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Pseudopheochromocytoma in the Conflict Zone of Northwest Syria: A Case Report and Literature Review

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Abstract

Background: Pseudopheochromocytoma is a rare clinical entity characterized by symptoms resembling those of pheochromocytoma, despite the absence of an adrenal medullary tumor. Its diagnosis remains difficult due to overlapping features with various other conditions and the absence of definitive diagnostic markers.

Methods: We report the case of a 47-year-old male school teacher who developed pseudopheochromocytoma, likely precipitated by psychological stress associated with prolonged exposure to the war-torn environment of Northwest Syria.

Results: The patient presented with repeated episodes of sudden-onset severe hypertension, along with palpitations, excessive sweating, headaches, chest discomfort, and facial flushing. A comprehensive workup ruled out endocrine and structural causes. The psychological burden linked to displacement and chronic instability was believed to be a significant contributing factor. Given the patient's asthma, beta-blockers were avoided. Management with the calcium channel blocker (Diltiazem) and the antidepressant (Sertraline) resulted in substantial clinical improvement.

Conclusion: Pseudopheochromocytoma can closely imitate true pheochromocytoma, making careful evaluation essential. In selected cases, calcium channel blockers combined with antidepressant therapy may offer effective symptom control. More studies are needed to establish standardized treatment strategies for this underrecognized condition.

Introduction

Pseudopheochromocytoma (PPCC) is a rare and often overlooked condition, believed to occur significantly more frequently than pheochromocytoma (PCC) - by as much as 50 to 100 times [1]. Because its clinical features closely mimic those of pheochromocytoma, distinguishing between the two can be difficult. The term "pseudopheochromocytoma" was first introduced by O. Kuchel in 1985, and since then, only a limited number of cases have been described in the literature [2]. The disorder is typically characterized by sudden episodes of markedly elevated blood pressure, occasionally accompanied by a rapid heart rate. These hypertensive spikes may persist from several minutes to a few hours [3,4]. Although patients often show no adrenal mass and may have normal or only slightly elevated catecholamine levels, they still experience symptoms resembling catecholamine excess—such as palpitations, flushing, headaches, and profuse sweating [5-7].

In many cases, the patient appears completely well between episodes, which can make these attacks the only outward sign of the condition. As such, pseudopheochromocytoma is considered a diagnosis of exclusion. It is essential to first eliminate other possible causes such as obstructive sleep apnea, primary aldosteronism, kidney parenchymal disease, hyperthyroidism, pheochromocytoma, carcinoid syndrome, and panic disorder [3,7,8]. Recent studies have linked the sudden onset of paroxysmal hypertension to previous exposure to psychological stressors [4,6,9-11], which is evident in our case, where the patient developed PPCC following his grief and displacement in a war-torn region of Northwest Syria (NWS).

Methods

This case was identified in NWS for A 47-year-old male, smoker, asthmatic and with a history of allergic rhinitis, presented with episodic palpitations, diaphoresis, headache, flushing, and chest pain associated with severe hypertension (peak SBP 260 mmHg). He denied alcohol or drug use, consumed two cups of coffee daily, had a BMI of 24, and reported no sleep disturbances.

Investigations included plasma and 24-hour urinary metanephrines, catecholamines, thyroid function tests, ECG, echocardiography, and abdominal CT to evaluate for pheochromocytoma and other hypertensive secondary causes. Due to the episodic nature of symptoms and the absence of adrenal pathology, a psychological cause was proposed. The patient was managed with antihypertensives and Anxiolytics .

A literature review was conducted using PubMed and Google Scholar, concentrating on PPCC, episodic hypertension, and stress-induced hypertension. Relevant case reports and reviews from the past two decades were explored. The conclusions support the role of psychological stressors in triggering hypertensive crises in patients without adrenal tumors, highlighting the need for a multidisciplinary approach.

The patient has provided informed consent for publication, However, ethical approval was not obtainable due to the challenges of conducting research in a war-torn region like Northwest Syria, where formal ethics committees are not always accessible.

Results

Clinical Presentation

The patient was utterly asymptomatic between the episodes. The patient reported prior similar episodes; the first one happened ten years ago, after grieving about the loss of his sibling. His past episodes were treated symptomatically by sublingual nitroglycerin and oral captopril over the last year and then stopped altogether. The episodes recurred two months before attending the clinic; each episode lasted up to an hour in ten days and became more frequent until it became daily. He experienced these episodes after he was displaced into an area of armed conflict, where civilians often bore the brunt of violence. The patient's displacement into a near front-line zone posed considerable extra challenges, including limited access to healthcare services, resource constraints, and medication shortages. Chronic psychological stress from exposure to brutality likely exacerbated hypertensive attacks, emphasizing the complex interplay between autonomic dysfunction and trauma. The evaluation of possible secondary causes of hypertension was essential, as summarized in Table 2. By the end of the episode, his heart rate declined to 70-90/minute, and his blood pressure was normalized.

Emergency Visits and Blood Pressure Trend

His systolic blood pressure during episodes was between 250 and 260 mmHg. He received treatment multiple times in the emergency department, including sublingual nitroglycerin and oral captopril. After administering the maintenance medications, the values of systolic pressure became 180 – 150 mmHg, and the episodes have been interrupted for over one year. To date, the blood pressure is stable between 110/60 mmHg and 130/80 mmHg.

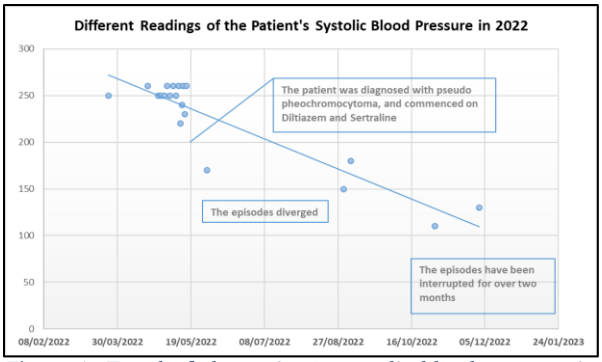

Figure 1: Trend of the patient's systolic blood pressure in 2022, showing initial hypertensive episodes, treatment initiation, and subsequent symptom resolution.

Diagnostic Investigations

Blood test results were within normal limits, including unremarkable electrolytes and urine tests (Table 1), with no evidence of renal impairment. Hormonal findings excluded the presence of hyperaldosteronism,hyperthyroidism, carcinoid tumor, or pheochromocytoma. While adrenaline and noradrenaline levels were elevated in plasma, urinary vanillylmandelic acid levels remained within the normal range.

Imaging and Cardiac Assessment

Electrocardiography, chest X-ray, and echocardiography were normal (no signs of ventricular hypertrophy, cavity dilatation, or impaired cardiac output were reported). In addition, the cerebral CT scan was normal, and fundoscopic examination revealed no retinopathy. The patient also underwent an abdominal CT scan and MRI, which demonstrated no adrenal masses and kidneys without renal artery stenosis. A review of selected published cases of pseudopheochromocytoma, including their management strategies, is presented in Table 3.

Diagnosis and Follow-up

The patient was clinically diagnosed with PPCC after excluding other differentials: pheochromocytoma, hyperaldosteronism, thyrotoxicosis, carcinoid syndrome, obstructive sleep apnea, alcohol withdrawal, cocaine use, anti-Parkinsonian drugs, and anxiety state (panic attack).

Due to the patient's history of asthma, beta-blockers were contraindicated. As an alternative, he was started on Diltiazem, a calcium channel blocker, at a dose of 60 mg twice daily. Additionally, Sertraline 50 mg once daily was prescribed to address the suspected underlying psychiatric component of the condition. Both drugs contributed to controlling episodes and reducing their frequency, as the systolic pressure readings remained below 180 mm Hg during the different attacks. The episodes were interrupted for over two months. To date, the pressure is stable between 110-130/60-80 mmHg (Figure 1). Over the past 2 years, the patient has been followed up regularly, with no reported attacks. Furthermore, the patient has received rigorous safety-netting advice to ensure proper management if episodes recur.

Laboratory Variables	Results	Laboratory References
WBC	9100	4500 – 10500/mm^3
RBC	4,930,000	4,000,000 - 5,400,000/ml
PLT	333,000	150,000 - 450000/ml
HGB	15.7	12 - 16 g/dL
HCT	45.6	35 – 47%
MCV	92.5	78 – 96 Fl
MCH	31.8	27 – 32 g/dL
MCHC	34.4	31 – 35 g/dL
Glucose	105	65 – 110 mg/dL
Urea	34	15 – 45 mg/dL
Creatinine	0.7	0.5 – 1.2 mg/dL
CRP	1.21	Up to 6 mg/L
LDH	334	220 - 450 U/L
ALT	30	5 - 45 U/L
D-Dimer	186	Up to 500 ng/ml
Cholesterol	197	Below 200 mg/dL
Triglycerides	73	Below 150 mg/dL
Electrolytes:		
Na	137	135 - 145 mmol/L
K	3.6	3.5 - 5 mmol/L
Ca++	4.4	4.4 - 5 mmol/L
Hormonal Analysis		
TSH	2.11	0.3 - 5 mIU/L
Cortisol	355	> 300 nmol/l
Adrenaline	6.99	< 0.1 ng/ml
Noradrenaline	4.29	< 0.6 ng/ml
Plasma Renin	12.9	4 - 50 µmU/ml
Plasma Aldosterone	14	18 - 230 pg/ml
Urine 24-h collection		
VMA	10.2	Up to 13.6 mg/24 h
5-HIAA	6	0.7 - 8 mg/24 h

WBC: White Blood Cells; RBC: Red Blood Cells; PLT: Platelets; HGB: Hemoglobin; HCT: Hematocrit; MCV: Mean Corpuscular Volume; MCH: Mean Corpuscular Hemoglobin; MCHC: Mean Corpuscular Hemoglobin Concentration; Glucose: Blood Glucose Level; Urea: Serum Urea; Creatinine: Serum Creatinine; CRP: C-Reactive Protein; LDH: Lactate Dehydrogenase; ALT: Alanine Aminotransferase; D-Dimer: D-dimer (a fibrin degradation product); Cholesterol: Total Cholesterol Level; Triglycerides: Total Triglycerides Level; Ca++: Calcium; K: Potassium; Na: Sodium; TSH: Thyroid-Stimulating Hormone; Cortisol: Cortisol Hormone Level; Adrenaline: Epinephrine; Noradrenaline: Norepinephrine; Plasma Renin: Plasma Renin Activity; Plasma Aldosterone: Plasma Aldosterone Concentration; 5-HIAA: 5-Hydroxyindoleacetic Acid; VMA: Vanillylmandelic Acid.

Table 1: The patient's laboratory and hormonal test results, including biochemical markers assessed during the diagnostic evaluation for pseudo pheochromocytoma.

Discussion

An essential aspect of evaluating patients with paroxysmal hypertension is the thorough investigation of secondary causes to determine whether the condition is chronic or episodic. Vascular disorders of the kidneys, primary aldosteronism, Kidney parenchymal disorders, obstructive sleep apnea, Cushing's syndrome, hyperthyroidism, and PCC are the most common causes of secondary hypertension (Table 2). The term "pseudo pheochromocytoma" has been utilized in literature to define paroxysmal hypertension with symptoms indicative of excess catecholamine but without an associated tumor.

Frequent underlying causes of secondary high blood pressure `			
Cause	**Prevalence in patients with HTN**	**Characteristic manifestations and findings**	Preliminary diagnostic tests
Obstructive sleep apnea	5-10%	Snoring; obesity; wakeup headache; daytime somnolence.	Epworth score and ambulatory polygraphy.
Renal parenchymal disease	2-10%	Generally without symptoms; diabetes; hematuria; renal mass (adult), polycystic chronic kidney disease.	U&Es, urine dipstick, urinary albumin, creatinine ratio, Kidney ultrasound.
Renovascular Disease			
Atherosclerotic renovascular disease	1-10%	Elderly; Diffuse atherosclerosis; diabetes; smoking; abdominal bruit; Frequent flash; pulmonary oedema.	Renal artery Doppler, CT angiography, or MRI.
Atherosclerotic renovascular disease		Younger age; common in females; abdominal bruit.	
Endocrine Causes			
Primary Aldosteronism	5-15%	Mainly asymptomatic; muscle weakness (rare)	Aldosterone: renin ratio; and hypokalemia
Pheochromocytoma	<1%	Episodic: paroxysmal hypertension, palpations, pounding headache, perspiration, and pallor; labile high BP.	Plasma metanephrines or 24-hour urinary metanephrines
Cushing's syndrome	<1%	Central obesity, moon face, skin atrophy, bruising and striae, diabetes, Long-term corticosteroid therapy.	24-hour urine cortisol excretion
Thyroid disease (Over or underactive)	1-2%	Signs and symptoms of hyper/ hypothyroidism	Thyroid function tests
Hyperparathyroidism	<1%	Hypercalcemia, hypophosphatemia	Parathyroid hormone, Calcium
Other causes			
Coarctation of the aorta	<1%	Usually identified in childhood or adolescents; different BP (>20/10 mmHg) between upper-lower limbs and/or between the right-left arm; delayed radial-femoral pulsation; low ABI; interscapular ejection murmur; rib notching on CXR.	Echocardiogram

Table 2: Common causes of secondary hypertension, along with associated clinical symptoms and diagnostic screening methods [9].

Case's Title	Author	Year	Age/Y	Gender	Management
Pseudopheochromocytoma due to obstructive sleep apnea: a case report [3]	Aria Jazdarehee et al	Feb 2022	65	Male	Alpha-blocker with CPAP therapy.
Pseudopheochromocytoma Associated with Domestic Assault [7]	H M Le et al	2016 Sep	45	Female	Alpha and beta antagonists, along with anxiolytics and mental health support
Pseudopheochromocytoma induced by anxiolytic withdrawal [12]	Alida Pall et al	2014 Oct	55	Female	Alpha and beta antagonists, along with anxiety-relieving medications
Lateralizing sensorimotor deficits in a case of Pseudopheochromocytoma [18]	Joome Suh et al	2014 Dec	54	Female	Alpha- and beta-blockers
Obstructive sleep apnea presenting as Pseudopheochromocytoma [4]	HeLa Marmouch et al	2016 Mar	52	Female	ACE inhibitors and calcium channel blockers were added, as well as Prazosin.
Pseudopheochromocytoma: An uncommon cause of malignant hypertension [15]	SM Seck et al	2009 Jul	42	Male	Alpha and beta antagonists, along with anxiolytics and mental health support
Clozapine use presenting with Pseudopheochromocytoma in a schizophrenic patient: a case report [6]	Jaskanwal Sara et al	2013 Jan	49	Female	Stopped Clozapine
Obstructive sleep apnea presenting as pseudopheochromocytoma [19]	Michael K Cheezum et al	2010 Apr	39	Male	CPAP and antihypertensives
Paroxysmal hypertension in a 48-year-old woman [20]	Jennifer Hunt et al	2008 Aug	48	Female	Alpha- and beta-blockers and psychological support
Unexplained Symptomatic Paroxysmal Hypertension: A Diagnostic and Management Challenge [14]	Kelly Dyer MD et al	2019 Nov	58	Female	Alpha-beta blockade and psychological support addition selective serotonin reuptake inhibitors (SSRI)
A RARE CASE OF PSEUDOPHEOCHROMOCYTOMA WITH PANIC ATTACK WITHOUT AGORAPHOBIA – A CASE REPORT [13]	Iskandar Mirza Amran et al	2022 Nov	26	Male	Alpha and beta antagonists, along with anxiolytics and mental health support
PSEUDOPHEOCHROMOCYTOMA–CASE REPORT AND REVIEW OF THE LITERATURE [16]	Lenz et al	2016 Sep	43	Male	AT1-blocking, then gradually intensified to standard triple therapy, plus an antidepressant.
Pseudopheochromocytoma of Pregnancy [17]	Baiju R. Shah et al	2003 Oct	33	Female	Delivery

Table 3: The following table shows a literature review of some of the published cases of PPCC, including management.

Other potential sources of elevated catecholamine include psychological stress, pheochromocytoma, certain medications, and the misuse of amphetamines or cocaine [9,11,12]. Hypertension episodes in PPCC are sudden in onset, and physical symptoms often accompany those episodes, including headaches, nausea, dizziness, chest pain, diaphoresis, and palpitations [9,13]; these mimic the symptoms associated with PCC. These episodes range from daily to less than one per month, and the episodes may range from minutes to days [10]. A clear correlation exists between elevated blood pressure and emotional distress in cases of labile hypertension, distinguishing it from paroxysmal hypertension. A panic disorder, rather than PPCC, is characterized by the presence of a specific trigger, such as anxiety or fear, along with a moderate increase in blood pressure that does not surpass 180 mmHg [7,11].

The protracted conflict in Northwest Syria has led to a shortage of medical equipment, staff, and essential medications, as well as limited availability of intensive care unit beds. In our case, the trigger was war-related, grief and displacement. H. M. Le et al., reported a case triggered by physical and verbal abuse [7], Alida Pall et al. related it to anxiolytic medication withdrawal [12], Jaskanwal et al., described a case with schizophrenia on clozapine [6], and Amran reported a case with a panic attack [13].

In our case, endocrinological disturbances, particularly PCC, were excluded. Although sleep studies were not performed, the patient's medical history and physical examination did not suggest sleep apnea. Laboratory testing excluded thyrotoxicosis and carcinoid, and there was no evidence suggesting a history of alcohol withdrawal; therefore, a diagnosis of PPCC was made.

The pathophysiology of PPCC remains poorly understood [14]. Literature review shows that beta-blockers, alpha-blockers, and psychopharmacological interventions could be used in PPCC [15-17] (Table 3). It is believed that pseudo pheochromocytoma exhibits hypersensitivity to beta—and alpha-1-adrenoceptors, and the usefulness of alpha—and beta-blockers further supports this theory [16]. However, sometimes, these drugs have not been effective [12]. In our case, due to our patient's asthma, he was started on calcium channel blockers (Diltiazem) as a maintenance treatment for blood pressure. The patient showed significant improvement in controlling blood pressure and the frequency of the episodes, with Sertraline as an antidepressant. This might indicate that calcium channel blockers could be as effective as beta-blockers in managing PPCC; however, more studies are needed.

In all admissions, the patient was not allocated to the intensive care unit (ICU) and did not receive intravenous medications. In low-resource war-torn territories, ICU bed availability is limited to only intubated patients and war-related life-threatening cases. In contrast, severely hypertensive patients without target organ damage are managed in the Emergency Department using basic approaches. Nevertheless, these approaches were deemed appropriate in our present case and resulted in significant improvement in the patient's condition.

PPCC is often misdiagnosed as PCC, and its management can vary depending on the individual case. Our case highlights the importance of considering alternative treatments, such as calcium channel blockers and antidepressants, in patients with comorbidities. This case elucidates the importance of a multidisciplinary approach in managing patients with PPCC, particularly in resource-limited settings. Further research is needed to expand the knowledge of alternative management options for this challenging condition.

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Authors' contributions

JN and ZA completed the initial structure, data collection, literature review, and study drafting. JN, ZA, OAA, GM, and HA contributed to the design, supervision, data analysis, and multiple stages of revision.

Availability of data and material

The data used was made available with permission from Idlib University Hospital.

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Conflict of Interest

The authors state that they have no known competing financial interests or personal relationships that could have emerged to affect the work reported in this report.

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