

Pheochromocytoma presenting as a mimic of acute coronary syndrome

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Abstract

Chest pain with elevated serum troponin is a common clinical presentation and is normally managed as suspected myocardial infarction or acute coronary syndrome (ACS). We report a 49 year old man who presented with central chest pain sweating and breathlessness. He had a significantly elevated serum troponin I level and a subsequent angiogram showed near normal coronary arteries. He was subsequently investigated for fever and found to have a 3cm right sided adrenal mass consistent with a pheochromocytoma. After confirmation and appropriate blockade laparoscopic adrenalectomy was performed.

Pheochromocytoma may present as a mimic of acute coronary syndrome but this is often unrecognized and leaves the patient at risk of future phaeo crisis events which may be fatal.

Keywords

Pheochromocytoma, Acute coronary syndrome (ACS), Metanephrines, Crisis, Interleukin 6 (IL6)

Teaching Points

- Pheochromocytoma should be considered in the differential diagnosis for patients presenting with troponin positive chest pain, particularly when the coronary arteries are normal at angiography.
- A history of recurrent unexplained episodes of chest pain, breathlessness or sweating should raise suspicion of pheochromocytoma
- Delay in diagnosis is believed to increase the risk of fatal pheochromocytoma crisis
- The diagnostic test is serum metanephrines (or 24 hour urine metanephrines) although this test may be falsely elevated in acutely unwell patients, so deferred testing may be needed.

Case History

A previously well 49 year old man presented with central crushing chest pain radiating to his left arm. He was not previously known to have ischaemic heart disease and took no regular medication. He smoked 20 cigarettes per day and there was a family history of fatal myocardial infarction affecting his father aged 62. Clinical examination was unremarkable, with pulse 97/min, sinus rhythm and BP 156/107. Investigations showed serum Troponin I was elevated 893 ng/L (normal <16), sample taken 5 hours after the onset of pain. Serial ECGs demonstrated sinus rhythm with no ST elevation or T wave inversion. CRP was raised at 42mg/L (normal <5). He was admitted and managed as suspected non-ST elevation myocardial infarction (NSTEMI). During the admission he had a further episode of chest pain and pallor associated with a transient BP rise to 232/141 (See Image 1). Coronary angiography was performed on Day 3 of the admission which demonstrated normal coronary arteries apart from mild LAD disease which did not require intervention.

The raised inflammatory markers were thought to be secondary to the cardiac event and no source of infection was detected. He was discharged on the fourth day of admission taking Aspirin 75mg, Ticagrelor 90mg bd, Ramipril 2.5mg, Bisoprolol

10mg, Atorvastatin 80mg, omeprazole 20mg and GTN spray.

He re-presented 2 weeks later, again with symptoms of central crushing chest pain. Serum troponin I was not elevated on this second occasion and the ECG was unchanged from the previous admission. He was treated with Fondaparinux 2.5mg but continued to have chest pains with palpitations. He also reported sweating and episodes of feeling feverish. His temperature was recorded as intermittently elevated up to 38.2°. Blood pressure was normal (123/78). Inflammatory markers were raised (CRP 146mg/L) with no obvious source of infection. Chest Xray, urine dipstick assessment and blood cultures did not show any abnormality. Echocardiogram (trans-thoracic and trans-oesophageal) revealed no vegetations and a normal left ventricle with good systolic function. Autoimmune profile, respiratory viral screen, malaria screen and HIV test were all negative.

Low grade fever with raised CRP persisted. CT scan of chest, abdomen and pelvis was requested to look for any intra-abdominal source of infection, and to exclude malignancy or lymphoma. The scan did not reveal a collection, abscess or lymphadenopathy, but showed a 3.6cm right adrenal mass (see image 2).

Previous history taking had been focused on the features of suspected cardiac chest pain. Eliciting a

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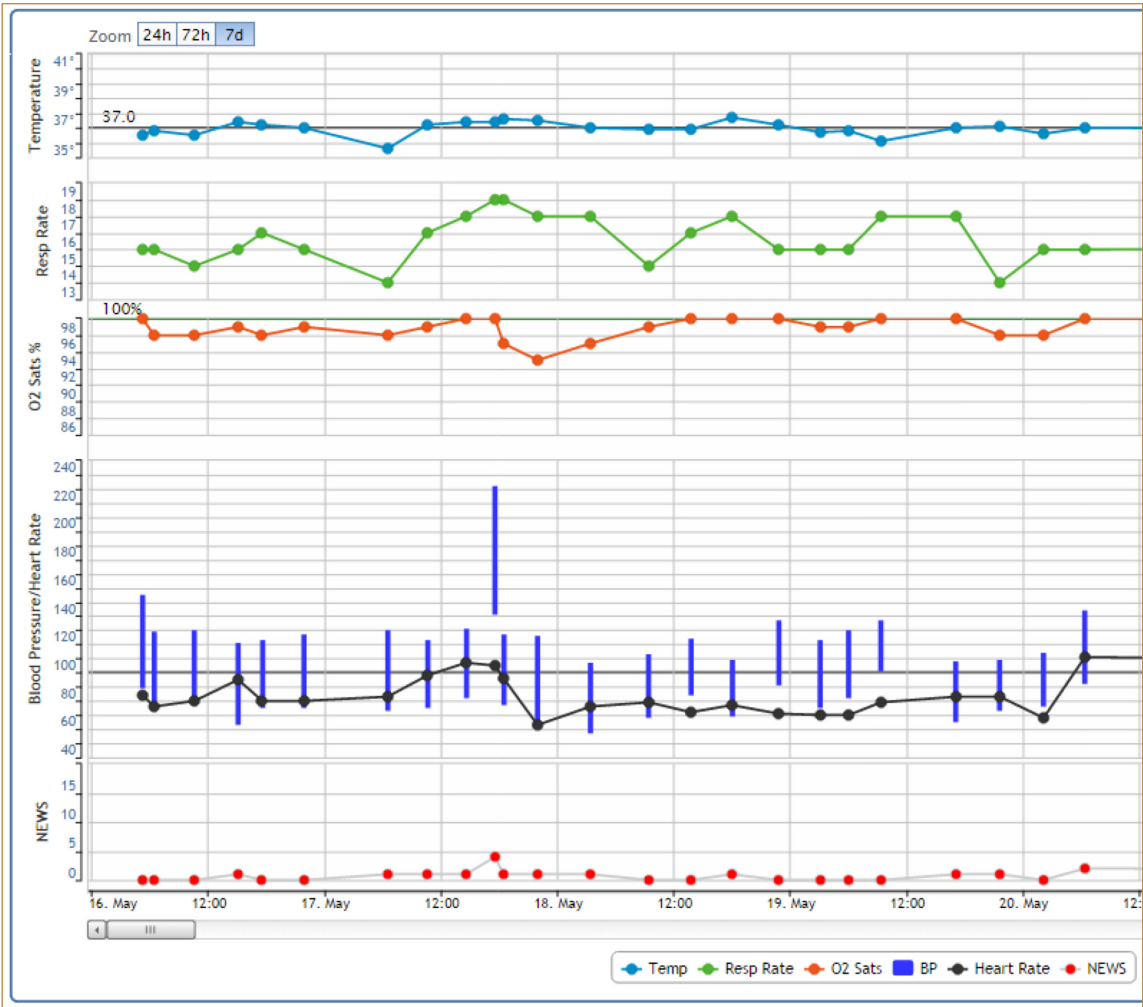


Figure 1. Observation chart from 1st admission, showing one isolated episode of transient severe hypertension.

broader history revealed episodes of intermittent palpitations and heat during which he became extremely pale and unwell and also intermittent fevers and night sweats. He also reported weight loss, but was unable to quantify the amount. The patient reported he had attended A&E three times over the previous 18 months. Two of these episodes were dominated by palpitations and headache one episode involved chest pain. BP was not elevated on these occasions, troponin I was not measured and no specific diagnosis was made for those previous presentations.

Plasma normetadrenaline was found to be more than ten times the upper limit of normal: 14808 pmol/L (normal <1180) confirming the diagnosis

of pheochromocytoma (see table 1). MIBG scan confirmed a solitary right pheochromocytoma (see image 3). Alpha-blockade with oral phenoxybenzamine was initiated and bisoprolol was withheld. Serum cytokine panel was demonstrated elevated IL6 (34.5 ng/L, normal range 2-29) and VEGF (684.4 ng/L, normal <150) which could potentially explain the fever.

After appropriate alpha blockade with phenoxybenzamine the patient proceeded to laparoscopic adrenalectomy which was uncomplicated. The histology demonstrated a fully excised 35mm pheochromocytoma with which was histologically of low risk. There was no vascular or peri-neural invasion with low Ki67 (1-2%). There was intra-

Table 1. Pre and post operative plasma metanephrines

	Pre-Operative	Post-Operative	Normal Range
Plasma metadrenaline	144	153	80-510 pmol/L
Plasma normetadrenaline	14808	492	120-1180 pmol/L
Plasma 3-methoxytyramine	147	<120	<120 pmol/L

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Figure 2. Right sided 3cm adrenal mass, heterogeneous appearance consistent with pheochromocytoma.

operative evidence of peri-adrenal inflammation. Post operatively serum normetadrenaline normalized (see table 1) and the patient made a good recovery.

Discussion

This case describes a patient with an underlying diagnosis of pheochromocytoma which was not initially identified. Pheochromocytomas can present with a wide variety of different clinical symptoms,¹⁻³ but the classic symptomatic presentation is with hypertension, headache, palpitations and sweating.⁴ The cardiac manifestations of a pheochromocytoma are normally described as hypertension, arrhythmia, ischemia and cardiomyopathy.⁵ Although there are case reports of pheochromocytoma presenting with chest pain, elevated serum troponin and unobstructed coronary arteries, it is a presentation associated with delayed diagnosis.⁵⁻⁸ The patient also re-presented with low grade pyrexia and raised CRP, in absence of infection, which is another rare presenting feature of pheochromocytoma.⁹⁻¹¹

What were the missed opportunities to diagnose pheochromocytoma?

There are clinical features in this patient's history, such as paroxysmal episodes of palpitations, heat and looking pale which are highly suggestive of pheochromocytoma. The episode of sudden severe hypertension with pallor during the first admission is also very suggestive. Catecholamine release usually causes profound vasoconstriction leading to both hypertension and pallor.

The early diagnostic labelling of this patient with acute coronary syndrome (ACS) probably presented a barrier to reaching the correct underlying diagnosis. The risk of missing the diagnosis is likely to be exacerbated by taking a history focused only on the presence or absence of cardiac chest pain (with or without a proforma) rather than a history of the broader presentation.



Figure 3. MIBG scan confirms solitary right sided 3cm pheochromocytoma.

guidelines¹² suggest sepsis, hypovolemia, atrial fibrillation, heart failure, pulmonary embolism, myocarditis, myocardial contusion, and renal failure as potential explanations for this presentation. Pheochromocytoma should also be considered in this situation.

The particular clues that a patient may have a pheochromocytoma are suggested to be:¹³

- Multiple hyperadrenergic (headache, palpitations, sweating) symptoms
- Symptoms which occur in paroxysms, lasting < 30 mins

How should we investigate or confirm the diagnosis of pheochromocytoma?

The most significant obstacle to making the diagnosis of pheochromocytoma is to consider the diagnosis in the first place. Once the question has been raised, diagnosis is normally confirmed or refuted on the basis of a combination of biochemistry and radiology. In a clinically stable patient the best biochemical investigation is plasma metanephrines.¹⁴ 24 hour urine metanephrine assessment is an equally good diagnostic test but normally less convenient.¹⁴ Certain drugs can give falsely elevated metanephrine levels including alpha blockers, beta blockers, tricyclic antidepressants, selective serotonin reuptake inhibitors and monoamine oxidase inhibitors.¹³

Diet does not have a significant impact on the two main metanephrines which are measured (metadrenaline and normetadrenaline). A diet high in bananas, nuts and cereals does cause elevated 3-methoxytyramine levels.¹³

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In an acutely unwell patient biochemical investigations are more difficult to interpret.¹⁵ Patients who are in intensive care or who have renal impairment often have elevated catecholamine and metanephrines. In such cases moderately elevated metanephrines are difficult to interpret. Radiological imaging, such as adrenal CT scan, may be more useful in this setting when there is significant clinical suspicion of pheochromocytoma.¹⁵ However it is important to note that adrenal masses found on abdominal imaging are common; the majority of unexpected adrenal masses identified will be non-functioning adenomata, rather than pheochromocytoma. Early involvement of an endocrinologist is advisable, given the rarity of this diagnosis. If confirmed: further radiological investigation (mIBG or FDG PET scan) may be requested and peri-operative alpha blockade will be needed.¹⁴

What is the importance of making the diagnosis?

Patients who are identified with pheochromocytoma often have been symptomatic for 1-3 years without achieving a correct diagnosis.¹⁶ In addition to the unpleasant symptoms which remain untreated, pheochromocytomas can be dangerous. About 8-18% of patients with a pheochromocytoma will, at some point, have a pheo crisis which is an acute episode of severe haemodynamic instability and end organ damage or dysfunction. The mortality of pheo crisis is estimated to be 15%.¹⁷ Although there are no definitive studies it is widely believed that early diagnosis improves outcomes, whereas undiagnosed pheochromocytoma is associated with significant mortality.^{14, 18}

Statement of conflict of interest

The authors declare that they have no conflict of interest.

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