

Takotsubo Cardiomyopathy (TTC)

Background

1. Definition

- Acute onset reversible left ventricular apical ballooning (during systole), with chest pain, ECG changes and no, or minimal, elevation of cardiac enzymes in absence of significant CAD
- Also known as:
 - Broken heart syndrome, transient LV apical ballooning, stress induced cardiomyopathy
- 1st described in Japan in 1991
- Takes its name from unusual shape, resembling Japanese octopus jar, the left ventricle assumes during systole in affected patients

Pathophysiology

1. Pathology of disease

- Hallmark is hypokinesis of the apex of left ventricle (LV)
 - As the base of LV contracts, the apparently stunned apex balloons outward, forming characteristic shape
- Exact etiology not well understood
- Catecholamines play major role in development of TTC
 - Patients present in times of acute stress, when sympathetic outflow is frequently increased
- Catecholamines have been shown to induce myocardial damage both clinically (pheochromocytoma) and experimentally
- In patients with stress cardiomyopathy
 - Plasma catecholamine levels
 - 2-3 times higher than in MI
 - Up to 34 times higher than in healthy pts
 - Catecholamine-induced myocardial stunning is a proposed mechanism of TTC
- Unique anatomic features (greater response to adrenergic stimulation, limited coronary circulation) of the left apex may explain its vulnerability to TTC
 - Main consequence of significant TTC is heart failure

Diagnostics

1. Impossible to distinguish between TTC and myocardial infarction on the basis of Hx and PE alone

- Studies typically used to evaluate chest pain (ECG, cardiac enzymes) may confound Dx rather than clarify it

2. History

- Chest pain, often at rest
- Dyspnea
- Syncope
- Recent emotional trauma (typical feature)
 - Unexpected death of a loved one

- Domestic abuse
 - Arguments
 - Financial losses
 - Accidents
 - Court appearances
 - Any high stress event
 - Physical stressors
 - Varied physical stressors
 - Exhausting physical activity
 - Asthma attacks
 - Exacerbation of other systemic disorders
 - Medical procedures (endoscopy, colonoscopy)
3. Physical exam
- Findings nonexistent or subtle
 - Significant findings, if present, usually due to left heart failure
 - Blood pressure: normal - shock
 - Systolic cardiac murmurs occasionally noted
 - Ejection murmur heard over aorta or base
 - Mitral regurgitation
 - Pulmonary crackles 2° to pulmonary edema
4. Diagnostic testing
- ECG abnormal in most cases
 - ECG of limited value
 - Lack of reciprocal ECG changes and Q waves
 - Q waves have been noted but are transient
 - Corrected QT interval tends to be significantly longer in patients with TTC
 - Cardiac enzymes
 - Limited value
 - May not rise at all, may rise and fall in pattern similar to MI
 - Peak levels at presentation, with faster normalization than is seen in infarction
 - BNP markedly elevated during acute phase
 - Echocardiography
 - Large area of apical hypokinesis
 - Cardiac catheterization
 - Cath findings do not correspond to presenting symptoms
 - No treatable coronary lesions
 - Ventriculography
 - Classic finding of apical ballooning accompanied by hyperkinetic activity at the base of ventricle
5. Criteria (Mayo Clinic):
- Transient akinesis or dyskinesis of left ventricular apical and midventricular segments
 - Regional wall motion abnormalities must extend beyond single epicardial vascular distribution

- Exclusion of obstructive coronary disease or angiographic evidence of acute plaque rupture
- New ECG abnormalities
- Exclusion of recent head trauma, intracranial hemorrhage, hypertrophic cardiomyopathy, myocarditis, obstructive epicardial coronary artery disease, pheochromocytoma

Differential Diagnoses

1. Acute coronary syndrome
 - Associated with ST elevation on ECG
2. Aortic dissection
 - Widening of mediastinum on CXR
 - Ripping, tearing pain felt in intrascapular region
3. Pulmonary embolism
 - Seen on CT
4. Tension pneumothorax
 - Decreased breath sounds
 - Shifting of trachea
 - Seen on CXR
5. Pericarditis
 - Pericardial friction rub
 - Beck's Triad:
 - Jugular venous distention
 - Muffled heart sounds
 - Hypotension
 - Electric alternans on ECG
6. Hypertrophic obstructive cardiomyopathy
 - ECG will show LV hypertrophy
 - Echo may be diagnostic

Therapeutics

1. Supportive treatment
 - Beta blockers for dynamic intraventricular obstruction
 - Metoprolol 25 mg PO qD
 - Calcium channel blockers for coronary vasospasm
 - Diltiazem 120 mg PO BID
 - Beta blockers, ACE inhibitors and diuretics for heart failure
 - Furosemide 20 mg PO qD
 - Lisinopril 20 mg PO qD
 - Short-term anticoagulation until left ventricular function recovers
 - Often used prophylactically
2. Thrombolytic agents not indicated

Prognosis

1. Despite dramatic presentation, prognosis of TTC is positive

2. Mortality of 1-3%
3. Most patients regain full functional capacity within 2-4 weeks
4. Recurrence rate has not yet been identified

References

1. Dote K, Sato H, Tateishi H, et al. Myocardial stunning due to simultaneous multivessel coronary spasms: a review of 5 cases (in Japanese) *J. Cardiology* 1992; 21(2): 203-214.
2. Gianni M, Dentali F, Grandi AM, et al. Apical ballooning syndrome or Takotsubo cardiomyopathy: a systematic review. *European Heart Journal*. 2006; 27(13): 1523-1529
3. Bybee KA, Kara T, Prasad A, et al. Systematic review: transient left ventricular apical ballooning: a syndrome that mimics ST-segment elevation myocardial infarction. *Annals Internal medicine*. 2004; 141(11): 858-865.
4. Pavin D, Le Breton H, Daubert C. Human stress cardiomyopathy mimicking acute myocardial infarction syndrome. *Heart*. 1997; 78(5): 509-511
5. Wittstein IS, Thiemann DR, Jima JAC, et al. Neuro-humoral features of myocardial stunning due to sudden emotional stress. *New England Journal of Medicine*. 2005; 352(6): 539-548
6. Akashi YJ, Barbaro G, Sakurai T, et al. Cardiac autonomic imbalance in patients with reversible ventricular dysfunction takotsubo cardiomyopathy. *QJM*. 2007; 100(6): 335-343
7. Lyon AR, Rees PS, Prasad S, et al. Stress (takotsubo) cardiomyopathy: a novel pathophysiological hypothesis to explain catecholamine-induced acute myocardial stunning. *Nat Clin Pract Cardiovasc Med*. 2008; 59(1): 22-29
8. Virani SS, Khan AN, Mendoza CE, et al. Takotsubo cardiomyopathy, or broken-heart syndrome. *Tex Heart Inst Journal*. 2007; 34(1): 76-79
9. Sharkey SW, Lesser JR, Zenovich AG, et al. Acute and reversible cardiomyopathy provoked by stress in women from the United States. *Circulation*. 2005; 111(4): 472-479
10. Akashi YJ, Nakazawa K, Sakakibara M, et al. The clinical features of takotsubo cardiomyopathy. *QJM*. 2003; 96(8): 563-573
11. Hansen PR. Takotsubo cardiomyopathy: an under-recognized myocardial syndrome. *Eur J Intern Med*. 2007; 18(8): 561-565
12. Ogura R, Hiasa Y, Takahashi T, et al. Specific findings of the standard 12-lead ECG in patients with 'takotsubo' cardiomyopathy: comparison with the findings of acute anterior myocardial infarction. *Circ J*. 2003; 67(8): 687-690
13. Dhar S, Koul D, Subramanian S, Bakhshi M. Transient apical ballooning: sheep in wolves' garb. *Card Rev*. 2007; 15(3): 150-153
14. Alizadeh Dehnavi R, van der Wall EE. Transient left ventricular apical ballooning [letter]. *Ann Intern Med*. 2005; 142(8): 678
15. Ako J, Honda Y, Fitzgerald PJ. Transient left ventricular apical ballooning [letter]. *Ann Intern Med*. 2005; 142(8): 678

Authors: Dennys Maldonad, MD, & James Horton, MD, Mercy Health System FMRP, WI

Editor: Wail Malaty, MD, University of North Carolina FPRP