A Potpourri of Fascinating Cases to Learn From

Echo Hawaii

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Case 1

47-year-old woman with follicular lymphoma with large B cell lymphoma transformation presenting to MSKCC for an initial evaluation for CAR-T cell therapy.

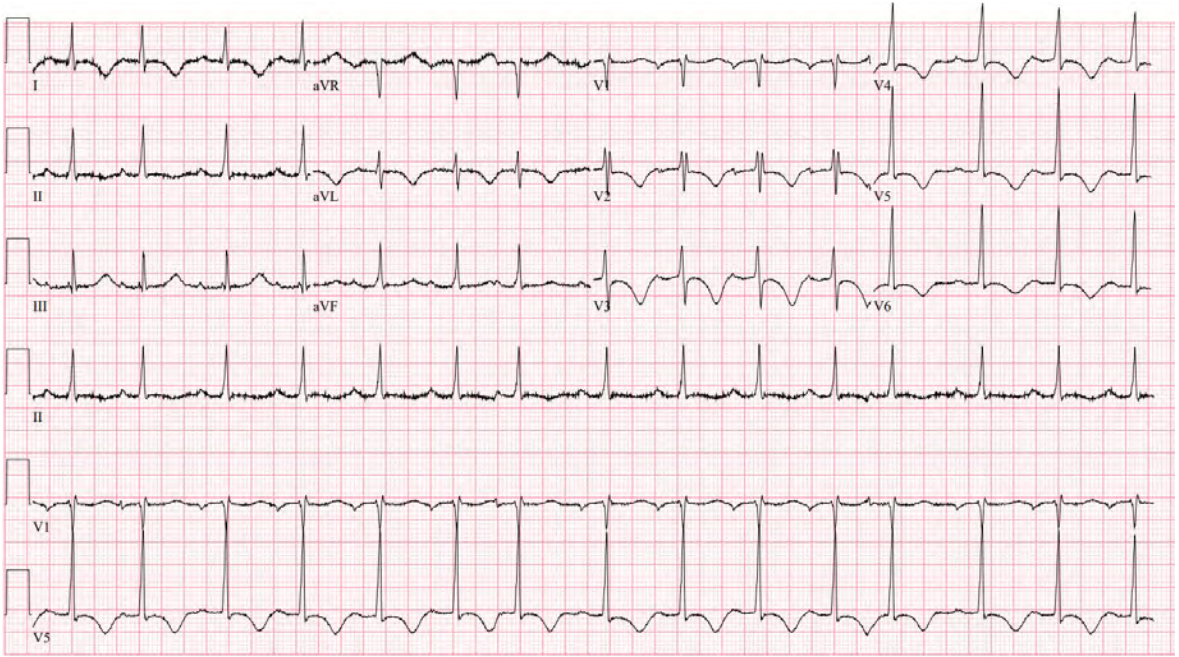
- Prior treatment with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) and autologous stem cell transplant

- Reports ~8-10 weeks of ongoing chest pain, wrapped around her entire chest, unrelated to activity or position, making it difficult to breath. Echo and ECG done at the onset of these complaints were normal. The pain was attributed to disk herniation at C4-C5, T7-12.

- No known cardiovascular disease. No HTN, DM, CKD or CHF

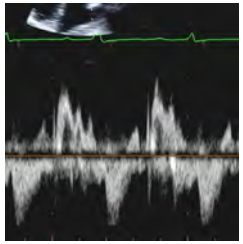
- Exam – NAD appearing
    - BP 104/71; HR 86, R 18, SpO2 100%, T 36.6C
    - Unremarkable. No signs of decompensated heart failure

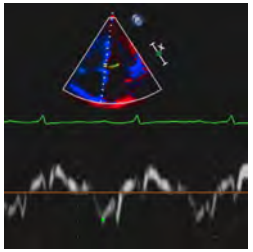
EKG at Presentation

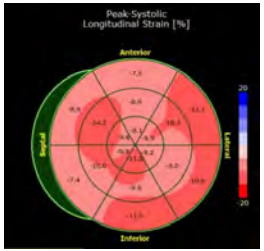


Sinus rhythm, 1st degree AV block, repolarization abnormality consider anterolateral ischemia; prolonged QT (QTc 537 msec)
Normal ECG a months ago per record

2D Echocardiogram







Measurements:

- IVS = 1.7 cm; PWT 1.3 cm
- LV mass/BSA = 141 gm/m2
- LVEF 47%
- Mitral E/A 1.2; medial e' 5 cm/sec
  E/e' = 15
- GLS -9.6%

Interpretation:

- Severe concentric LV hypertrophy
- Diffusely hypokinetic LV; mildly reduced LVEF; severely reduced GLS
- Diastolic dysfunction with elevated LV filling pressure

What is the diagnosis?

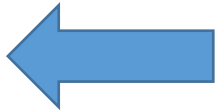
A. Hypertrophic Cardiomyopathy

B. Amyloid Cardiomyopathy

C. Myocarditis

D. Cardiac Lymphoma

E. Uncertain but likely something serious!



- **Labs**
  - TnI 9.0 ng/ml; BNP 1288 pg/ml

Next diagnostic step?

A. Cardiac MRI

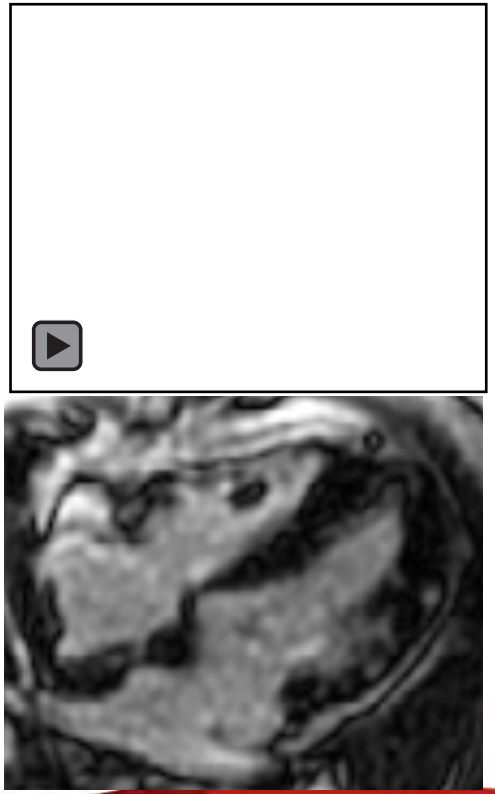
B. Chest CT to rule out PE

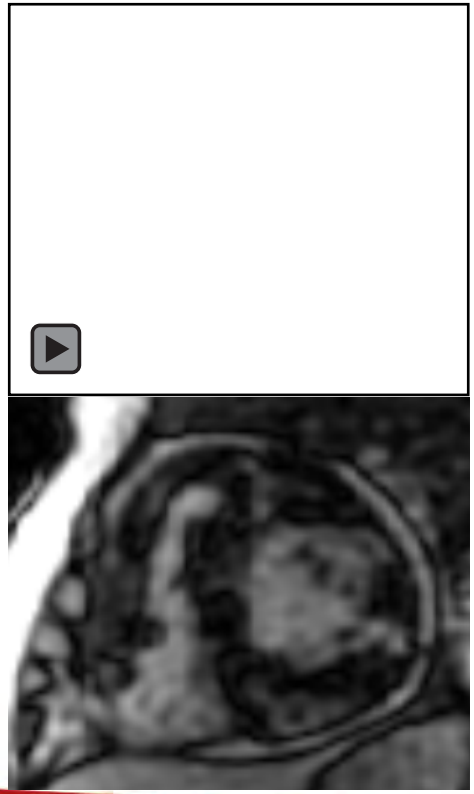
C. PET Scan

D. Right and left heart cath including endomyocardial biopsy

R/L heart cath: normal coronaries, LVEDP 17 mm Hg, PA 32/16 mm Hg
Endomyocardial biopsy performed.

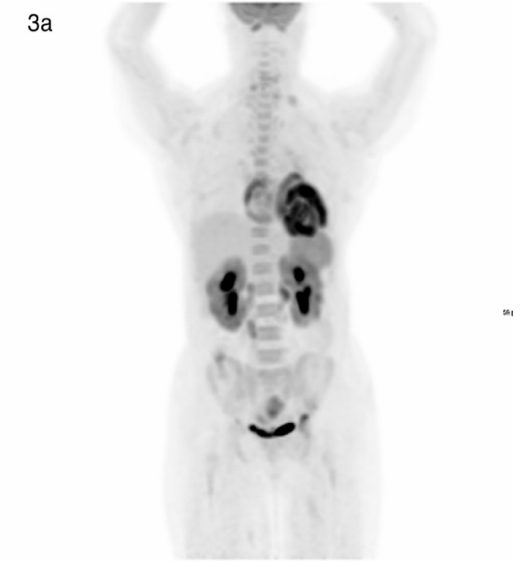
Cardiac MRI

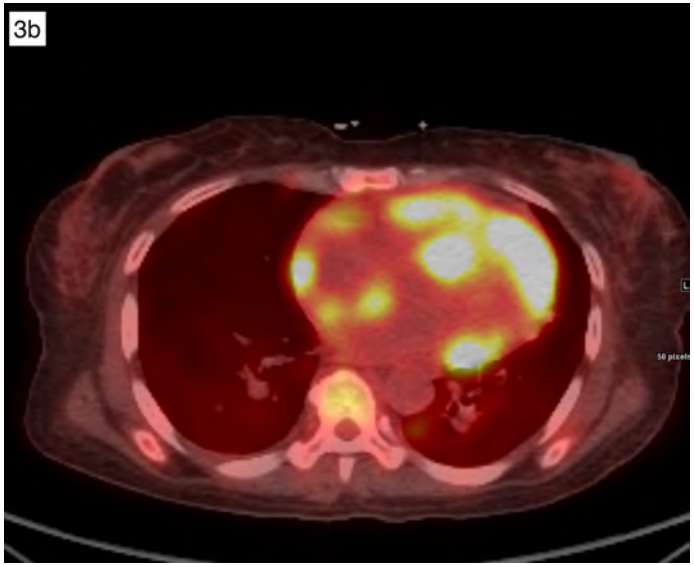




- Small LV size; LVIDd 4 cm
- IVSd= 1.6 cm; PWT 1.4 cm
- Concentric LV hypertrophy; LVEF 45%
- RV hypertrophy; RVEF 39%
- Diffuse foci of myocardial enhancement involving all LV walls, prominent epicardial involvement. Infarct/scar size 13%
- Enhancement of the RV free wall and inter-atrial septum

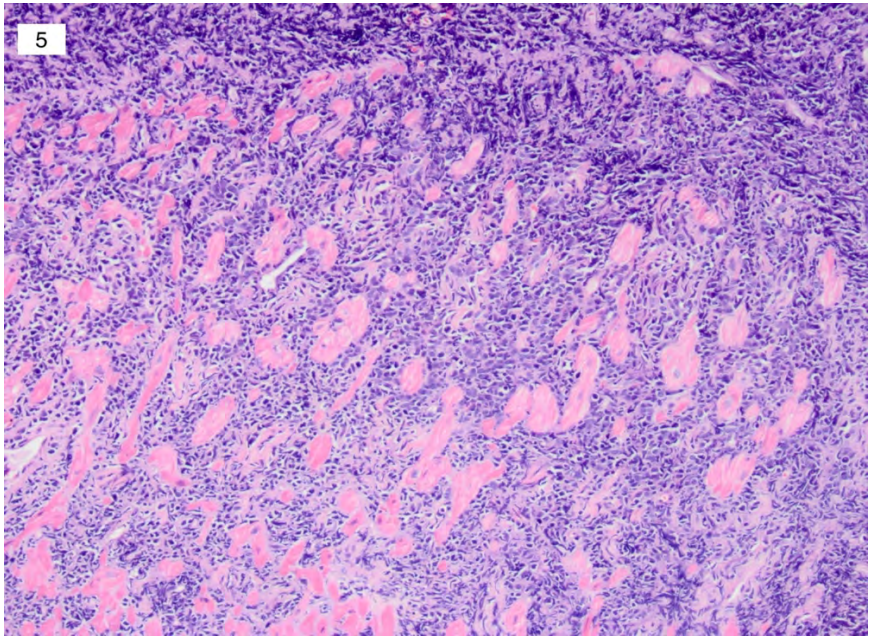
Whole Body PET





Intense patchy FDG accumulation in the myocardium; possibly lymphomatous infiltration; inflammatory etiology (e.g. sarcoid) also possible

Endomyocardial Biopsy



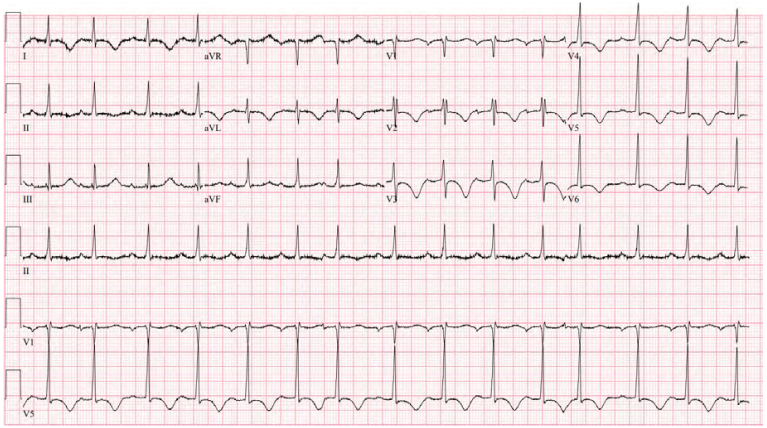
Myocardial Biopsy with diffuse lymphocytic infiltration

Treatment Course

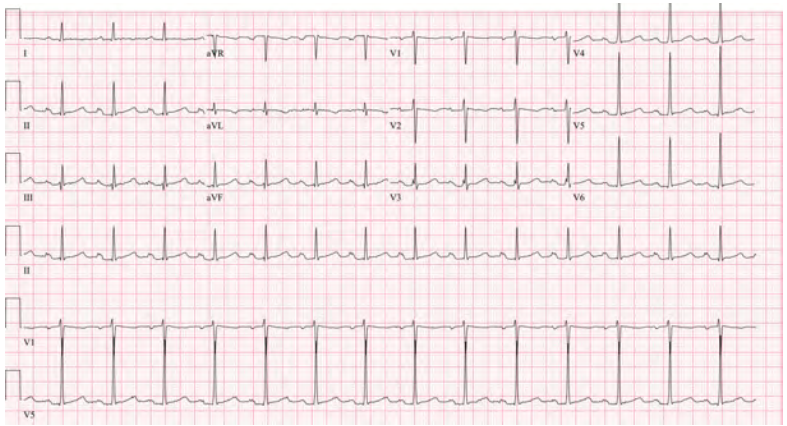
- Low dose regimen initiated with slow increase (prednisone followed by dose adjusted R-EPOCH).
- Monitored in the CICU for the initial cycles of treatment, due to the risk of rapid tumor destruction with antineoplastic therapy associated with lymphoma, may lead to significant cardiovascular complications such as ventricular rupture or life arrhythmia when there is extensive myocardial involvement.
- Tolerated the planned protocol without complications. Good response to therapy. Improvement of chest pain and dyspnea.

8 weeks after treatment

- **Troponin I 9.39 →0.05 ng/ml**
- **BNP1288 →169**



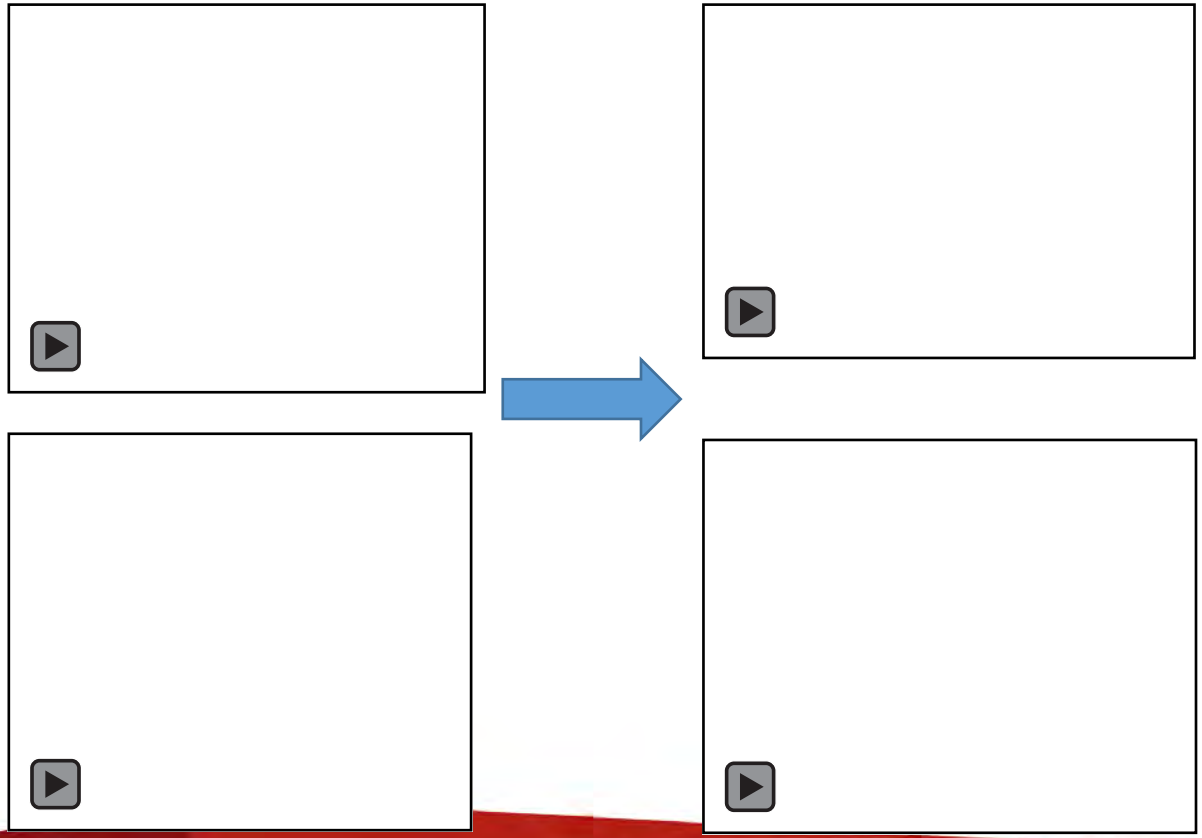
Baseline



Post Tx

Resolution of T wave inversion in the anterolateral leads; QTc normal

Cardiac MRI



8 weeks after treatment

- Improved LV systolic function; EF 52%
- Decreased ventricular hypertrophy; wall thickness; IVS 1.0 cm; PWT 0.8 cm
- Decreased myocardial enhancement

Cardiac Involvement with Lymphoma

- Incidence of cardiac involvement by lymphoma as identified by autopsy varies widely, ranging from 8.7% to 20%.
- Previously thought as a rarity, likely undetected clinically; now being reported with greater frequency antemortem, as a result of increased clinical awareness, improved imaging techniques
- Lymphoma metastasis can involve the pericardium, epicardium, myocardium and endocardium. Multiple masses or nodules more common, though diffuse infiltration of the myocardium can also occur; case reports of mimicking hypertrophic cardiomyopathy.
- Troponin elevations as a result of ischemia or myocardial damage from lymphomatous deposits.

Cardiac Involvement with Lymphoma

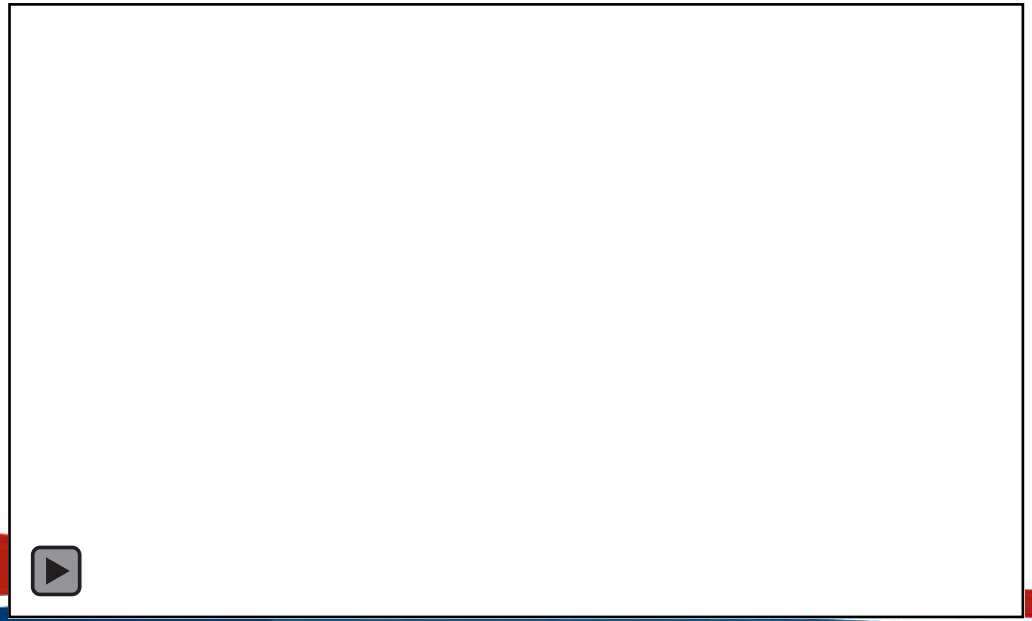
- Cardiac metastasis should be suspected or sought in any patient with known malignancy who develops new CV signs or symptoms.

- While tissue biopsy is the gold standard for diagnosis, multimodality imaging plays a central role in the evaluation of cardiac metastasis:
  - Accurately distinguishing cardiac metastasis
  - Guide management – medical, surgical or both
  - Assess response to treatment.

Case 2

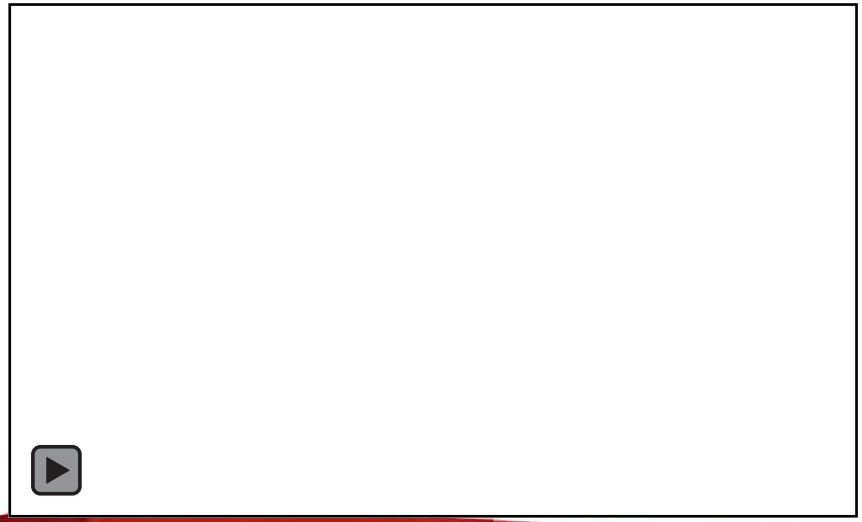
64 yo F metastatic endometrial cancer starting a clinical trial with dual immune checkpoint inhibitor therapy with durvalumab (PD-L1 inhibitor) and tremelimumab (CTLA-4 inhibitor).

- No CV history or risk factors.
- Pretreatment echo normal: LVEF 64% and GLS 18.1%.



6 weeks after starting immunotherapy:

- Complained of difficulty ambulating due to muscle weakness and progressive DOE.
- Afebrile, stable vital signs.
- Labs: transaminitis with AST 309, ALT 386 and CPK to 4,750 U/L.
- Steroid initiated for suspected immune check-point inhibitor induced myositis.
- Repeat echo: preserved LVEF of 60% though decreased GLS to 13.9% (GLS 18% at baseline). ECG: normal



Which of the following is true:

A. Immune check point inhibitor therapy has no cardiotoxic effects

B. A normal LVEF does not rule out ICI induced myocarditis

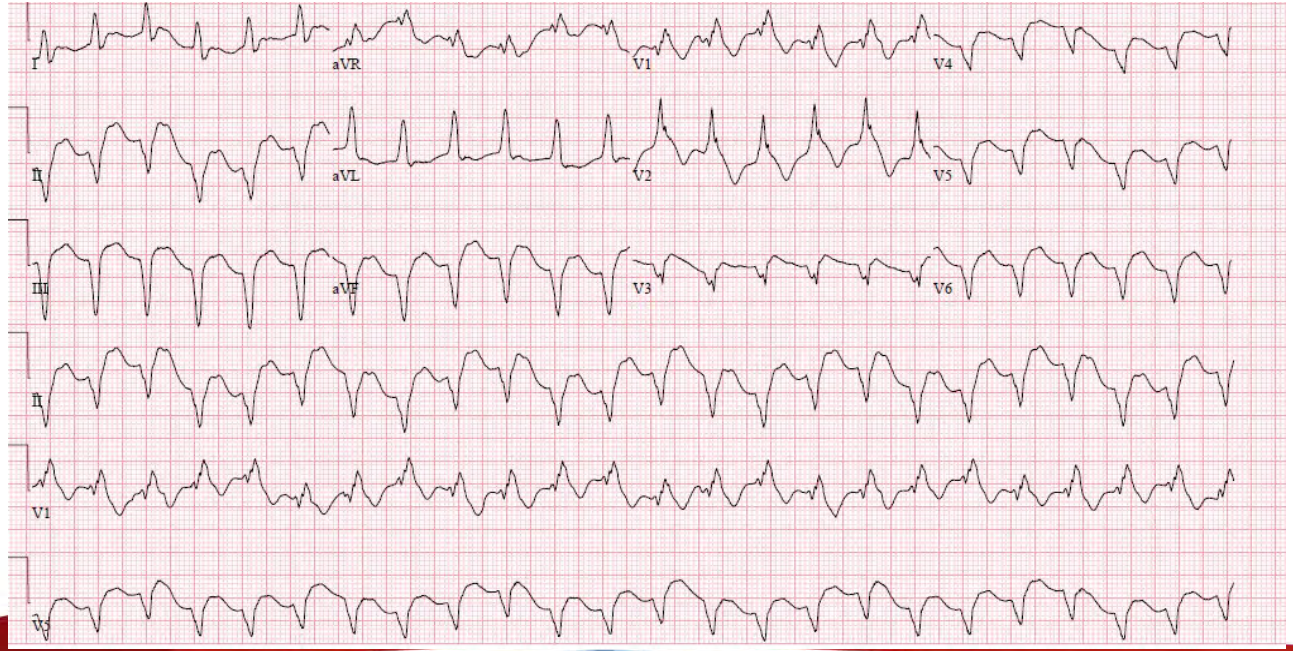
C. A drop of GLS to 13.9% must be incorrect since the LVEF remains normal

D. A normal ECG rules out myocarditis

Presents a few days later w/ weakness, dyspnea at rest, mild chest pressure, palpitations.

- VSS: 36.6C, BP 124/70, HR137bpm, 94% 2l NC

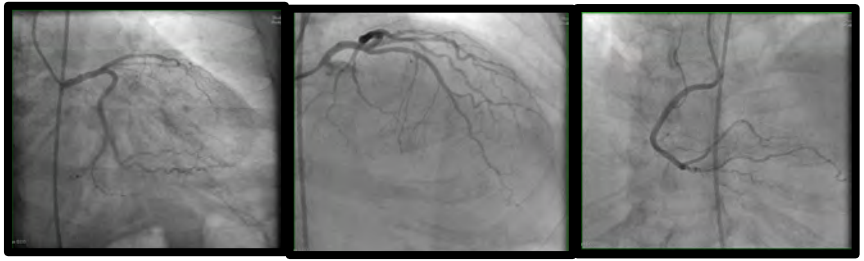
ECG – wide complex tachycardia



Trop 18 ng/ml
BNP 261 pg/ml,

Pt underwent emergent cardiac catheterization

- Coronary Angiography: Normal

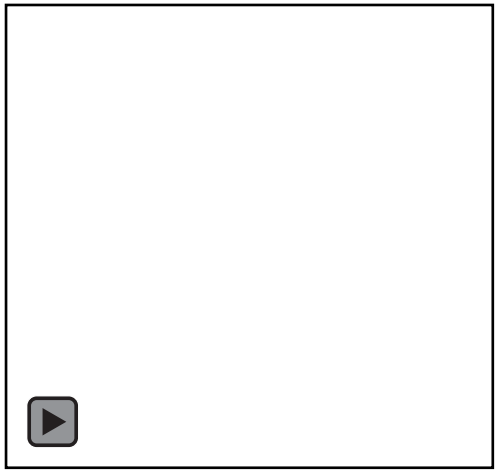


- Further decompensates with respiratory failure requiring intubation
- Myocarditis suspected. RV biopsy performed on cath
- Methylprednisolone 1 gm/day initiated

Hospital Day 2

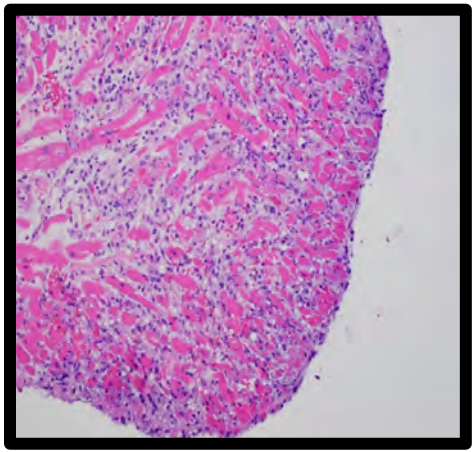
- Continued wide complex tachycardia despite DCCV x2 and antiarrhythmics
- Follow-up echo showing LVEF 28%
- IABP placed
- Continued clinical/hemodynamic deterioration
- Tn increased to 30, urine output dropped, on 3 pressors
- Placed on veno-arterial extra-corporeal membranous oxygenation (VA-ECMO)

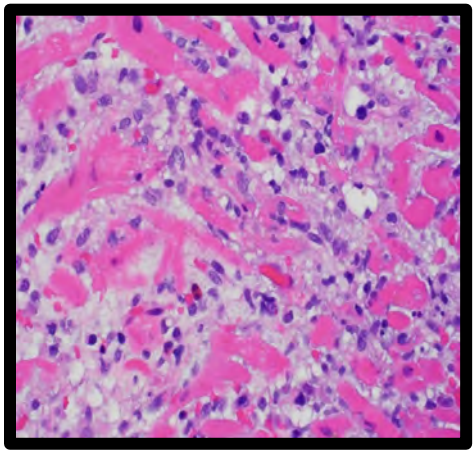
Follow-up Echo:



Echo: EF 30%. Severe hypokinesis of LV

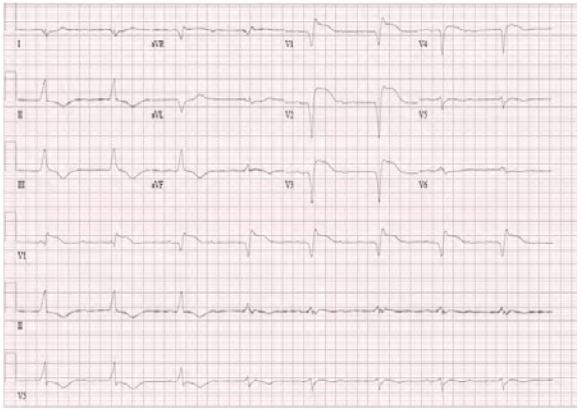
RV Biopsy

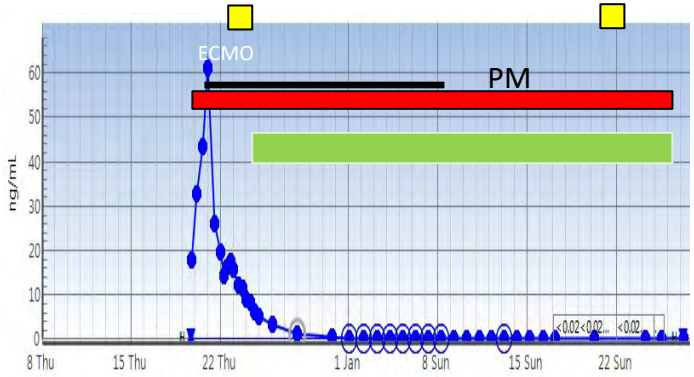




Pathology Report: Intense lymphocytic infiltration c/w extensive lymphocytic and lymphohistiocytic myocarditis

HD 3: VT resolves but CHB unveiled; marked ST elevation reflecting ongoing myocarditis; temporary PM placed. Troponin peaked at 61 and down to 6 a few days later, receiving with steroids, IVIG and mycophenolate; gradual improvement of clinical status
HD 9: ECMO explanted
HD 22: PM explanted, regained complete 100% AV conduction
HD 24 (pre-discharge): EF 55-60%





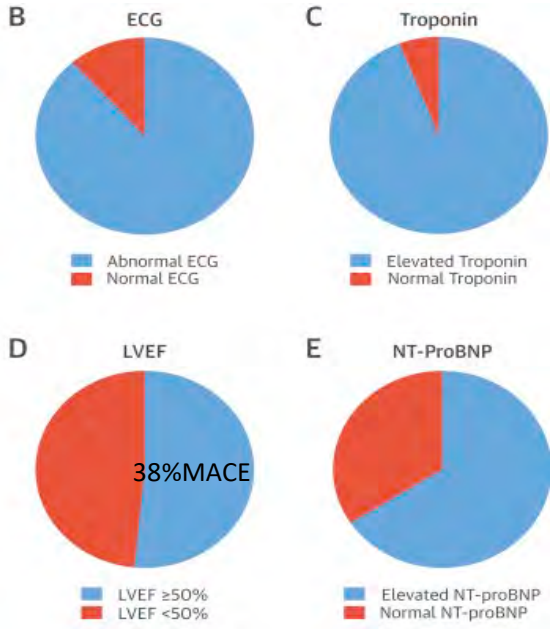
- Steroids: HD1 (pulse x 5 days) -> taper
- IVIG: HD3,4 and HD 31,32
- Mycophenolate mofetil HD4 500mg IV bid -> 1000mg po bid.

Immune Checkpoint Inhibitor Associated Myocarditis

- T cell infiltration of the myocardium; pathologically similar to transplant rejection
- Incidence: 0.27 to 1.14%. Higher risk in combination therapy (CTLA-4 inhibitor combined with a PD-1 inhibitor).
- Most cases occur early; 81% presenting within 3 months of starting therapy
- Cases range from mild signs and symptoms to fatal events
- Poor prognosis
  - Case fatality rate between 30-50% (vs 2-5% in general myocarditis)
  - High rate of major adverse cardiac event
    - cardiogenic shock, cardiac arrest, VT, complete heart block

Wang DY, JAMA Oncol 2018
Mahmood, JACC 2018

ICI Myocarditis: Clinical Manifestation (registry data)



Mahmood, SS. Et al. JACC 2018; 71(16): 1755-64

Symptoms

- SOB, chest pain, palpitation, general malaise

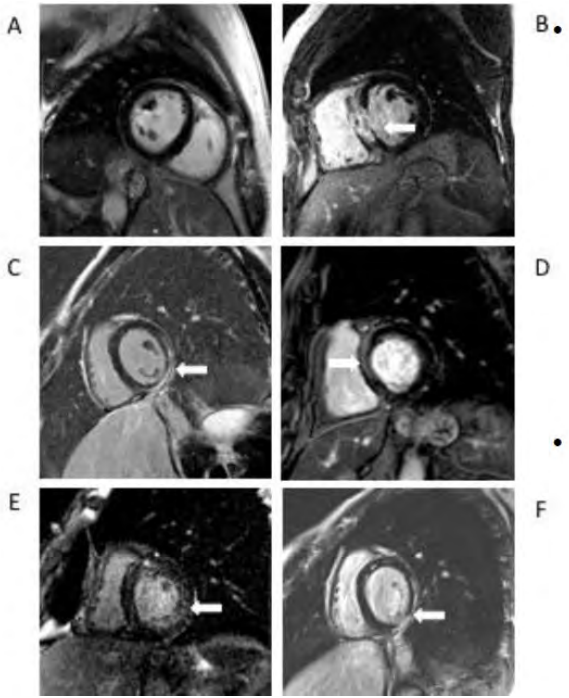
Elevated troponin present in nearly all cases (94%)

Abnormal ECG changes and elevated BNP or NT-proBNP common (83% and 66% respectively)

LVEF normal in ~50% of cases

- 38% MACE occurred in patients with normal LVEF
- Poor predictor of outcome

Cardiac MRI in ICI-Associated Myocarditis

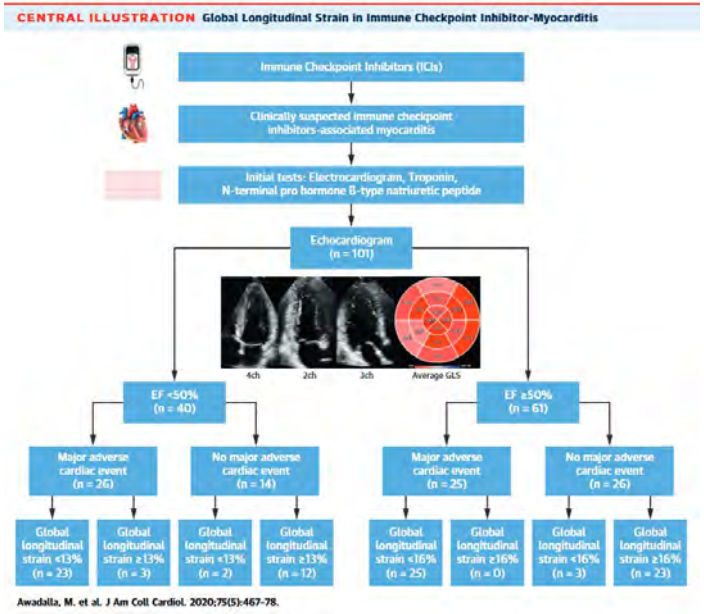


Zhang L, et al, EHJ 2020

LGE pattern: A. normal B. sub-endocardial/transmural
C. sub-epicardial myocardial D. mid-myocardial E. diffuse F. mixed

- Preferred imaging modality for diagnosis
- Tissue characterization techniques (T1 and T2 weighted sequences and LGE sequence) allow detection of edema, inflammation or necrosis
- Late gadolinium enhancement (LGE) patterns - variable

GLS and Cardiac Events in Patients with Immune Checkpoint Inhibitor-Myocarditis



- Drop in GLS is associated with ICI related myocarditis, even among patients with normal LVEF.
- GLS prognostic: Lower GLS and relative drop in GLS from baseline was associated with subsequent MACE (cardiogenic shock, arrest, complete heart block, and cardiac death) in both normal or reduced EF.

Awadalla M, Neilan T. JACC 2020;75:467-78

ICI Associated Myocarditis

- Associated with a high rate of major adverse cardiac events
- The diagnosis should be considered among patients on ICI presenting with cardiac signs and symptoms
- An elevated troponin is a common finding and a reasonable indicator of outcomes
- GLS decreases with the development of ICI induced myocarditis in patients with both normal and reduced LVEF, and is predictive of outcome
- Early diagnosis is essential as earlier treatment with high dose steroid may reduce the rate of major adverse events.