Granulomatous Myocarditis - An overlooked cause of cardiomyopathy

C. Narasimhan
CARE Hospital
Hyderabad, India.

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Medanta, New Delhi
Outline:

- Background
- Our experience (When to suspect, How to confirm)
- Clinical Approach to making a diagnosis
- Management
• The Pioneers:

- Jonathan Hutchinson
- Robert Koch
SARCOIDOSIS vs. TUBERCULOSIS

<table>
<thead>
<tr>
<th>Country</th>
<th>Prevalence per million</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweden</td>
<td>640</td>
</tr>
<tr>
<td>Germany</td>
<td>420</td>
</tr>
<tr>
<td>Ireland</td>
<td>400</td>
</tr>
<tr>
<td>USA</td>
<td>390</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>270</td>
</tr>
<tr>
<td>France</td>
<td>160</td>
</tr>
<tr>
<td>Italy</td>
<td>90</td>
</tr>
<tr>
<td>Japan</td>
<td>25</td>
</tr>
<tr>
<td>Spain</td>
<td>12</td>
</tr>
</tbody>
</table>


Estimated no. of TB cases by country 2000

- = >100 000
- = <20/100 000 population

Arch Intern Med 2003;163:1009-21
36 yrs  Opthalmologist

First presentation –

- Recurrent palpitations
- Documented VT 2004
- Moderate LV systolic function LVEf 35%
- NYHA II
- CAG – Normal

- No H/O viral illness, significant F/H. etiology ??

Medical treatment , amiodarone for VT
Cardiac MRI (2011)
Non compaction anterior and lateral wall
Gd enhancement – mid myocardial basal septal scar
EF – 30%

Dual Chamber ICD inserted 09/2011

Recurrent admission for Heart failure - 2013
2013

- Recurrent admissions for heart failure requiring inotropic reports

- Recent admission for heart failure and ventricular tachycardia (recurrent device therapy)

- Hoarseness of voice

- NYHA class IV

- EF – 25%

- Referred for further management
<table>
<thead>
<tr>
<th>Condition</th>
<th>Status</th>
<th>Measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral Valve</td>
<td>NORMAL</td>
<td>MACS - 2.0 CM</td>
</tr>
<tr>
<td>Aortic Valve</td>
<td>NORMAL</td>
<td></td>
</tr>
<tr>
<td>Tricuspid Valve</td>
<td>NORMAL</td>
<td></td>
</tr>
<tr>
<td>Pulmonary Valve</td>
<td>NORMAL</td>
<td></td>
</tr>
<tr>
<td>Right Atrium</td>
<td>NORMAL</td>
<td></td>
</tr>
<tr>
<td>Right Ventricle</td>
<td>NORMAL</td>
<td></td>
</tr>
<tr>
<td>Left Ventricle</td>
<td>DILATED 5.6 CM</td>
<td></td>
</tr>
<tr>
<td>IVS(s)</td>
<td>0.9 cm</td>
<td>LV(s): 6.2</td>
</tr>
<tr>
<td>IVS(d)</td>
<td>0.9 cm</td>
<td>LV(d): 6.9</td>
</tr>
<tr>
<td>PW(s)</td>
<td>1.1 cm</td>
<td>LVEF: 25%</td>
</tr>
<tr>
<td>PW(d)</td>
<td>0.8 cm</td>
<td>FS: 13%</td>
</tr>
<tr>
<td>IVS</td>
<td>INTACT</td>
<td></td>
</tr>
<tr>
<td>IAS</td>
<td>INTACT</td>
<td></td>
</tr>
<tr>
<td>AORTA</td>
<td>2.6 cm</td>
<td></td>
</tr>
<tr>
<td>Pulm Artery</td>
<td>NORMAL</td>
<td></td>
</tr>
<tr>
<td>Pulm Veins</td>
<td>NORMAL</td>
<td></td>
</tr>
<tr>
<td>Pericardium</td>
<td>NORMAL</td>
<td></td>
</tr>
<tr>
<td>SVS/IVC/CS</td>
<td>NORMAL</td>
<td></td>
</tr>
</tbody>
</table>

**DOPPLER STUDY**

- Mitral Flow: 0.7 m/sec
- Aortic Flow: 0.7 m/sec
- Pulmonary Flow: NOR m/sec
- Pulm Venous Flow: NOR m/sec

**COLOR DOPPLER**

- MR: SEVERE (MR JET AREA - 16.1 MM OF HG)
- AR: NIL
- TR: MILD (TR GRADIENT - 33 MM OF HG)
- PR: NIL

**HEMODYNAMIC DATA**

- E/A = E > A
- PG - 2.3 MM OF HG
- Airlifted on IV dobutamine.
- Was on inotropic support as cardiogenic shock (Norad / dobutamine), S. creat 2mg, elevated liver enzymes
- STAGE D heart failure with recurrent admissions for heart failure and recurrent VT option of CARDIAC TRANSPLANT was discussed.
Considering slow progressive disease, vocal cord involvement with myocardial scarring inflammatory/infiltrative cardiomyopathy suspected.

Cardiac FDG PET scan was performed.
- Started on methyl prednisolone
- Continued with high dose steroid, and MTX

- Dr returned to his work, cardiac rehab able to walk 20 mts- 30 mts, EF – 35 %

Vocal cord palsy completely recoverd.
45 yr old lady
With idiopathic VT
Tt with Amio & betablockers

4 years later had recurrent VT/ Vf mild LV dysfunction
ICD implanted

• 1996

• Long History, variable systemic symptoms
• remissions and relapses

• 2004
• developed LBBB
• CHF: CRTd
• implanted

• PG change 2009
• Diagnosed to have
• Sarcoid

Cardiac involvement in Sarcoidosis

- Autopsy series Systemic Sarcoidosis, myocardial granulomas in 27%, but clinically silent in over 35%
  
  *Silverman et al, Circulation 1978*

Myocardial involvement 24/123 patients (19.5%)

Clinical Cardiac involvement in 5%

*Iwai K et al, 1994 Autopsy in systemic sarcoidosis*
Cardiac sarcoidosis (TB) is generally diagnosed as a part of systemic Sarcoidosis, or in the following settings:

- VT with in non ischemic cardiomyopathy
- Ventricular arrhythmias with conduction system disease
- Cardiomyopathies (DCM, RCM) & conduction system disease

First pt ( 38 M ) with recurrent VT and normal Coronaries diagnosed to have possible Myoc TB in 2004
Investigation protocol

Step 1. Is there a Scar or inflammation

DE-CMR : mid-myocardial scar
HRCT chest : mediastinal lymph nodes
$^{18}$FDG PET-CT : increased myocardial & lymph node uptake
Biopsy (lymph node ± endomyocardial) : granuloma

Step 2. Determine the Aetiology

Tuberculin skin test
Investigations on the biopsied specimen
  Stain & culture for acid-fast bacilli
  *M. tuberculosis* DNA-PCR (IS 6110)
  Stain & culture for fungal elements
Investigation protocol (unexplained VT)

- ECG, Echo, Chest X-ray
- Gadolinium enhanced cardiac MRI
- HRCT - chest, neck and upper abdomen
- $^{18}$FDG PET-CT of heart, neck & abdomen

- Tuberculin skin test (5TU) ($\geq 10$mm = positive)

- Serum ACE levels / ESR/ CRP/ Soluble IL2
Investigations:

- Lymph node biopsy
- EMB (poor yield)

Analysis of biopsy samples:

- Histopathology
- Stain for acid fast bacilli
- Culture for Mycobacterial species
- DNA-PCR to detect *M. tuberculosis* (IS 6110 sequence)
- Stain & culture for fungal elements
Value of Endo Myocardial Biopsy

- First 14 patients underwent EMB:
- 12 were normal, one revealed a nonspecific necrosis
• Mapping and ablation of high voltage corridor between scars
Diagnosis groups

- AFB stain / \( M.\text{tuberculosis} \) culture positive = **TUBERCULOSIS**
  Rx : Anti-tuberculosis therapy (ATT)

- AFB stain
  M.tb culture
  M.tb DNA- PCR
  Tuberculin skin test negative = **SARCOIDOSIS**
  Rx : Corticosteroids ± Methotrexate

- AFB stain & M.tb Culture negative;
  POTENTIALLY ACTIVE TB
  skin test positive + or PCR = **LATENT TB**
  Rx : ATT + Corticosteroids ± Methotrexate

Sekar et al  Indian J of Medical Microbiology  2008
MRI findings

- Normal: 14%
- Involvement of septum only: 21%
- Involvement of other walls (not septum): 10%
- Diffuse delayed enhancement: 15%
- Other abnormalities: 20%
- Involvement of septum and other walls: 21%
Myocardial scar by MRI

- **Mid Myocardial scar**: 100%
- **Epicardial involvement**: 43% (Tuberculosis), 20% (Sarcoid)
- **RV involvement**: 29% (Tuberculosis), 0% (Sarcoid)
- **IAS**: 20% (Tuberculosis), 0% (Sarcoid)
Males (10/12)

Age: 42 ±11 yrs

Mean LVEF at presentation: 36.75 ± 10.3 %

LVESD - 42.1 ± 6.5 mm, LVEDD- 50.4 ± 6mm

RV dysfunction- 4 patients (25%)

Mitral regurgitation -6 (50%) patients.
Change in LVEF-24months follow up

Pre Treatment LVEF  Post Treatment LVEF

Patient1  Patient2  Patient3  Patient4  Patient5  Patient6  Patient7  Patient8  Patient9  Patient10  Patient11  Patient12
Clues to diagnosis

- ECG
- Echo
- Vt morphologies
Sinus rhythm ECG at presentation provides diagnostic clues

<table>
<thead>
<tr>
<th>ECG abnormality</th>
<th>Group A (n=20)</th>
<th>Group B (n=20)</th>
<th>p value for difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fascicular blocks</td>
<td>2(10%)</td>
<td>10(50%)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>- overall</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAHB</td>
<td>0</td>
<td>4(20%)</td>
<td>NS</td>
</tr>
<tr>
<td>LPHB</td>
<td>2(10%)</td>
<td>3(15%)</td>
<td>NS</td>
</tr>
<tr>
<td>Bifascicular block</td>
<td>0</td>
<td>3(15%)</td>
<td>NS</td>
</tr>
<tr>
<td>QRS notching</td>
<td>2(10%)</td>
<td>10(50%)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>- overall</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- on ascending limb of R wave</td>
<td>2(10%)</td>
<td>4(20%)</td>
<td></td>
</tr>
<tr>
<td>- on descending limb of R wave</td>
<td>2(10%)</td>
<td>4(20%)</td>
<td></td>
</tr>
<tr>
<td>- on ascending limb of S wave</td>
<td>1(5%)</td>
<td>2(10%)</td>
<td></td>
</tr>
<tr>
<td>- on descending limb of S wave</td>
<td>0</td>
<td>3(15%)</td>
<td></td>
</tr>
</tbody>
</table>

**Group A = True idiopathic VT**

**Group B = VT due to granulomatous infiltration**

Satish reddy: Subtle Electrocardiographic Findings In Idiopathic Ventricular Tachycardia - A Malignant Subset” - presented At HRS 2010
Sinus rhythm ECG at presentation provides diagnostic clues
DCM / VT (no f/H)

- Atypical morphology
- Minor Echo abnormalities
- IRBBB/prolonged PR interval/LAFB, etc.
- Constitutional/systemic manifestations
- LV function abnormalities

Contrast Enhanced MRI/FDG-PET

- Normal
  - RFA
- Myocardial scarring
  - IVS/RV surface
    - EM Biopsy
- Scarring at other sites
  - Biopsy of mediastinal node
Granulomatous myocarditis-

- Not rare
- Paucity of systemic manifestations
- Long duration, variable progression.
- Disease specific therapy results in improved outcome.
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- **Dept Of Electrophysiology:**
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- **Dept of Rhematology**
  - Jugal Kishore MD
  - Ravikiran MD
CONCLUSIONS

- Ventricular Dysfunction and VT may be the only manifestation of myocardial tuberculosis or cardiac sarcoidosis.

- Several clinical clues aid diagnosis

- Early disease-specific therapy controls the arrhythmia, and prevents ventricular dysfunction. (potentially preventable form of Cardiomyopathy)