# Phaeochromocytoma - a classic (but easily forgotten) cause of anxiety

We report on a patient with recurrent panic attacks, depression, and palpitations caused by a phaeochromocytoma. The diagnosis was missed for ten years, and was only considered after she developed a potentially catastrophic intraoperative hypertensive crisis. The anxiety symptoms resolved completely after removal of the tumour. It is important to consider cathecholamine producing tumours in the work up for organic causes of psychiatric disorders.

#### Case

A 51 year old woman presented to a breast surgeon with a longstanding history of a nipple discharge. She did not volunteer any significant past medical history and the referral letter contained no further information. She had no family history of relevance. After a breast evaluation she was advised to have a microdochectomy.

On the day of admission she was noted to be hypertensive (160/110) and tachycardic. She mentioned she was anxious about the procedure and had an impending sense of doom. Fifteen minutes after induction of general anaesthesia, the patient developed an uncontrollable tachycardia and a significant hypertensive surge, with the systolic blood pressure exceeding 250 mm/Hg. After administration of 5 mg IV labetolol (mixed  $\alpha$ - $\beta$  blocker) she became profoundly hypotensive. An intraoperative diagnosis of a phaeochromocytoma was made, and she was treated according. The procedure was terminated and she was transferred to ICU, where she fortunately made an uneventful recovery.

On direct questioning, the patient and her general practitioner reported a long and significant history of medical and psychiatric symptoms. There were numerous episodes during the preceding decade of consultations with her doctor and local emergency unit relating to "panic attacks", "pressure on her chest", shallow breathing, palpitations, a feeling of her "heart in her throat", tremors, severe headache, visual disturbances, feeling faint and having "strange turns". She found it increasingly problematic to function in her job as an executive in a travel company, and she noted particular difficulty at board meetings and public presentations, during which she was occasionally overcome with palpitations, profuse sweating and dizziness. She said: "I didn't actually feel that anxious, but I felt as if my body grossly overreacted and behaved as if I was!".

She had been diagnosed with paroxysmal supraventricular tachycardia, functional chest pain, migraine, generalized anxiety disorder, depression, and panic attacks. Besides her GP and emergency room physicians, a neurologist, a physician and a psychologist evaluated her. Her therapy over the years included multiple analgesic combinations for headaches, propranolol, and

**Correspondence** Dr J Edge email: jennyedge1234@gmail.com various courses and doses of lorazepam (Ativan), citalopram (Cipramil), escitalopram (Cipralex), amitryptyline (Trepilene), venlafaxine (Effexor) and diazepam (Valium). She spent a period of two weeks admitted to a local psychiatric clinic for the treatment of severe anxiety, and received long term cognitive behaviour therapy. During these years her blood pressure was recorded numerous times, and never noted to be abnormally elevated. Her neurological findings were always normal. Routine blood tests (serum electrolytes, full blood count, liver function tests, thyroid function tests) were repeatedly normal.

Urgent investigations after the anaesthetic induced crisis, confirmed an excess of cathecholamine secretion: the 24 hour urine normetanephrine/creatinine ratio was elevated, 639 nmol/24hr (range 26-300) and the metanephrine/creatinine ratio was 100 times above the normal range, 10833 nmol/24hr (5-90). A CT Scan of the abdomen showed a massive 15 cm solid/cystic tumour localized to the right adrenal gland (Fig 1). The diagnosis of a phaeochromocytoma was thus unequivocally confirmed, and after a 3 week period of pre-operative -blockade with prazosin (Minipress), the tumour was removed surgically without complications.

In the immediate post operative period she reported a complete and dramatic resolution of her feelings of anxiety, stress and "panic": "it was as if someone switched off the tap". At a six months follow up she had fully recovered, was working normally and her pre-existing symptoms of palpitations, anxiety, tremor had completely disappeared.

To add a further twist to this interesting story, four months after surgery, she was diagnosed with thyrotoxicosis. This was treated

Figure 1: CT Image Phaeochromocytoma: 15 cm solid and cystic tumour of the right adrenal causing a pressure effect on the right lobe of the liver



successfully with carbimazole (Neomercazole) and bisoprolol (Cardicor). She is awaiting definitive radioactive iodine ablation. Her thyroid function tests were normal at the time of the diagnosis of the phaeochromocytoma.

Pheochromocytomas are neuroendocrine tumors of the medulla of the adrenal glands which secrete excessive amounts of catecholamines. Extra-adrenal paragangliomas (often described as extra-adrenal pheochromocytomas) are closely related, but less common, tumors that originate in the ganglia of the sympathetic nervous system.

The signs and symptoms of a pheochromocytoma are the result of sympathetic nervous system hyperactivity. They are many and variable and include abnormal skin sensations, flank and abdominal pain, (occasionally so severe that it may mimick an acute abdomen), tachycardia, arrhythmias, palpitations, pallor, weight loss, hypertension, excessive sweating, anxiety and headaches. It is not uncommon for the diagnosis to be missed for many years. Some patients may have been symptomatic for as long as 30 years prior to diagnosis, with a mean time to diagnosis of 42 months.<sup>1</sup> With increasing use of radiology, up to 25% of phaeochromocytomas are diagnosed incidentally, and the symptomatology becomes evident only in retrospect.<sup>2</sup>

The characteristic clinical feature is hypertension, but it's incidence is variable. Many large series note up to 90% patients are hypertensive.<sup>3</sup> This is typically paroxysmal, severe and potentially fatal, but it can be more moderate and sustained, and importantly some patient may even be occasionally hypotensive. With improvement of imaging techniques and clinical awareness, more people with normal blood pressure have been diagnosed with phaeochromocytomas.<sup>4</sup> Apart from the preoperative reading, our patient's blood pressure was normal at all times.

Our patient's only consistent symptoms were those of anxiety and palpitations, with occasional headaches. The majority of the literature underestimates the significance of psychiatric symptoms in patients with phaeochromocytoma, and these are much more common when asked for retrospectively. Mannelli and colleagues sent a questionnaire to 284 patients with phaeochromocytoma and asked retrospectively about their symptoms. From a list of 14, the commonest 5 symptoms noted were: palpitations (58%), headache (52%), sweating (49%), anxiety (35%) and tremors (26%).1

In conclusion we illustrate a case of phaeochromocytoma, misdiagnosed and incorrectly treated as an anxiety disorder for many years, in whom general anaesthesia precipitated a potentially disastrous hypertensive crisis. When evaluating new or atypical cases with an anxiety disorder, or cases particularly refractory to treatment, it is relevant to think of a phaeochromocytoma. The most reliable way to test for this is to request a 24 hour urine collection for cathecholamine metabolites. Because of the episodic nature of cathecolamine secretion, at least three separate urine collections should be checked. Blood levels of adrenaline are too variable, and not routinely used for diagnosis.

This case illustrates that a woman with seemingly benign, and longstanding anxiety disorder may have an occult life threatening organic disease. Appropriate diagnosis and intervention can be a life saving event.

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### **IMPORTANT NUMBERS TO REMEMBER**

Suicide Crisis Line: 0800 567 567 or SMS 31393 Pharmadynamics Police and Trauma Line: 0800 20 50 26 AstraZeneca Bipolar Line: 0800 70 80 90 Sanofi Aventis Sleep Line: 0800-SLEEPY (0800 753 379) Dept. of Social Development Substance Abuse Line: 0800 12 13 14 or SMS 32312 Dr Reddy's Helpline: 0800 21 22 23 Office Lines: 011 262 6396 Website: www.sadag.co.za