A case of ‘unusual’ Acute Coronary Syndrome

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Clinical features

- 28-year old, fit man
- Current smoker, 20 cigarettes/day
- No history of hypertension, diabetes or dyslipidemia
- No family history of cardiac disease
- No relevant previous clinical events
Clinical scenario

At awakening...

...sudden onset of dizziness, diaphoresis, stomach-ache, nausea and vomiting
Clinical scenario

Persistent stomach-ache and vomiting during the day

In the evening

Emergency Department (ED) at Velletri (RM)
ED Admission

- Phisical examination: unremarkable

- Blood Pressure: 140/80 mmHg

- ECG: sinus tachycardia (105 beats/min), ST-segment depression in leads V4-V6

- Blood tests: TnT I = 15 ng/ml, consensual CK-MB & total CK

- Echocardiogram: mild anterior septal hypokinesis
Transfer to our Coronary Care Unit
On CCU Admission

- Regression of symptoms
- Blood pressure: 140/80 mmHg
Electrocardiogram
“Severe left ventricular dysfunction with contractile abnormalities consisting of akinesia of the basal and midventricular segments and hyperkinesis of the apical segments”
Initial Medical Treatment

- Aspirin 160 mg loading dose, then 100 mg/daily
- Clopidogrel 300 mg loading dose, then 75 mg/daily
- Fondaparinux 2.5 mg/daily
- β-receptor blockers
Do you think that this initial medical treatment was appropriate?

1. Yes
2. No
Appropriate initial medical treatment
NSTE-ACS Guidelines

- **Aspirin** is recommended for all patients presenting with NSTE-ACS without contraindication at an initial loading dose of 160–325 mg (non-enteric) (I-A), and at a maintenance dose of 75–100 mg long-term (I-A)

- For all patients, an immediate 300 mg loading dose of **clopidogrel** is recommended, followed by 75 mg clopidogrel daily (I-A)

- **Fondaparinux** is recommended on the basis of the most favourable efficacy/safety profile (I-A)

- **Beta-blockers** are recommended in the absence of contraindications, particularly in patients with hypertension or tachycardia (I-B)

(Bassand, Hamm, et al, EHJ 2007)
Do you think that an urgent cardiac catheterization was necessary?

1. Yes
2. No
Percutaneous Coronary Intervention
NSTE-ACS Guidelines

(Bassand, Hamm, et al, EHJ 2007)
According to guidelines, two days later...
Coronary angiography (left dominant)

No angiographic evidence of atheroma
Normal coronary angiogram in Acute Coronary Syndrome
Normal angiogram in ACS

“About 15% of patients with proven NSTE-ACS have normal or nearly normal coronary arteries. The pathophysicsology is heterogeneous and possible mechanisms include…”

(Bassand, Hamm, et al, EHJ 2007)
Diagnostic Hypothesis

1. Coronary artery spasm:
   - Prinzmetal’s angina
   - Nicotine or cocaine
   - Chemotherapeutic drugs

2. Coronary embolism

3. Congenital anomalies

4. Acute thrombosis followed by recanalization

5. Others:
   - Myocarditis
   - Tako-tsubo syndrome
Intracoronary ergonovine test (32 mcg)

Basal

After ic ergonovine

After ic nitrates
Normal left ventricular function (EF 65%)
Medical History

Mumble ... mumble...

- Elevated Troponin levels, ECG abnormalities
- Normal coronary arteries
- Transient wall motion abnormalities
Diagnostic Hypothesis

Coronary artery spasm:
- Prinzmetal’s angina
- Nicotine or cocaine
- Thyreotoxicosis
- Chemotherapeutic drugs

Acute thrombosis followed by recanalization

Others:
- Myocarditis
- Tako-tsubo syndrome

Coronary embolism

Congenital anomalies
Cardiac Magnetic Resonance

Left Ventricular Hypertrophy (IVS=15 mm)

No delayed enhancement
Diagnostic Hypotesis

Others:
Myocarditis
Tako-tsubo syndrome
Tako-tsubo cardiomyopathy

- Described for the first time in Japan (J Cardiol 1991; 21:203-14)
- Primarily characterized by transient LV apical and medio-apical dysfunction with hyperkinesis of the basal segments
- Initial clinical presentation mimics classical ACS with chest pain, dyspnea, ECG changes, such as T-wave inversion in V3-V6 and possible ST segment elevation, minor increase of cardiac markers (including troponin) in absence of significant coronary artery disease
Tako-tsubo cardiomyopathy

- Occurs most commonly in post-menopausal women; often preceded by episodes of “intense emotional or physical stress” with associated elevation of catecholamine levels.

- More recently, a variant of this syndrome, the “inverted-Tako-tsubo” pattern has been described. It is characterized by dysfunction of the basal and mid-ventricular segments with preserved function of the apical segments.
**Takotsubo cardiomyopathy**

Diagnostic criteria (Mayo Clinic):

- Transient akinesia or dyskinesia of the left ventricular apical and mid-ventricular segments with regional wall-motion abnormalities extending beyond a single epicardial vascular distribution;

- Absence of obstructive coronary disease or angiographic evidence of acute plaque rupture;

- New electrocardiographic abnormalities

- Absence of: Recent significant head trauma, Intracranial bleeding, Pheochromocytoma, Myocarditis, Hypertrophic cardiomyopathy

*Bybee K, Ann Intern Med 2004; 141:858-865*
Mumble … mumble…

Meanwhile
Clinical scenario

At awakening...

...sudden onset of dizziness, diaphoresis, stomach-ache, nausea and vomiting
Electrocardiogram
What to do?

1. Urgent coronary angiography
2. Echocardiogram
3. Laboratory tests: Troponin
Abdominal Echography

“Presence of 76x68 mm mass in the right hepatorenal space with dishomogeneous echogenicity and fluid areas”
Abdominal Computed Tomography

GE MEDICAL SYSTEMS LightSpeed
16-apr-2010 11.57.04
120kV, 79mAs
SC 500 mrr
SW 5.0 mrr

Study Desc: TAC addome (con MDC

6.5x6.5 mm
Abdominal Magnetic Resonance

28Y4M,M,25013533
Scan:3-37
Sl:37
Pos:-30,293
Acc# IU113GYX4PC0
Tra
Ec: 1
Patient Pos: FFS

6.5x6.5x6 mm
Biochemical dates

Urinary catecholamine:

- adrenaline: 86.4 µg/24 h (2.0-22.0)
- noradrenalin: 76.4 µg/24 h (12.0-86.0)
- metanephrine: 5780 µg/24 h (50-340)
- normetanephrine: 2104 µg/24 h (90-445)
- vanilmandelic acid: 12 mg/24 h (2.0-7.0)

Chromogranin: 610.5 ng/ml (19.4-98.1)
Pheochromocytoma

• Rare catecholamine-secreting tumor typically located in the adrenal medulla or along the sympathetic ganglia

• Distant effects by secretion of catecholamines
Pheochromocytoma

- It usually presents with classic symptoms: headache, sweating, tachycardia, pallor and hypertension.

- It has also been reported to cause several cardiac symptoms....
Patients presenting to the Chan Gung Memorial Hospital between January 2003 and December 2007 with a final diagnosis of pheochromocytoma (25 patients):

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>16/25 (64%)</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>9/25 (36%)</td>
</tr>
<tr>
<td>Palpitation</td>
<td>9/25 (36%)</td>
</tr>
<tr>
<td>Angina</td>
<td>8/25 (32%)</td>
</tr>
<tr>
<td>Headache</td>
<td>7/25 (28%)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>6/25 (24%)</td>
</tr>
<tr>
<td>Syncope</td>
<td>5/25 (20%)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>4/25 (16%)</td>
</tr>
<tr>
<td>Fever</td>
<td>3/25 (1%)</td>
</tr>
<tr>
<td>labile</td>
<td>2/25 (18%)</td>
</tr>
<tr>
<td>persistent</td>
<td>8/25 (32%)</td>
</tr>
<tr>
<td>paroxysmal</td>
<td>6/25 (24%)</td>
</tr>
</tbody>
</table>
Six of these patients had abnormal ECG ST-T changes

Suspected Acute Coronary Syndrome

Coronary Angiography

All of them had normal coronary arteries

American Journal of Emergency Medicine, 2000
Takotsubo cardiomyopathy

Diagnostic criteria (Mayo Clinic):

• Transient akinesis or dyskinesis of the left ventricular apical and mid-ventricular segments with regional wall-motion abnormalities extending beyond a single epicardial vascular distribution;

• Absence of obstructive coronary disease or angiographic evidence of acute plaque rupture;

• New electrocardiographic abnormalities

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Bybee K, Ann Intern Med 2004; 141:858-865
A case of Pheochromocytoma presenting as Inverted Tako-tsubo
Pheochromocytoma and inverted Tako-tsubo cardiomyopathy: a case report and review of the literature.

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aUniversité de Montréal, Canada bDepartment of Internal Medicine, Division of Cardiology, Canada cDepartment of General Surgery, Hôpital Maisonneuve-Rosemont, Montréal, Québec, Canada.

Abstract
The classical entity of Takotsubo cardiomyopathy is well established in the literature, but mechanisms explaining it remain unelucidated. Recently, the uncommon inverted Takotsubo type (sparing apical ballooning) has been more frequently described. We report the case of a 26-year-old man admitted with gastrointestinal symptoms, whose clinical presentation for a stress-related cardiomyopathy, which usually presents with cardiopulmonary symptoms, was rather atypical. The cardiac assessment including echocardiography and cardiac magnetic resonance imaging (MRI) demonstrated a dilated cardiomyopathy, whereas coronary angiography showed the absence of atherosclerotic disease. The abdominal computed tomography (CT) scan revealed a left adrenal mass, and elevated urinary catecholamine levels were highly suggestive of a pheochromocytoma. Prompt medical and surgical treatments were instituted. During the left adrenalectomy the patient suffered from brief electromechanical dissociation requiring aggressive resuscitation. Postoperative course was unremarkable. Reverse Takotsubo heart failure is a recently recognized syndrome and a systematic review of the literature of 10 cases of pheochromocytoma-induced inverted Takotsubo is presented in the present article.
In a recently published series of patients with left ventricular dysfunction after emotional stress, plasma catecholamine levels were significantly higher than in patients with Killip Class III AMI.

Wittstein and at, New England Journal Medicine, 2005

Myocardial stunning

Increased catecholamines release

Direct myocyte injury

Intracellular calcium overload

Formation of highly toxic substance and free radicals

Cathecolamine oxidation

Focal, mononuclear, inflammatory areas of fibrotic response

Contraction bands

Multivessel epicardial spasm

Microvascular spasm

Acute and transient coronary microvascular dysfunction

β-receptors

Pathophysiological links

Pheocromocytoma

Tako-tsubo
Mumble ... mumble...

What to do?
Regression of ECG and echocardiogram abnormalities after surgical resection of pheochromocytoma.
Medical perioperative management

- Combined $\alpha + \beta$ blockade
  - Phenoxybenzamine
  - Selective $\alpha_1$-blocker (ex. Prazosin)
  - Propanolol

- Phenoxybenzamine
  - *Drug of choice*
  - Covalently binds $\alpha$-receptors ($\alpha_1 > \alpha_2$)
  - Start 10 mg po bid → increase q2d by 10-20 mg/d
  - Increase until BP cntrl and no more paroxysms
  - Maintenance 40-80 mg/d (some need > 200 mg/d)
Pheochromocytoma management

• β blockade
  • Used to control reflex tachycardia and prophylaxis against arrhythmia during surgery
  • *Start only after effective α-blockade (may ppt HTN)*
  • If suspect CHF/dilated CMY → start low dose
  • Propanolol most studied in pheo prep
Take home message

In patients with an unexpected Acute Coronary Syndrome, normal or minimally diseased coronary arteries and (inverted) Takotsubo-like left ventricular dysfunction, a pheochromocytoma may be suspected in order to avoid mistakes in treatment.
Our young patient, on treatment with Phenoxybenzamine, is waiting for surgical intervention.
Thanks for your attention

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