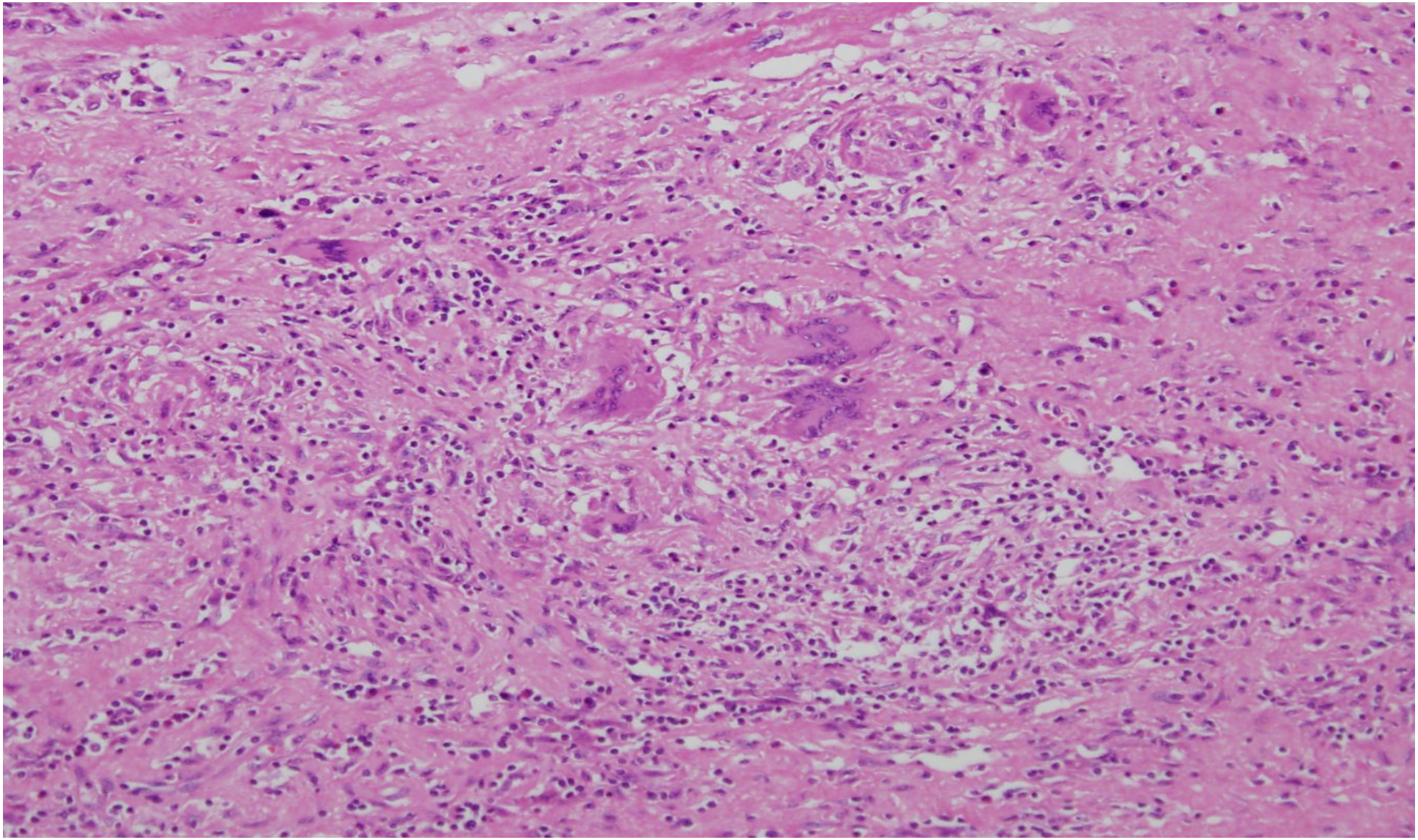
Giant Cell Myocarditis



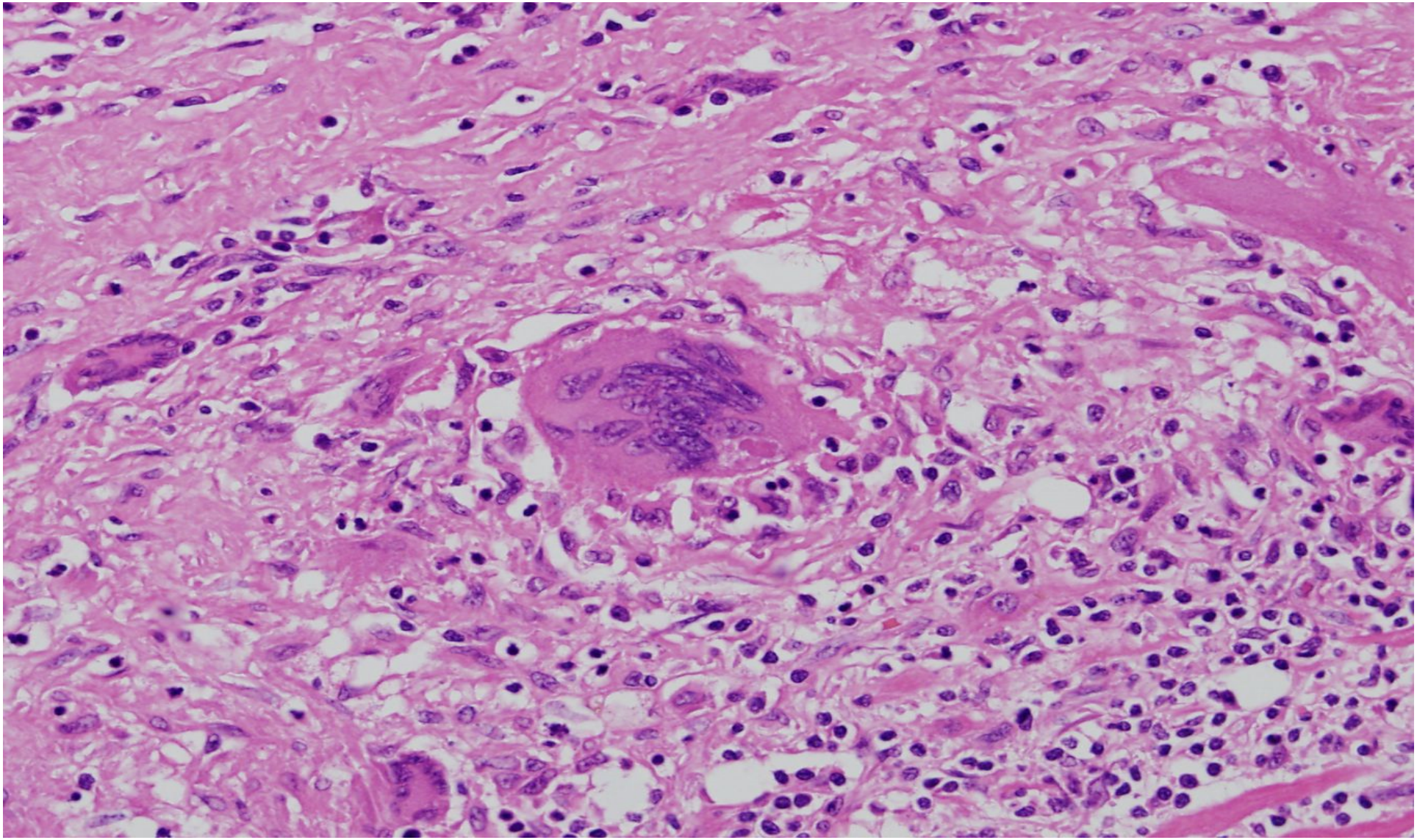
Giant Cell Myocarditis



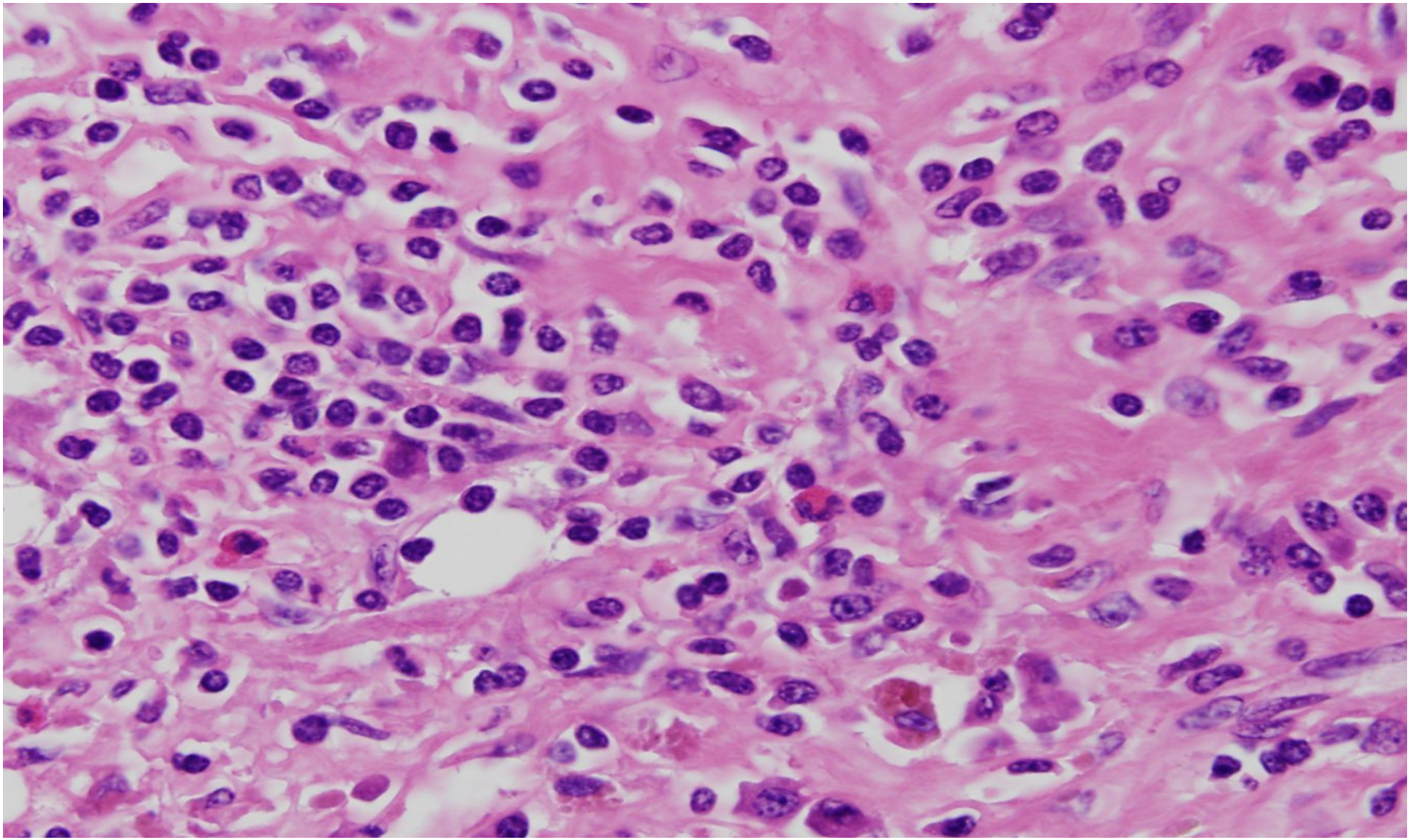
Giant Cell Myocarditis



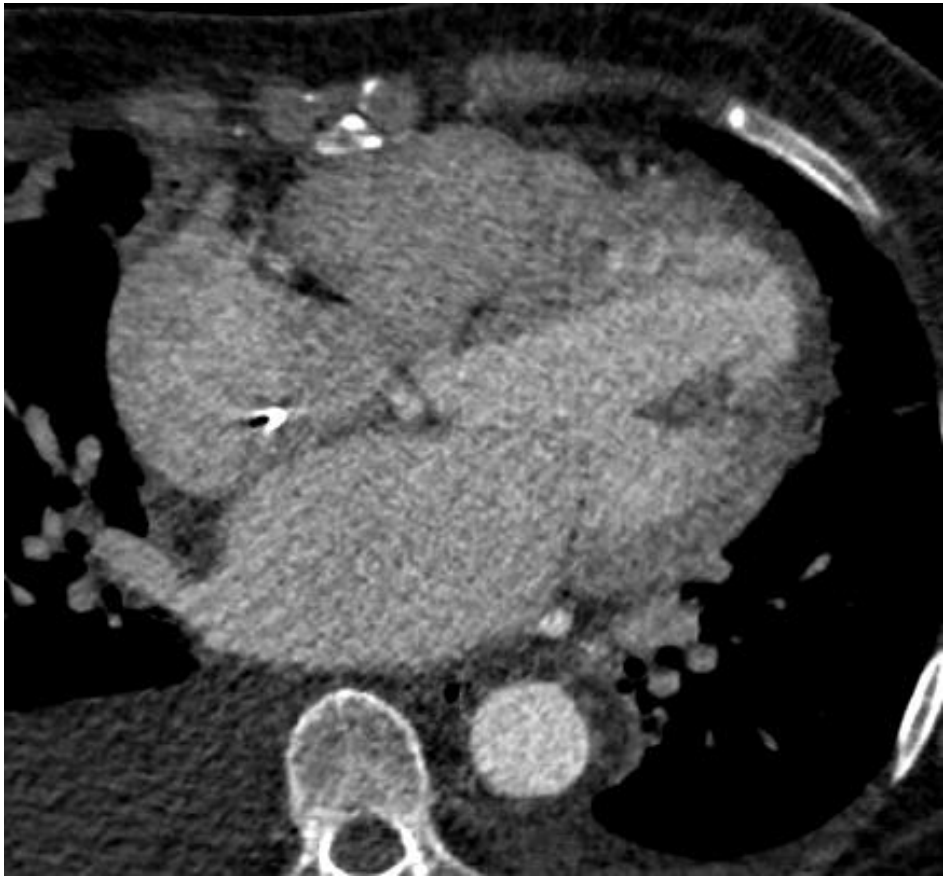
Giant Cell Myocarditis

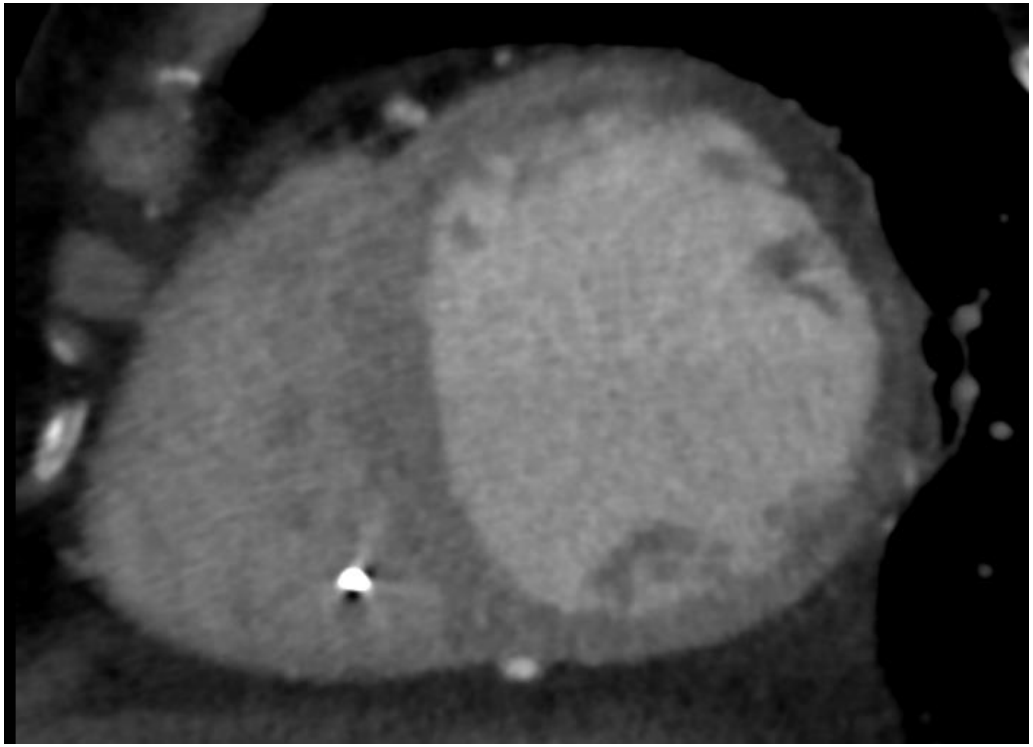


Giant Cell Myocarditis

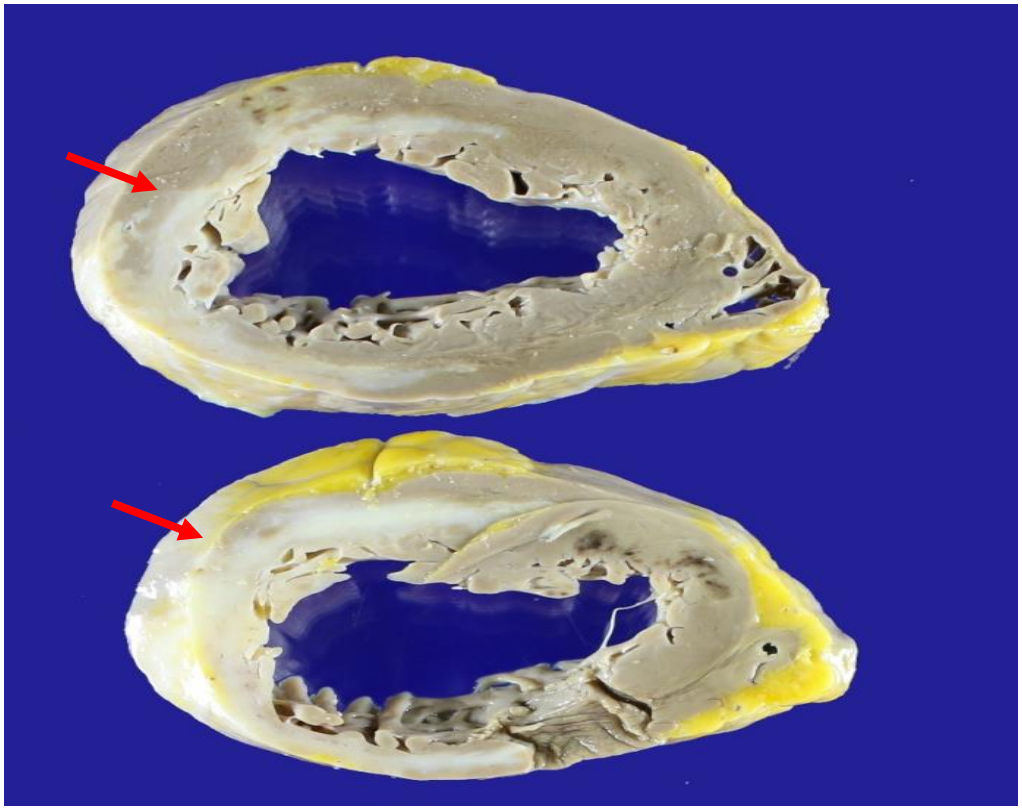


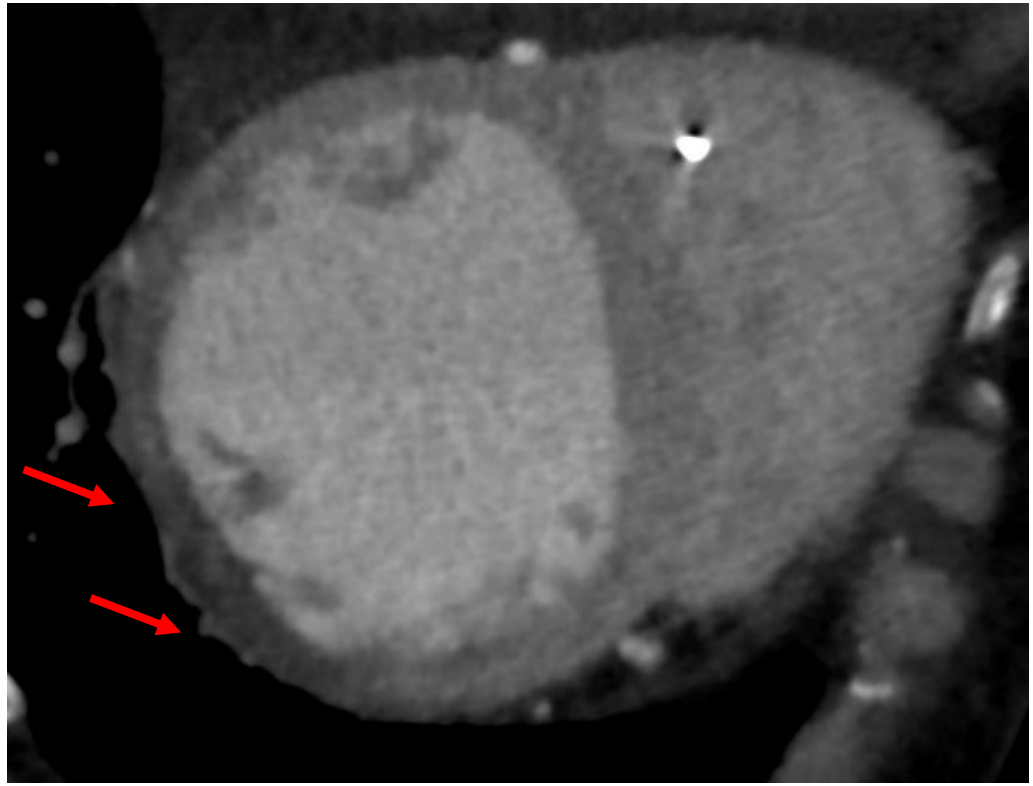
CT Heart (HOD#30)

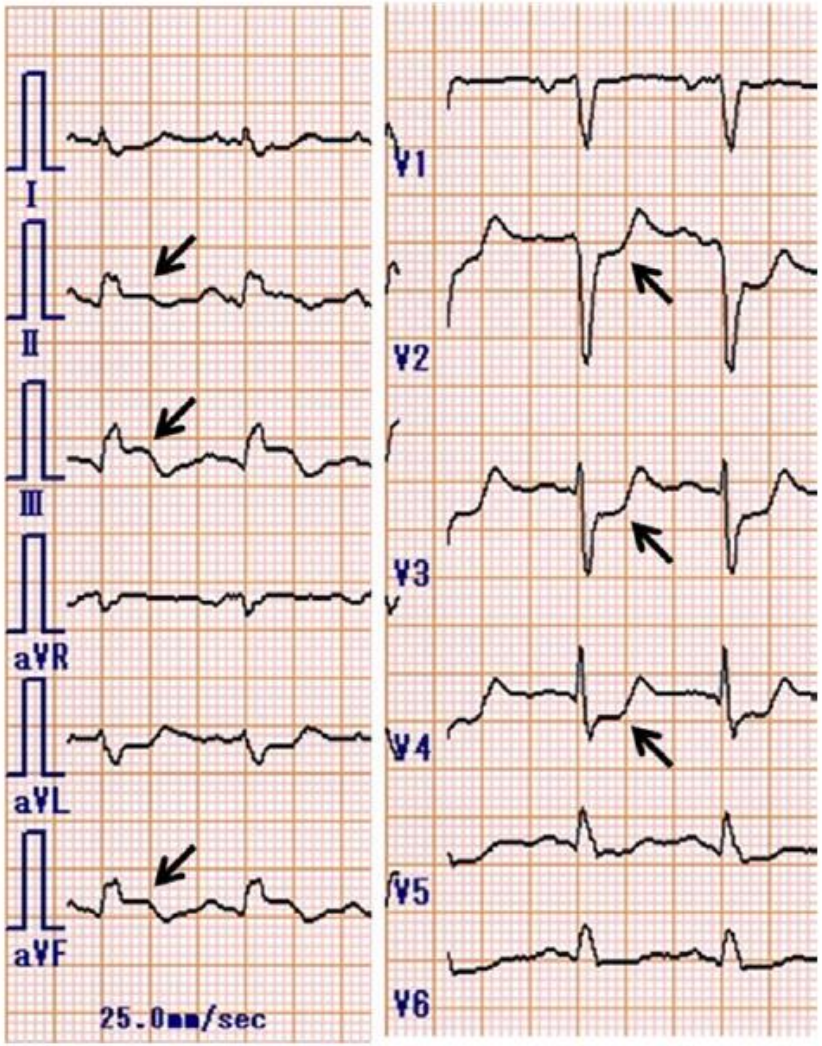


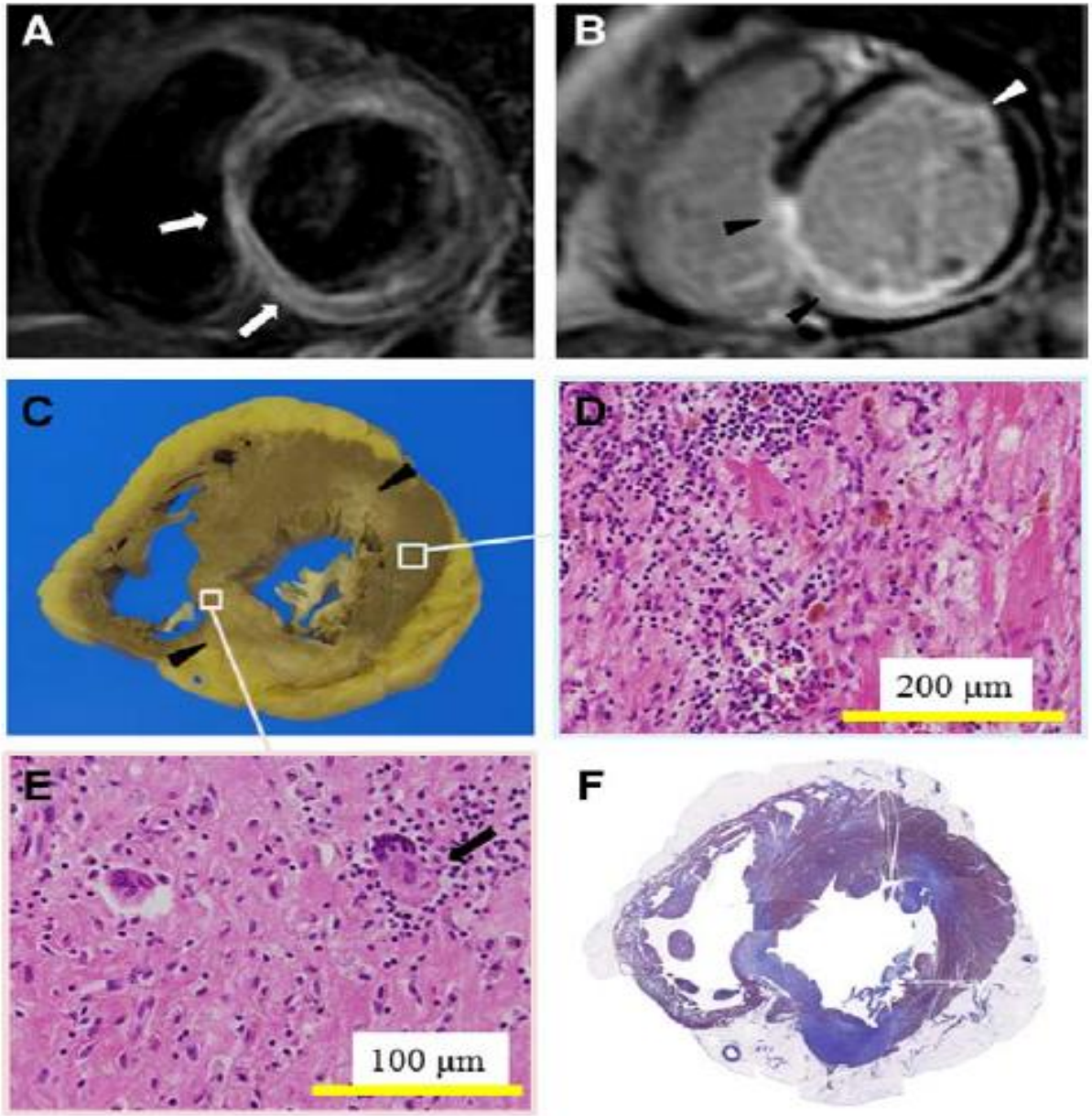


Giant Cell Myocarditis









Sujino et al. Circulation 2014;129:e467

Long-term outcome and its predictors in giant cell myocarditis

Kaj Ekström[1]*, Jukka Lehtonen[1], Riina Kandolin[1], Anne Räisänen-Sokolowski[2], Kaisa Salmenkivi[2], and Markku Kupari[1]

[1]Heart and Lung Center, Helsinki University Central Hospital, Helsinki, Finland; and [2]Department of Pathology, HUSLAB, Helsinki University Central Hospital, Helsinki, Finland

Main presenting clinical manifestation, *n* (percentage of 46)	
Heart failure	19 (41)
Distal atrioventricular conduction block	13 (28)
Ventricular tachycardia or fibrillation	8 (17)
Syndrome mimicking myocardial infarction	4 (9)
Other[a]	2 (4)
NYHA functional class, *n* (percentage of 44)	
1	16 (36)
2	12 (27)
3–4	16 (36)
LVEF at echocardiography, %	41 ± 15
Plasma cardiac troponin T[b], *n* (percentage of 38)	
>85 ng/L	19 (50)
>500 ng/L	15 (40)
Plasma NT-proBNP, ng/L[c]	3727 (94–57 443)
Late gadolinium enhancement on CMRI, *n* (percentage of 20)	20 (100)
Abnormal myocardial uptake on 18 F-FDG PET, *n* (percentage of 14)	13 (93)

Ekstrom et al. Eur J Heart Fail 2016;18:1452

Atrial Giant Cell Myocarditis
A Distinctive Clinicopathologic Entity

Brandon T. Larsen, MD, PhD; Joseph J. Maleszewski, MD; William D. Edwards, MD;
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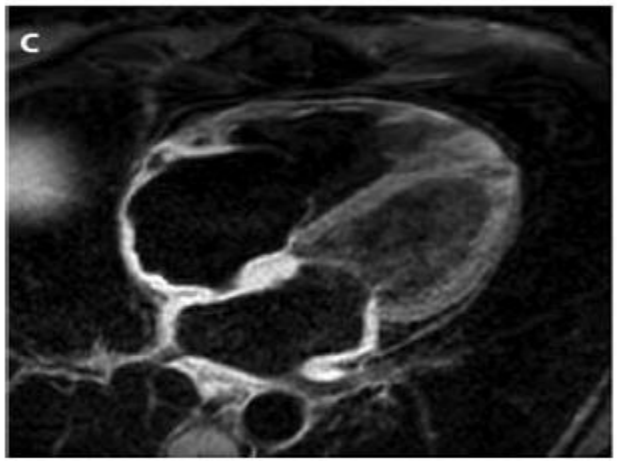
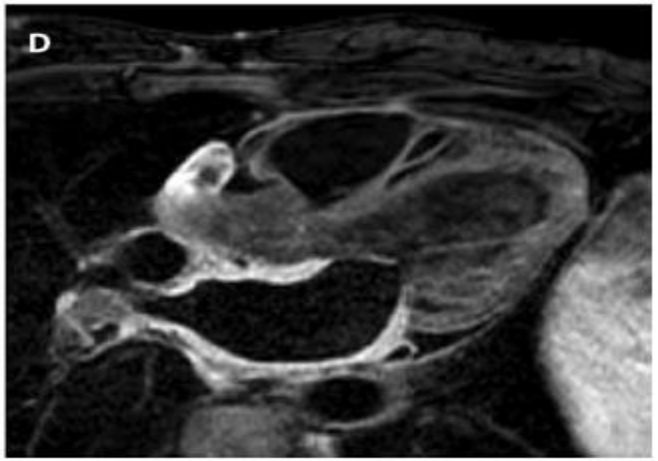




- **Benign atrial variant**
- **<u>Disguised for years in a monosymptomatic heart block & DCMP</u>**

Larsen et al. Circulation 2013;127:39

Discussion

- Fever from IE or GCM ?
- Slow progression of ventricular GCM ?
- Progression from aGCM to vGCM ?
  - From AVN to Ventricles

The Phantom Menace

Thank You
for Your Attention

Giant Cell Myocarditis (GCM)

- Rapidly progressive & fatal unless HTPL

- TPL free survival at 5 years : 52%
- GCM-targeted therapy : 63%

- May present as
  - Benign atrial variant (Circ. 2013;127:39)
  - Disguised for years in a monosymptomatic heart block & DCMP

Table 2 Therapy in the 46 patients with giant cell myocarditis

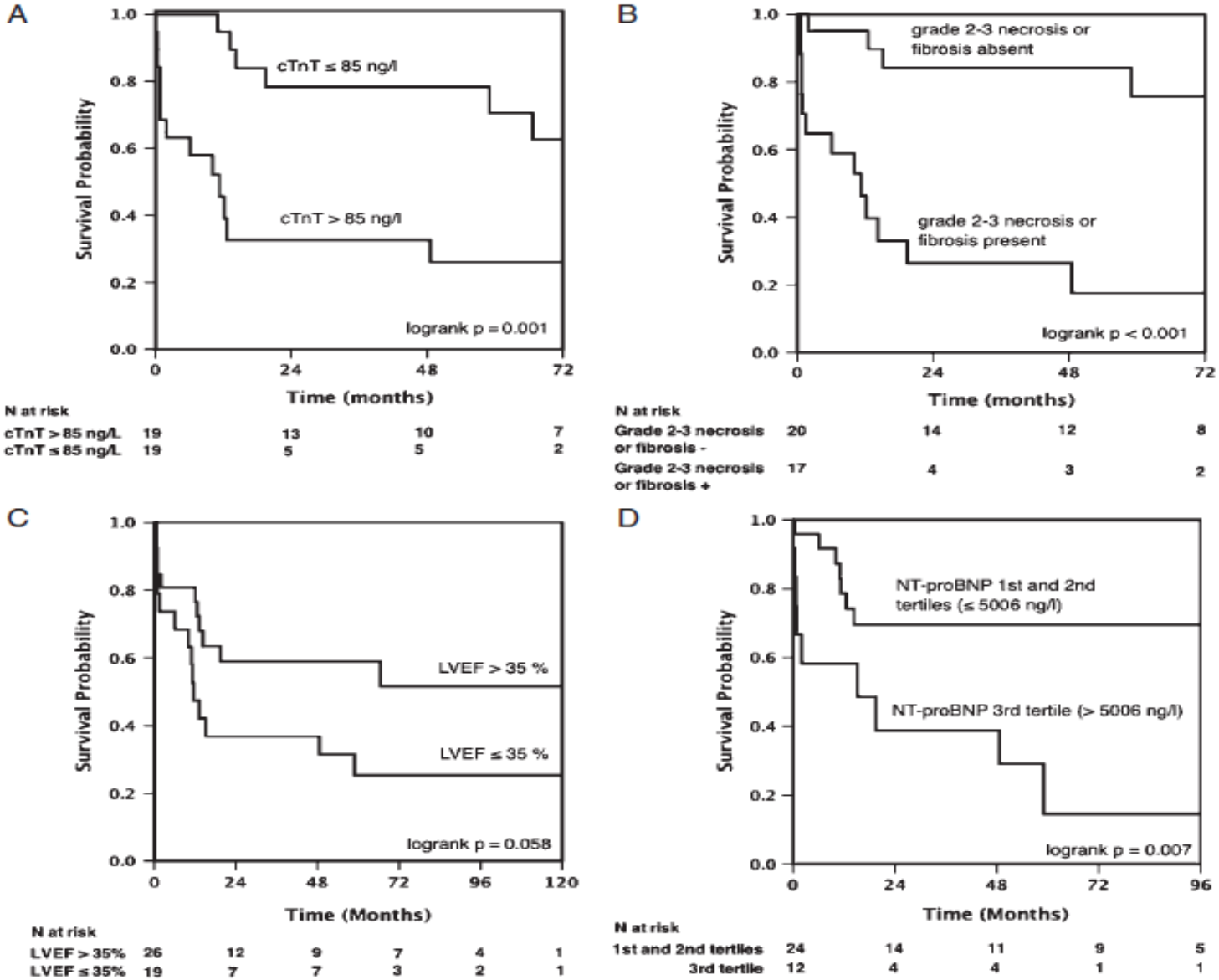
Immunosuppressive therapy[a]	37/38 (97)
Prednisone	37/37 (100)
Azathioprine	31/37 (84)
Cyclosporine	28/37 (76)
Other[b]	7/37 (19)
Triple combination therapy[c]	26/37 (70)
Beta-adrenergic blockers	39 (85)
ACE inhibitors	33 (72)
Amiodarone	28 (61)
ICD implanted (total)	26 (57)
Primary prevention	21 (46)
Secondary prevention	5 (11)
Permanent pacemaker	8 (17)
Left ventricular assist device	2 (4)
Extracorporeal membrane oxygenation	2 (4)

Ekstrom et al. Eur J Heart Fail 2016;18:1452

Table 3 Predictors of transplant-free cardiac survival in giant cell myocarditis by Cox regression analysis

Predictor	e/n	HR (95% CI)	*P*-value
LVEF by echocardiography, per +5%	25/45	0.87 (0.75–0.99)	0.047
Plasma NT-proBNP, per +1000 ng/L	16/36	1.06 (1.03–1.10)	<0.001
Plasma cardiac troponin-T >85 ng/L (median)	19/38	4.57 (1.63–11.28)	0.003
Grade 2–3 myocyte necrosis[a]	17/37	4.29 (1.63–11.28)	0.003
Grade 2–3 myocardial fibrosis[a]	17/37	2.37 (0.83–6.82)	0.109
Grade 2–3 necrosis or fibrosis[a]	17/37	7.17 (2.29–22.40)	<0.001
Triple-drug immunosuppression[b]	17/37	0.39 (0.15–1.01)	0.051

Ekstrom et al. Eur J Heart Fail 2016;18:1452



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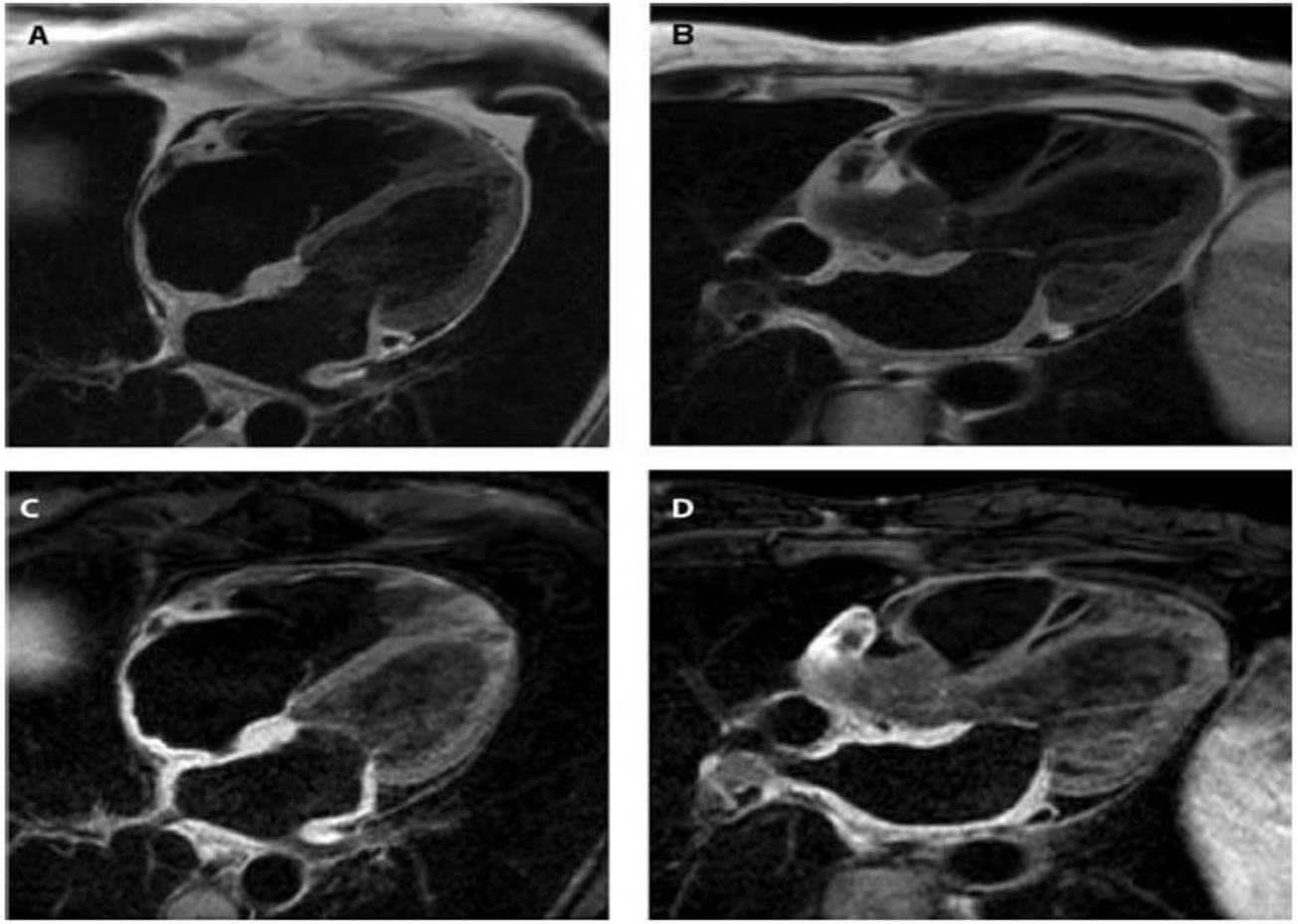


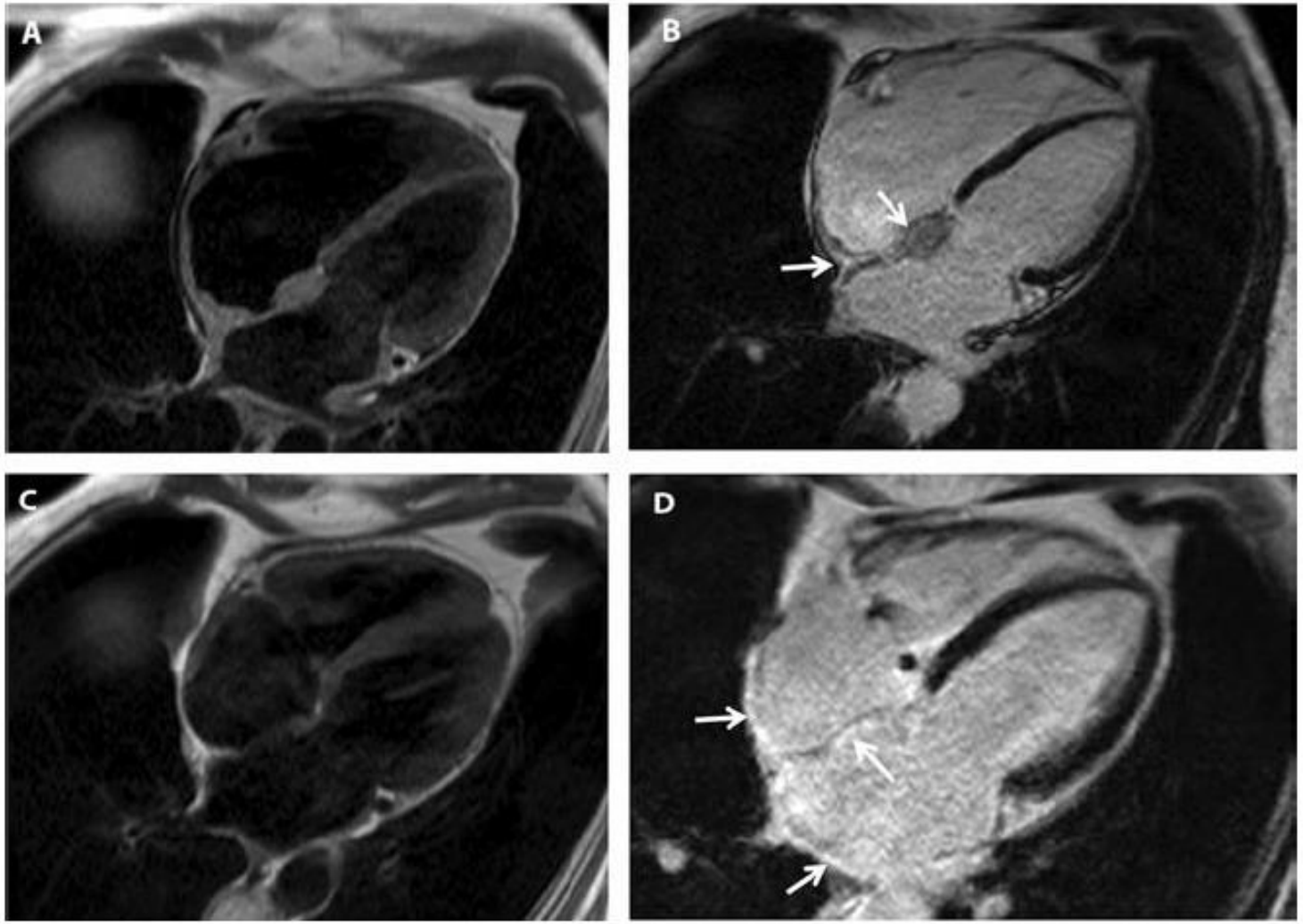
Larsen et al. Circulation 2013;127:39

Case # (ref.)	Valve Disease	Atrial Dilatation	Atrial Wall Thickening	Mural Thrombus	LVEF/LV Function	RV Function	Treatment	Duration of Course	Disease-Free Follow-Up
1*	None†	None†	None†	No†	Unknown	Unknown	n/a	n/a	n/a
2*	MS (severe), MR (mild)	LA (severe), with akinesis	Unknown	Yes	50% to 59%	Normal	Warfarin, pacemaker	2 wk	4 mo
3*	TR (severe), TV annular dilatation	RA (severe)	Yes (Bilateral, marked)	No	Normal	Normal	Steroids, cyclosporine	8 wk	12 mo
4*	MR (mod.), TR (mild-mod.)	LA (severe), RA (mild)	Yes (LAA)	No	58%	Normal	Warfarin	Unknown	8 wk
5*	MS (severe), MR (mild)	LA (severe)	Unknown	Yes	60% to 65%	Normal	Warfarin	2 wk	6 wk
6*	AR (trace), MR (mild), TR (mild)	LA (severe), with hypokinesis	Unknown	Yes	Normal	Normal	Warfarin	4 wk	8 wk
7 (18)	MS (severe), MR (mild)	LA (severe)	Yes (LAA)	Yes	Normal	Normal	Pacemaker	Unknown	2 y
8 (17)	MR (severe)	Biatrial (severe)	None	No	Normal	Normal	Pacemaker, amiodarone	Unknown	6 mo
9 (16)	MS, AR‡	Biatrial (severe)†	None†	No†	Unknown	Unknown	Supportive	n/a§	n/a§
10 (15)	MS‡	Unknown	Unknown	Yes	Normal	Normal	Unknown	Unknown	6 y
11 (15)	MS‡	Unknown	Unknown	Yes	Normal	Normal	Unknown	Unknown	4 y
12 (15)	MS‡	Unknown	Unknown	Yes	Normal	Normal	Unknown	Unknown	3 y
13 (14)	MS (mod.), MR (trace)‡	LA	Unknown	Yes	Normal	Normal	Anticoag., digoxin	Unknown	8 mo

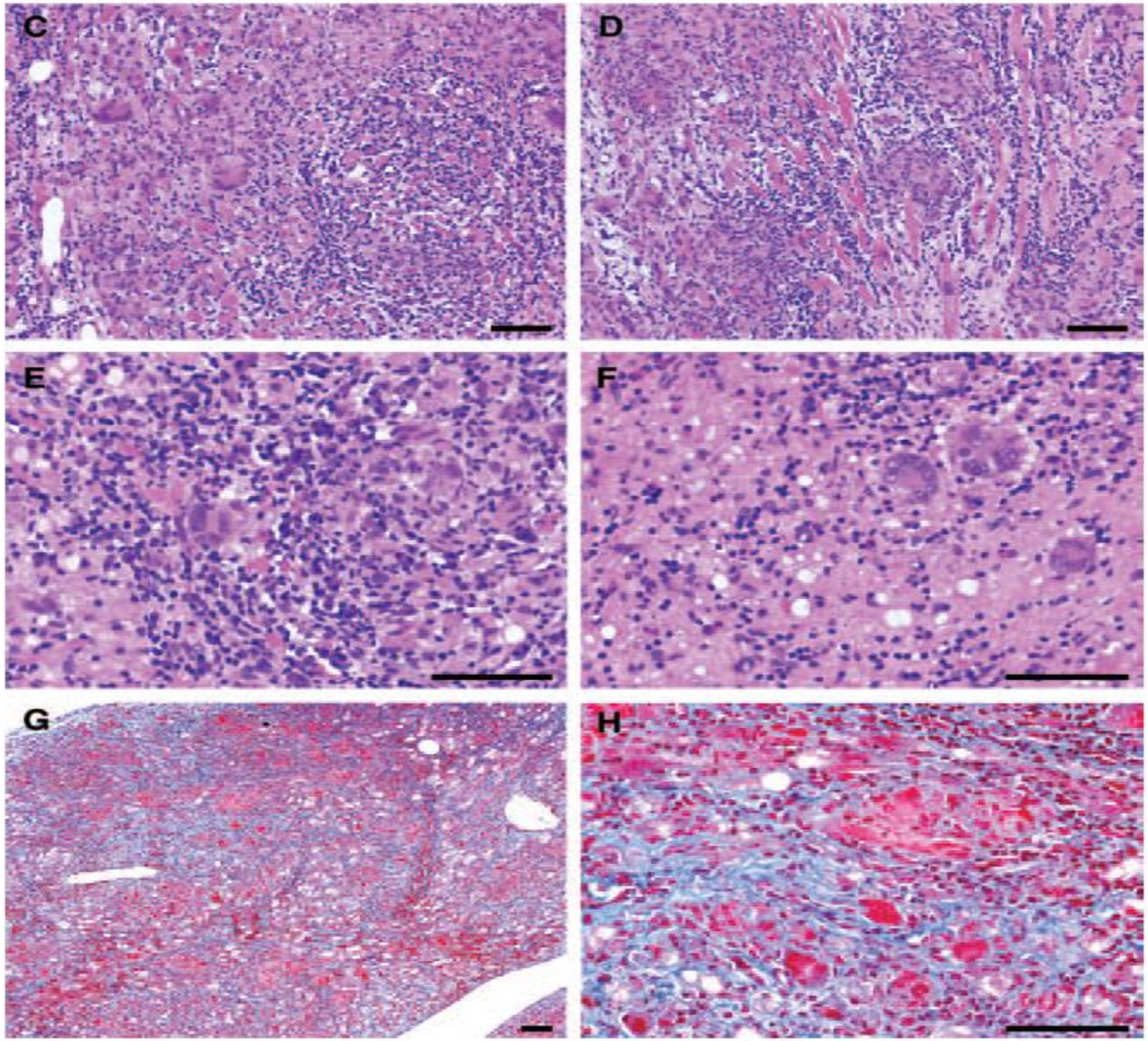
Larsen et al. Circulation 2013;127:39

Case #	Year (ref.)	Sex	Age (y)	Race	Symptoms	Symptom Duration	AF	Sarcoid	Rheumatic Valve Disease	Other Connective Tissue Disease	Other Past Medical History
1	2012*	M	42	W	None	n/a	Unk.	No	No	No	COPD, asthma, bipolar disorder
2	2012*	M	58	W	SOB, dyspnea, chest pain	Several weeks	Yes	No	Yes	No	HTN, HL
3	2012*	F	65	W	SOB, DOE, orthopnea, pedal edema	6 wk	Yes	No	No	No	Asthma
4	2012*	M	70	W	Chest pain	Several hours	Yes	No	No	No	HL, DM, CAD, MI
5	2012*	F	72	W	DOE, fatigue	Many years	Yes	No	Yes	No	HTN, HL, cerebral aneurysm
6	2012*	M	73	W	Fatigue, sudden left sided weakness	Several days	Yes	No	No	No	CAD, HTN, HL, DM, sleep apnea
7	2010 (18)	F	51	Unk.	CHF	Unk.	Yes	No	Yes	No	COPD, brachial artery thrombosis
8	2006 (17)	M	70	Unk.	CHF	Several years	Yes	No	No	Unk.	Unknown
9	1968 (16)	F	60	W	PND	9 y	Yes	No	Yes	Unk.	Popliteal artery embolism
10	1965 (15)	F	42	Unk.	CHF during pregnancy	1 y	Yes	No	Possibly	Unk.	Unknown
11	1965 (15)	F	54	Unk.	DOE	5 y	Yes	No	Possibly	Unk.	Unknown
12	1965 (15)	F	41	Unk.	DOE	3 y	Yes	No	Possibly	Unk.	Unknown
13	1964 (14)	M	37	Unk.	DOE, chest pain, myalgia	5 y	Yes	No	Yes	Unk.	Unknown

Larsen et al. Circulation 2013;127:39



Larsen et al. Circulation 2013;127:39



Larsen et al. Circulation 2013;127:39