Ambulatory Care Conference

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Case Presentation

- 50 year old white female presents to ED with substernal chest pain. Pain started while driving, is left substernal in location “like an elephant sitting on my chest.” She has radiation to the left arm and a tightness in her neck. She rates the pain a 9/10. The pain has now been going on over an hour.

Past Medical History

- Sleep apnea x 2 years, on CPAP
- Hypertension x 1 year
- Family history significant for DM, CHF

Physical Exam

- T 97^4 BP 122/72 P 67 R 20
- General: Obese WF in acute distress
- Neck: No JVD or bruits
- Heart: RRR with 2/6 SEM RUSB
- Lungs: CTA B
- Abdomen: Benign
- Extremities: No C/C/E, good pulses

Therapeutics

- ASA 325 mg po given
- Placed on 2L O_2 nasal cannula
- SL nitroglycerin attempted x 2 without change in chest pain
- GI Cocktail administered – no response

Laboratory Data

- CBC normal
- Electrolytes normal
- Chest Xray normal
- EKG NSR with <1mm lateral ST segment depression with flattening of t waves
- First Cardiac Enzymes negative

Hospital Course

- Attempted GXT-Thalium
  - 7 minutes, 1-2 mm ST down sloping in inferolateral leads (+) with associated chest pain
  - Small persistent anterior wall perfusion abnormality
  - EF 59% at rest → 70% with exercise
- Started on heparin IV (CAD protocol)
- Admitted to telemetry
- Pain resolved spontaneously
- No further recurrence
- Cardiac Enzymes all negative

Next morning

- Followup EKG demonstrated similar lateral ST segment changes
- Cardiac Catheterization
  - Normal LV function
  - Normal coronary vasculature
  - Acetylcholine challenge negative
- Discharged from hospital with diagnosis of non cardiac chest pain and instructed to followup with primary care in 1-2 weeks.

Subsequently…

- Patient continued to experience similar episodes of chest pain about 1-2 times per day.
- Each episode had similar pattern
  - Nonexertional
  - Anginal quality
  - Lasted around 1 hour
  - Spontaneous resolution
- Ultimately went on disability due to pains

Differential Diagnosis of chest pain with a normal angiogram

- Anxiety
- Esophageal spasm
- GERD
- Prinzmetal's Angina (epicardial coronary vasospasm)
- Systemic Hypertension
- Left Ventricular Hypertrophy
- Valvular Heart Disease

Cardiac Syndrome X

- Described by H.G. Kemp in editorial
- Etymology
  - 1973 Study by R. Arbogast and M. G. Bourassa
  - Grouped patients with chest pain into 2 groups:
    - Patients with CAD
    - Patients without angiographic evidence of CAD
  - Compared EKG and hemodynamic response to atrial pacing during cardiac catherization

Etymology

- Study found that patients with normal coronary arteries (Group X) had normal left ventricular function despite having typical ischemic EKG changes
- Group X arbitrarily named as such

Cardiac Syndrome X is not Metabolic Syndrome [X]

- Metabolic Syndrome [X]
  - Truncal Obesity
  - Hypertriglyceridemia
  - Hypertension
  - Diabetes mellitus type 2
  - Implicated with coronary artery disease

A Clinical Definition

- Angina
- Positive stress test
- Normal coronary angiogram
  - About 10-20% of patients with chest pain
- Exclusions
  - Vasospasm, Hypertension
  - Extracardiac sources of pain

Chest Pain

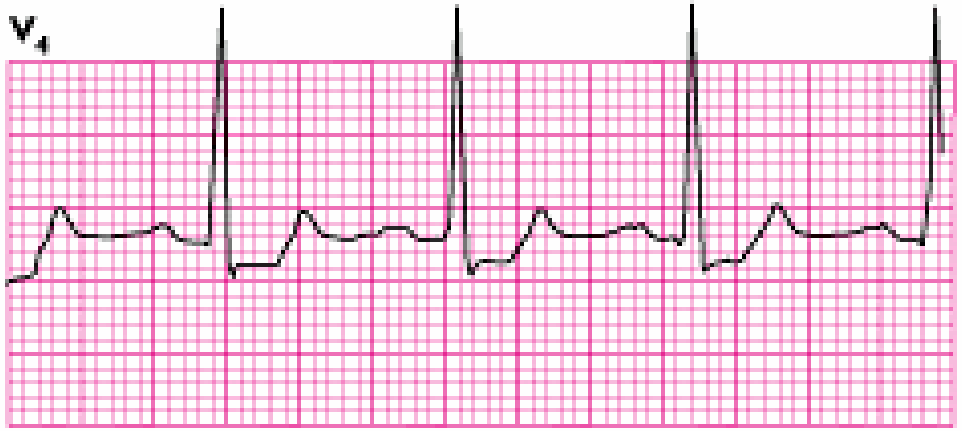
- Similar in character and radiation to angina
- Occurs at rest (41%)
- Long lasting (10 minutes to hours)
- Relieved by nitroglycerin about 50%
- Pain does not cause LV dysfunction!

EKG Changes

- Stress testing
  - 20% with abnormal stress tests
  - Many patients unable to complete test due to pain
  - EKG changes similar to patients with ischemic disease
  - Changes appear at higher HR-BP product
- Holter monitoring
  - circadian distribution similar to ischemic disease
  - ST segment depression much more common than elevation
  - ST segment changes last longer than those with angina

Before Exercise

Peak Exercise and Angina

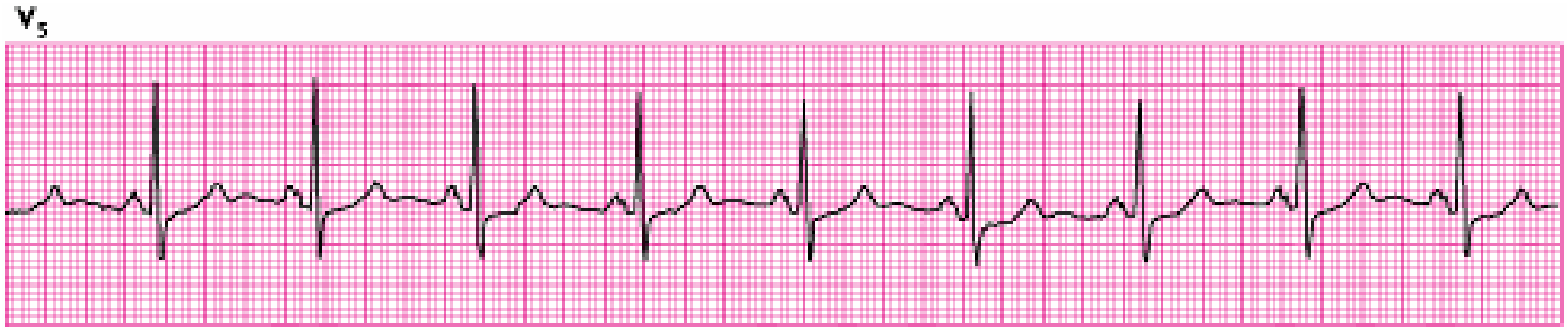


Nine Minutes After Exercise

Stress Testing

- Normal Baseline
- ST Segment depressions at peak exercise
- Positive Test
- ST depression persists longer than expected

Ambulatory Monitoring



Baseline

Fast Walking and Angina

Left Ventricular Function

- Normal LV function with episodes of pain and ST segment changes
- Contrast to ischemic disease which does show decreased LV function

Theories of Syndrome X

- Ischemic vs. Abnormal Pain Perception (or a combination)
- Microvascular Dysfunction
- Estrogen Deficiency
- Abnormal Pain Perception
- Enhanced activity of Sodium-Lithium Countertransport pump
- Autonomic Dysregulation

Myocardial Perfusion

- 30% of Syndrome X show transient abnormalities
  - Relative differences in myocardial perfusion
  - Perfusion is heterogeneous in Syndrome X
- New studies indicate ischemic source of abnormalities

Microvascular Dysfunction

- 1981 Opherk showed myocardial lactate production during atrial pacing in some patients with syndrome X
- Decreased endothelial response to vasodilatory signals
  - Nitric Oxide
- Increased Endothelin (vasoconstrictor)

Pathogenesis of Endothelial Dysfunction

- Conventional CAD risks
  - Smoking
  - Hyperlipidemia
  - Estrogen deficiency
  - Insulin resistance

Estrogen Deficiency

- Most patients with Syndrome X are peri or post-menopausal women
- Acute administration of transdermal estradiol improves coronary vasodilation
- Two months of estrogen replacement maintained vasodilator response

Abnormal Pain Perception

- Adenosine infusion results in more pain in syndrome X patients than those with CAD
- Intracardiac catheter manipulation produced typical chest pain without evidence of blood flow abnormality

Sodium-Lithium Countertransport

- Insulin resistance causes enhanced activity of sodium-lithium countertransport pump
  - Responsible for maintaining intracellular calcium concentrations
  - High intracellular calcium leads to increased coronary microvascular tone
  - High tone may lead to perfusion deficits

Autonomic System

- Increased sympathetic drive
- Increased response of coronary arteries to sympathetic stimulation

Prognosis

- 96% 7-year survival rate
  - 1/3 of deaths cardiovascular in origin
  - Hypertension and Smoking predicted mortality
  - Stress test response did not affect mortality
- Pain may cause severe morbidity
- Conflicting data on progression of Left Ventricular dysfunction
- Few patients show progression to CAD on second angiogram

Treatment

- Goals
  - Control Pain
  - Improve Function
- No one standard therapy
- Often must be individualized

Cardiac Medications

- Calcium channel blockers
  - Diltiazem widely used
- Nitrates
  - Beneficial in 40-50% of Syndrome X patients
- β-Blockers
  - Useful for patients with increased sympathetic activity
- ACE inhibitors?
  - Possible renin-angiotensin activity in Syndrome X?

Other Medications

- Tricyclic antidepressants
  - Imipramine
  - Amitriptyline
- Aminophylline
  - Blocks adenosine purinergic receptors
- Estrogen
  - Transdermal 17-β estradiol

Multidisciplinary Treatment

- Psychological Assessment
- Control risks for endothelial dysfunction
  - Smoking
  - Hyperlipidemia
  - Estrogen deficiency
  - Insulin resistance
- Trial and error treatment
- Pain recurrences

Case Presentation

- Patient started on
  - Elavil 25 mg qhs
  - Atenolol 50 mg qd
  - Estrogen/progestin
- No further episodes of chest pain
- Returned to work in 2 weeks
- Attempts to withdraw medications once a year – each time has recurrence of chest pain
- Recently stopped estrogen/progestin without exacerbation
- Recent GXT-thalium negative

Bibliography

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