Hong Kong College of Physicians
Case report for Interim Assessment
Specialty Board of Advanced Internal Medicine (AIM)

For AIM Training, case reports should be submitted in the prescribed format together with the application form for Interim Assessment at least EIGHT Weeks before the date of Interim Assessment

Name of candidate (print and sign): IP WHITNEY CHIN TUNG
Hospital and Unit: QUEEN MARY HOSPITAL Specialty: AIM AND GERIATRICS
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Date(s) and place (hospital) of patient encounter: 04/11/2021, 25/11/2021 QMH
Date of report submission: 6 MARCH 2023

Case report

Note: Failure to follow the prescribed format (including the number of words) results in a FAILURE mark (score between 0 and 4) for the Case Report.

Title: Just a simple headache?

Case history:

Mr. Tong WP, a 57-year-old gentleman, was referred to the Queen Mary Hospital triage clinic for the management of episodic headache on 4 November 2021.

Mr. Tong presented with three episodes of severe headaches to the emergency department one year ago (on 21 January 2020, 25 January 2020, and 30 January 2020). At that time, he complained of recurrent right-sided headache, right periorbital, and right facial pain with increased blood pressure up to 170/130 mmHg. It was associated with vomiting and nausea. There was no head injury or other neurological symptoms. He was given intravenous tramadol with symptomatic improvement. Chest X-ray was normal. Repeated computer tomography scans of the brain at the emergency department showed no remarkable findings. Mr. Tong was treated as right trigeminal neuralgia and discharged directly from the emergency department. He was referred to the triage clinic for further management.

The patient's history of presenting illness was further clarified at the triage

clinic. He had less frequent headaches, approximately four times yearly, since January 2020. Each time the headache lasted for three days and was localized at the right temporal region. It was associated with pain rated 4/10. It was associated with fast-tapping regular palpitations, sweating, facial flushing, and elevated blood pressure. He required occasional use of oral paracetamol for pain relief. The pain was self-limiting and therefore he did not seek for further medical attention. There were no triggers identified, no jaw claudication, no tremor, no visual involvement and aura, no vomiting, no diarrhea, no weakness, no autonomic symptoms, no rash, no fever, and no constitutional symptoms. The patient had snoring during night-time but he did not report any excessive daytime tiredness. He had a home blood pressure monitoring of 110-130/80-90. Mr. Tong had a good past health. He did not take any over-the-counter medications or herbs. There was no family history of endocrinopathy but a positive family history of breast cancer. He lived at home with his wife. He was a non-smoker and non-drinker and was working as a businessman. The headache did not affect his daily activities. There were no active symptoms during the time of consultation.

On physical examination, he has a blood pressure of 132/88 mmHg and a heart rate of 76 bpm. He had a body mass index of 22.5 kg/m^2. He was not diaphoretic nor anxious. There were no signs of hyperthyroidism and no neck mass. The cranial nerve examination was unremarkable. There were no focal neurological deficits. There were no heart murmurs. The chest was clear. The abdomen was soft without palpable mass. There were no renal bruits detected.

The complete blood count, liver function, and renal function tests were unremarkable. The thyroid function test and fasting glucose level were normal. The urine protein creatinine ratio was normal. The chest X-ray was normal. The 24-hour urine and plasma fractionated metanephrines were grossly elevated: urine normetanephrine was 814 nmol/D (N(normal range) < 240 nmol/D), urine metanephrine was 3368 nmol/D (N < 275 nmol/D), plasma normetanephrine was 2660 pmol/L (N: 110-740 pmol/L), and plasma metanephrine was 8590 pmol/L. A biochemical diagnosis of pheochromocytoma or paraganglioma was made.

Phenoxybenzamine followed by propranolol were started and were well tolerated. Flourodopa-F18 (18F-FDOPA) positron emission tomography-computer tomography (PET-CT) confirmed the presence of a

mass lesion at the medial limb of the right adrenal gland with an intense 18F-FDOPA activity compatible with phaeochromocytoma. The patient was referred to the endocrine surgery team and a right laparoscopic adrenalectomy was performed on 13 April 2022. Histology confirmed phaeochromocytoma. The patient stopped anti-hypertensive medications after surgery. Repeated plasma catecholamine level one month after surgery were normalized. The patient continued to follow up at the endocrine clinic without recurrence of symptoms.

Discussion and literature review

Pheochromocytoma is a rare catecholamine-secreting neoplasm arising from the chromaffin cells of the adrenal medulla. When the condition arises from extra-adrenal paraganglia, it is referred to as "paraganglioma". Although the two conditions have different associated neoplasms and genetic conditions, both are treated with similar management approaches.[1,2]

Pheochromocytoma accounts for 0.1% of all causes of hypertension. It mainly affects middle-aged men, with a mean age of presentation at 47, as suggested by a previous local retrospective study. Of which there was female predominance, and 24% of the cases were related to a familial form of pheochromocytoma. The time interval between the first symptom presentation and diagnosis ranged from 1 to 132 months.[3]

Pheochromocytoma is considered a "great masquerade" as it often mimics other medical conditions.[4] Differential diagnoses include hyperthyroidism, carcinoid syndrome, insulinoma, mastocytosis, panic attacks, primary headaches, autonomic epilepsy, etc. Regarding clinical presentation, a recent study showed that 61% of the diagnoses were made by the incidental finding of an adrenal mass on cross-sectional imaging. 27% of the patients presented with catecholamine-related symptoms, and 12% were detected by mutation-based detection screening.[5]

In our patient, a classical triad of paroxysmal headaches, palpitations, and

profuse sweating was presented, yet the patient presented with infrequent symptoms leading to a delay in diagnosis. The classical triad occurs in only 14% of the patients.[2] The sensitivity and specificity of this classical triad had been reported to be up to 90%.[3,5] Other symptoms of pheochromocytoma include orthostatic hypotension, cardiomyopathy, insulin resistance, hyperglycaemia, etc. These symptoms are directly related to the increase and types of catecholamines released. Pheochromocytoma crisis is a rarely seen fulminant presentation with an estimated mortality of up to 15%. It presents with multi-organ failure, hyperthermia, and encephalopathy, systemic and pulmonary vascular resistance requiring emergency tumor resection.[6]

The 24-hour urine fractionated metanephrines or plasma fractionated metanephranes can be used as the initial test for the biochemical diagnosis of pheochromocytoma. Some studies suggested using urine metanephrines as the test of choice for those with a low risk of pheochromocytoma due to its high sensitivity and specificity (98% and 98% respectively).[1,7] Radiological evaluation for tumor localization should be performed only after biochemical confirmation of catecholamine excess.

In patients with biochemical adrenergic phenotype, phaeochromocytoma is suspected. Computed tomography of the adrenal glands is usually considered as the first-line imaging for tumor localization, and it is superior to magnetic resonance imaging due to its superior spatial resolution of the abdomen. Recent advances in molecular imaging have improved the accuracy of radiological assessment of phaeochromocytoma and paraganglioma. 18F-FDOPA PET-CT is currently the radiotracer of choice for phaeochromocytoma. It is helpful for the detection of small phaeochromocytoma as there is limited physiological uptake of 18F-FDOPA in normal adrenal glands. Therefore, 18F-FDOPA PET-CT is more sensitive for lesion detection compared with other types of molecular imaging and anatomic imaging.[8]

In view of the high prevalence of germline and somatic mutations, genetic test is now recommended in every patient with phaeochromocytoma/paraganglioma. The strong genotypic-phenotypic correlation will inform clinicians and patients regarding the clinical behaviour and prognosis of phaeochromocytoma/paraganglioma, providing guidance on the personalized follow-up plan including the best strategy of radiological

monitoring. Indeed, genetic testing has been shown to have a positive impact on management and outcomes for these patients.[9]

Once the diagnosis of phaeochromocytoma is made, timely administration of the appropriate anti-hypertensive agents is recommended to relieve symptoms related to catecholamine excess, control blood pressure and prevent acute cardiovascular complications, both before and during definitive surgery. Alpha-adrenergic receptor blockers (e.g. phenoxybenzamine, doxazosin), which reverse catecholamine-mediated vasoconstriction, are the recommended first-line treatments. Beta-adrenergic receptor blockers can be added to control reflex tachycardia, but only after adequate alpha blockade in order to avoid unopposed alpha-adrenergic receptor-mediated vasoconstriction.[10]

The definitive treatment of pheochromocytoma remains to be surgical resection. Successful tumor removal can be confirmed by normalization of biochemical testing 2 to 4 weeks after surgery. Risk factors of recurrence after resection include advanced age, familial disease, tumor site, and tumor size greater than 5cm.[1,2]

In summary, clinicians should be alert to the catecholamine-related symptoms and signs to promptly initiate the workup of pheochromocytoma. Definitive treatment, which is surgical removal, should be performed to prevent morbidities and mortalities including life-threatening high blood pressure and other serious complications such as end-organ damage.

Tables and figures (where applicable) (no more than two figures)

Reference (not more than 10)

1. Lenders JW, Duh QY, Eisenhofer G, et al. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline [published correction appears in J Clin Endocrinol Metab. 2023 Feb 08;:]. J Clin Endocrinol Metab. 2014;99(6):1915-1942. doi:10.1210/jc.2014-1498
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4. Reyes HA, Paquin JJ, Harris DM. Pheochromocytoma, "the Great Masquerader," Presenting as Severe Acute Decompensated Heart Failure in a Young Patient. Case Rep Cardiol. 2018;2018:8767801. Published 2018 Apr 29. doi:10.1155/2018/8767801
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9. Nölting S, Bechmann N, Taieb D, et al. Personalized Management of Pheochromocytoma and Paraganglioma [published correction appears in Endocr Rev. 2021 Dec 14;:] [published correction appears in Endocr Rev. 2021 Dec 14;:]. Endocr Rev. 2022;43(2):199-239. doi:10.1210/endrev/bnab019
10. Berends AMA, Kerstens MN, Lenders JWM, Timmers HJLM. Approach to the Patient: Perioperative Management of the Patient with Pheochromocytoma or Sympathetic Paraganglioma [published correction appears in J Clin Endocrinol Metab. 2021 Mar 8;106(3):e1503]. J Clin Endocrinol Metab. 2020;105(9):dgaa441. doi:10.1210/clinem/dgaa441

No of words in Case History and Discussion (excluding references): **1316**

(should be between 1000-2000)

Declaration

I hereby declare that the case report submitted represents my own work and adheres to the prescribed format. I have been in clinical contact with the case selected. The case report has not been submitted to any assessment board or publication and it is NOT related to my second specialty(ies), if any. My consent is hereby given to the College to keep a copy of my case report, in written and/or electronic, at the College Secretariat and allow the public to have free access to the work for reference.

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(signature of Trainee)

Endorsed by Supervisor *

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