



CASE REPORT EVALUATING HYPERTENSION IN YOUNG PATIENTS: A CASE REPORT HIGHLIGHTING THE NEED TO CONSIDER PARAGANGLIOMA

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Abstract

Paragangliomas are rare neuroendocrine tumors that secrete catecholamines thus leading to hypertension and tachycardia. This is because paragangliomas in young patients may manifest symptoms that are periodic and thus may be confused with other diseases such as panic disorders and primary hypertension. This case report presents a 17-year-old boy who was diagnosed with hypertension, palpitations, and severe panic attacks for the last two months. He was not a steady candidate of constant blood pressure throughout the day and he had many cases of tachycardia. Biochemical investigations revealed elevated plasma normetanephrine levels suggesting the presence of a catecholamine-producing tumour. These were further supported by a 24-hour urine test which came out higher than the normal range of urinary normetanephrine level. Follow-up MRI and PET-CT scans showed neck lesions in close apposition to the carotid artery but there was no evidence of metastatic disease. Therefore the diagnosis of paraganglioma was made and the patient was scheduled for surgical removal of the tumours. This case emphasizes the diagnostic challenges in patients with paraganglioma especially when they are young and present with episodic hypertension and panic-like symptoms. Both biochemical and imaging studies should be implemented during the first stage of the disease to prevent complications such as hypertensive crises or tumor metastasis and to give adequate treatment.

Keywords: Paraganglioma, Hypertension, Catecholamines, Neuroendocrine tumor, Panic attacks.

1. Introduction

Hypertension is a lifelong condition, which refers to high blood pressure that is above the normal level and is a common ailment in modern society that affects over one billion people worldwide. While hypertension is prevalent in the elderly because of age-related factors such as arterial stiffness and other vices such as lack of exercise and poor diet, hypertension is also prevalent in the young. For youth below the age of 40 years, hypertension is mostly secondary and not primary as is the case with older persons (Zhou et al., 2017). This is clinically important because secondary hypertension may be

cured if the underlying cause is diagnosed correctly and managed appropriately; therefore, a detailed diagnostic workup should be undertaken, especially in young people in whom hypertension is not common. Secondary hypertension accounts for 5-10% of hypertension in the general population and is even more common in young people (Calhoun et al., 2008). In young patients, there should always be a search for potentially reversible causes because otherwise the patient is exposed to cardiovascular danger they do not require. There are several causes of secondary hypertension and endocrine diseases are considered to be significant as they can cause severe and resistant hypertension. Of the secondary causes of hypertension, paragangliomas are regarded as rare neuroendocrine neoplasms. Paragangliomas arise from the paraganglia which is a cluster of neuroendocrine cells found in various sites of the body about the sympathetic and parasympathetic nervous system (Fishbein et al., 2017). Paragangliomas are very similar to pheochromocytomas which are tumours that originate from the adrenal medulla. Pheochromocytomas are located only in the adrenal medulla while paragangliomas can occur in any site of the body. The most dangerous aspect of paragangliomas is that they secrete catecholamines such as epinephrine and norepinephrine which regulate blood pressure. Catecholamine elevates the blood pressure episodically or chronically and other symptoms such as palpitations, headaches, and sweating. Such symptoms are similar to common cardiovascular and psychiatric diseases, which makes it difficult to diagnose paragangliomas (Sharma & Fishbein, 2023). Paragangliomas are not very common but they can lead to a lot of issues if the tumor is not detected or if it is not managed. Paragangliomas are rare tumors and this makes them difficult to diagnose for clinicians. These tumors are reported to develop in 2-8 per million people per year (Lenders et al., 2014). Although they are not as common as other types of tumors, paragangliomas are of medical significance because they can become malignant and cause serious cardiovascular issues such as a stroke or heart attack due to excessive secretion of catecholamine (Y-Hassan & Falhammar, 2020). In addition, 25–40% of paragangliomas are hereditary, and most of the hereditary cases are linked to SDH genes. Such tumors should therefore be diagnosed at an early stage not only for the treatment of the patient but also to screen the other members of the family who may be at risk (Jain et al., 2020). Because of the challenges in diagnosing paragangliomas, this case report aims at enhancing the understanding of the clinical suspicion of this disease particularly in young patients with hypertension.

1.1 Importance of the Case

This case is worthy of discussion in detail because the patient was young and the cause of hypertension was paraganglioma. High blood pressure in young people is rare and is usually a result of a specific disease and is thus not called essential hypertension which is more frequent in the elderly population. Secondary hypertension should therefore always be suspected in patients with secondary hypertension and physicians should always look for secondary causes of hypertension since failure to do so means that the patient is being managed wrongly and will end up having long-term cardiovascular complications (Calhoun et al., 2008). This case provides clinicians with a reason to be very cautious of secondary causes of hypertension in young patients even when other risk factors such as obesity, diabetes, or family history of essential hypertension are not apparent. The diagnosis of paraganglioma in this case is also quite rare because this tumor is rare and is not commonly linked with hypertension. Paragangliomas are even rarer and are estimated to constitute less than 0. In secondary hypertension, renal parenchymal disease is seen in 2% of the cases only (Siddiqui et al., 2021). However, paragangliomas should be considered in the list of differential diagnoses when young patients have unexplained or refractory hypertension, particularly if they have episodic symptoms such as palpitations, headaches, or diaphoresis (Tanabe & Naruse, 2020). In this case, the patient's hypertension did not respond to conventional antihypertensive medications and this is a pointer towards a secondary cause and therefore requires a thorough workup to look for such rare conditions as paragangliomas. Paragangliomas should be diagnosed and treated early because the condition is life-threatening to the patients. If not controlled, excessive catecholamine from paragangliomas may cause a hypertensive crisis, arrhythmia, or myocardial infarction (Ma et al., 2022). The condition is normally diagnosed at an early stage and this normally calls for surgery where the surgeon has to

remove the tumor. Other imaging studies such as CT, MRI, or functional imaging studies such as MIBG can be employed to identify the tumor while biochemical tests to assess metanephrines can be used to diagnose the disease (Beninato & Duh, 2018). In this case, the patient was hypertensive but this was well controlled after the tumor was removed and this goes to show that early and correct diagnosis is important.

Therapeutic management of paragangliomas varies depending on their location, size, and genetic background. For example, the treatment of a thyroid paraganglioma, a rare entity, involved fine-needle aspiration biopsy correlated with histopathological findings, highlighting the role of minimally invasive diagnostic techniques in managing rare presentations (Çetin, Kir & Yilmaz, 2016).

1.2 Diagnosis Problems and Their Consequences for Practice

The greatest challenge in diagnosing paragangliomas is that patients may have a range of complaints that are nonspecific and rather vague (Shen et al., 2018). Paragangliomas may be asymptomatic for years or the patient may be diagnosed with other conditions such as essential hypertension, anxiety disorders, or migraines. Development of severe morbidity as patients are still vulnerable to the effects of excessive secretion of catecholamines (Schmittinger et al., 2012). This case therefore requires health care providers to exercise a lot of caution when dealing with hypertension in young people, especially those whose hypertension is resistant to conventional treatment. Thus, this case report underlines the importance of considering the non-conventional etiology of secondary hypertension, such as paraganglioma, in young patients with hypertension. These tumors are not very common but it is established that they have the potential to lead to severe cardiovascular complications if they are not detected and managed in good time. Clinicians have to remember this when dealing with patients who have uncontrolled hypertension, that is hypertension that cannot be controlled through normal medication. Thus, they can improve patient's quality of life and may potentially prevent the worse outcomes of the disease.

Advanced imaging modalities, such as PET/CT with radiopharmaceuticals like (68)Ga-DOTATATE, are increasingly utilized for localizing sporadic metastatic pheochromocytomas and paragangliomas, showing superiority over traditional imaging methods (Janssen et al., 2016). Such approaches enhance the detection of metastatic disease and guide therapeutic planning.

1.3 Atypical Presentations of Paraganglioma: Paragangliomas can present atypically in various patient groups, including children and young adults. For instance, a case study described a pediatric patient with seizures due to a paraganglioma, highlighting the rare neurological manifestations of this tumor type in children (Oyenusi et al., 2023). Another case of a young woman diagnosed in a primary care setting underscored the importance of early clinical suspicion in atypical cases presenting with vague symptoms (Reus et al., 2021). Diagnosis of paragangliomas is often complicated by their variable presentations. As seen in the case of synchronous carotid body and glomus jugulare tumors, imaging plays a crucial role, yet it may not always clearly differentiate between benign and malignant lesions (Rahman et al., 2024). Additionally, cases involving multiple sites, such as head, neck, retroperitoneum, and duodenum, further complicate the diagnostic process and emphasize the need for comprehensive imaging studies (Kawanabe et al., 2023).

2. Case presentation

The patient was a 17-year-old male who had been referred to the endocrinology clinic with a two-month history of hypertension, palpitations, and panic attacks. He also had occasional headaches and sometimes dizziness but the symptoms were progressive. These symptoms took the patient to several health care facilities where he was diagnosed with high blood pressure. He said that palpitations were sudden and could last for a few minutes and his panic attacks involved unprovoked severe panic. The patient also had non-localized headaches without visual aura and dizziness more so after the episodes of tachycardia. He had no family history of cardiovascular or neuroendocrine diseases and had never smoked, drank alcohol, used drugs, or had other severe diseases. The patient consistently exhibited

elevated blood pressure throughout the day with the recorded pressure ranging from 132/90 mmHg to 160/87 mmHg. During episodes of palpitations, his heart rate indicated tachycardia although it was normal outside these episodes. No abnormalities were noted in the physical examination of the head, neck, abdomen, or extremities. Because the patient's blood pressure was persistently high, further evaluation was done to ascertain the underlying cause of the patient's hypertension.

2.1 Blood Pressure Monitoring

During physical examination, the patient's blood pressure levels were elevated and blood pressure variations were recorded while there were few instances of tachycardia. He was also monitored for his blood pressure for an extended period and it was noted that his pressure tended to rise in the evening. His heart rate also has variations during these hypertensive episodes and there is sometimes a rise in heart rate as well. The variability in blood pressure, specifically the rise in systolic and diastolic pressures, required evaluation for secondary causes of hypertension and thus biochemical and imaging studies. This table records blood pressure readings taken in the morning and evening during the examination.

Table 1: Blood Pressure Readings

Date	6 am	9 pm	12 am
10/12/23	132/90	151/91	140/87
11/12/23	139/93	159/93	137/92
12/12/23	143/77	145/93	130/87
13/12/23	148/87	151/83	141/76
14/12/23	136/81	148/92	137/78
15/12/23	125/94	149/87	148/84
16/12/23	154/75	158/87	143/92
17/12/23	160/87	149/93	146/94
18/12/23	136/86	-	-

The changes in the blood pressure values during the day and over the time of the study may indicate labile or borderline hypertension which may be influenced by physical activity, diet, medication adherence, and stress. Persistently elevated abnormal values need further assessment and may need pharmacological intervention, particularly in patients with paraganglioma-associated secondary hypertension.

2.2 Laboratory Investigations

The patient was subjected to extensive laboratory investigations in an attempt to find out the cause of his hypertension with special emphasis on biochemical markers suggestive of neuroendocrine tumors like paraganglioma. The testing process was to assess catecholamine metabolites and other hormones that may be relevant to the pathophysiology of the condition.

2.2.1 Initial Hormonal and Catecholamine Evaluation

The initial procedures included serum tests for calcitonin and free plasma metanephrines, which are important markers in neuroendocrine tumors. Elevated levels of metanephrines and normetanephrines

strongly indicate the presence of catecholamine-secreting tumours including pheochromocytomas and paragangliomas. The results obtained were as follows:

- Calcitonin, Serum: <2.00 pg/mL (normal<8.40 pg/mL)
- Metanephrines, Free, Plasma: 15.90 ng/L (normal: 7.90 - 88.70 ng/L)
- Normetanephrine, Free, Plasma: 192.00 ng/L (elevated; normal: 20.10 - 135.40 ng/L)
- 3-Methoxytyramine: 2.83 ng/L (normal:<18.40 ng/L)

The normetanephrine level of the patient was also high; this was evidence of the presence of a catecholamine-secreting tumor. Plasma metanephrines were a little high, but not over normal values, and near the upper limit of normal. There was no evidence of a dopamine-secreting tumor because the serum level of 3-methoxytyramine, which is another metabolite of catecholamines, was normal. The rise in normetanephrine pointed to a possibility of paraganglioma, and therefore, the need for imaging and biochemical evaluation of catecholamine levels in urine.

2.2.2 Plasma-Free Metanephrines Results

Two separate plasma-free metanephrine tests were performed to confirm the presence of paraganglioma.

Table 2: Plasma Free Metanephrines Results (First Test)

Parameter	Result	Unit	Standard Range
Free Metanephrines	52	ng/L	12 - 61
Free Normetanephrine	198	ng/L	18 - 112
Free 3-Methoxytyramine	ND	ng/L	1 - 15

The first test showed an increase in the free normetanephrine level, which is 198 ng/L and exceeds the limits of the reference range. This elevation is suggestive of hyperproduction of norepinephrine which is typical of paragangliomas. The free metanephrine level was within the normal range while 3-methoxytyramine was undetectable.

Table 3: Plasma Free Metanephrines Results (Second Test)

Parameter	Result	Unit	Standard Range
Free Metanephrines	39	ng/L	12 - 61
Free Normetanephrine	52	ng/L	18 - 112
Free 3-Methoxytyramine	ND	ng/L	1 - 15

The second test revealed that the free metanephrine level was 39 ng/L and the free normetanephrine level was 52 ng/L which are normal values. The lack of increased catecholamine metabolites in this sample could be due to the episodic secretion of paragangliomas that can cause variation in the levels.

2.2.3 24-Hour Urine Catecholamines

To get a more detailed evaluation and to explain the changes, the 24-hour urine metanephrines were collected:

- Metanephrines: 114. 33 µg/24 hrs (normal: 74.00-297.00/24 hrs)
- Normetanephrine: 5405. 70 µg/24 hrs (elevated; normal: 73. 00 – 808. 00 µg/24 hrs)
- Total Volume: 3700 mL

The 24-hour urine test result also indicated a high level of normetanephrine (5405.70 μ g /24hrs). The increase in urinary excretion corresponds to the clinical profile of permanent hypernorepinephrine secretion.

2.2.4 Electrolyte Levels and Aldosterone/Renin Ratio

Additional tests were also conducted with a view of ruling out other causes of secondary hypertension as described below:

2.2.4.1 Serum Electrolytes:

- Sodium: 135.00 mEq/L (normal: 136.00 – 146.00 mEq/L)
- Potassium: 3.50 mEq/L (normal: 3. (50 – 5. 10 mEq/L)
- Chloride: 102.00 mEq/L (normal: 101.00 – 109.00 mEq/L)

2.2.4.2 Aldosterone/Renin Ratio:

- Aldosterone: 6.93 ng/dL
- Renin, Direct: 112.30 mIU/L
- Aldosterone Renin Ratio (ARR): <20.60 (suggestive of primary aldosteronism)

Although the increased ARR indicated the possibility of primary aldosteronism, clinical manifestations and extremely elevated normetanephrine levels indicated paraganglioma more. Additional biochemical tests for primary aldosteronism were advised but did not appear to be as emergent as clinical suspicion for a catecholamine-secreting tumor.

2.3 Imaging Studies

Imaging was helpful in the determination of paraganglioma and in determining the extent of the disease. These investigations were important in ascertaining whether the tumor existed, where it was located, and if it had spread to other parts of the body or other structures. Two primary imaging modalities were utilized: Magnetic resonance imaging and positron emission tomography-computed tomography.

2.3.1 Magnetic Resonance Imaging (MRI)

MRI was done to define the location and size of the soft tissue in the neck and to identify paraganglioma. MRI Report was conducted at Batra MRI Health Institute to visualize the soft tissues in the neck and identify any abnormalities indicative of paraganglioma.

Some of the discoveries that have been made from the MRI include the following:

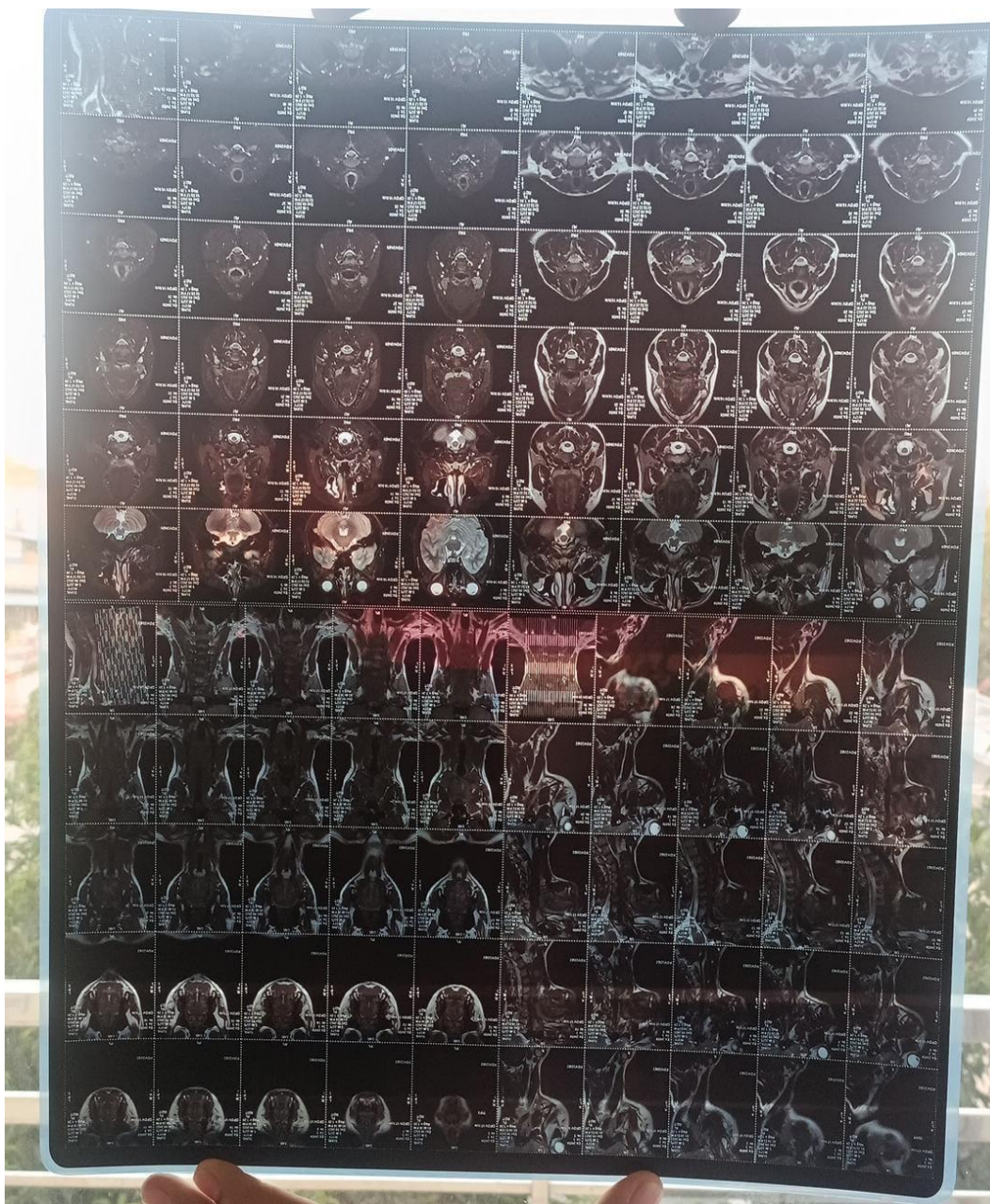


Fig 1: MRI Scan of the Head and Neck Region: Cross-Sectional Views for Diagnostic Evaluation of Cervical Pathology.

The key findings from the MRI included:

- Neck: No pathologic conditions were seen in the region of the neck.
- Lymph Nodes: In the bilateral deep cervical and submandibular chains small sub-centimeter nodes were present.
- Other Structures: There was no lesion in the larynx, glottis, subglottis, and paranasal sinuses.

In a way, it was comforting that there was no gross pathology in the neck but at the same time, one could worry that there may be a small localized tumor which might not be well seen on MRI. Small lymph nodes may be either a secondary deposit node or a reactive node. In the other structures, no other disease or complication was evidenced in the neck region based on the normal findings.

MRI gave a detailed picture of the anatomy, however, no major diseases were identified apart from the enlarged lymph nodes. It was beneficial in assessing the prevalence of local disease but not very beneficial in assessing metabolic activity.

2.3.2 Positron Emission Tomography – Computed Tomography (PET-CT) scan

Additional information about the metabolic activity of the lesions which helps diagnose and stage paragangliomas was obtained from PET-CT scan. PET-CT Scan Report was generated at RNM Imaging Therapy & Research Institute. The following was the result of the PET-CT scan:

- Right Neck: A non-tracer avid soft tissue lesion of 1.1 x 1.0 cm in size was identified and was in contact with the common carotid artery.
- Left Neck: A similar lesion, which was 0.8 x 0.8 cm in size, was detected on the left side of the patient.
- Lymph Nodes: Faintly tracer avid sub-centimeter bilateral cervical level II lymph nodes were noted.
- Other Areas: No focal tracer avid lesions were identified in the thorax, abdomen, pelvis, or skeletal system.

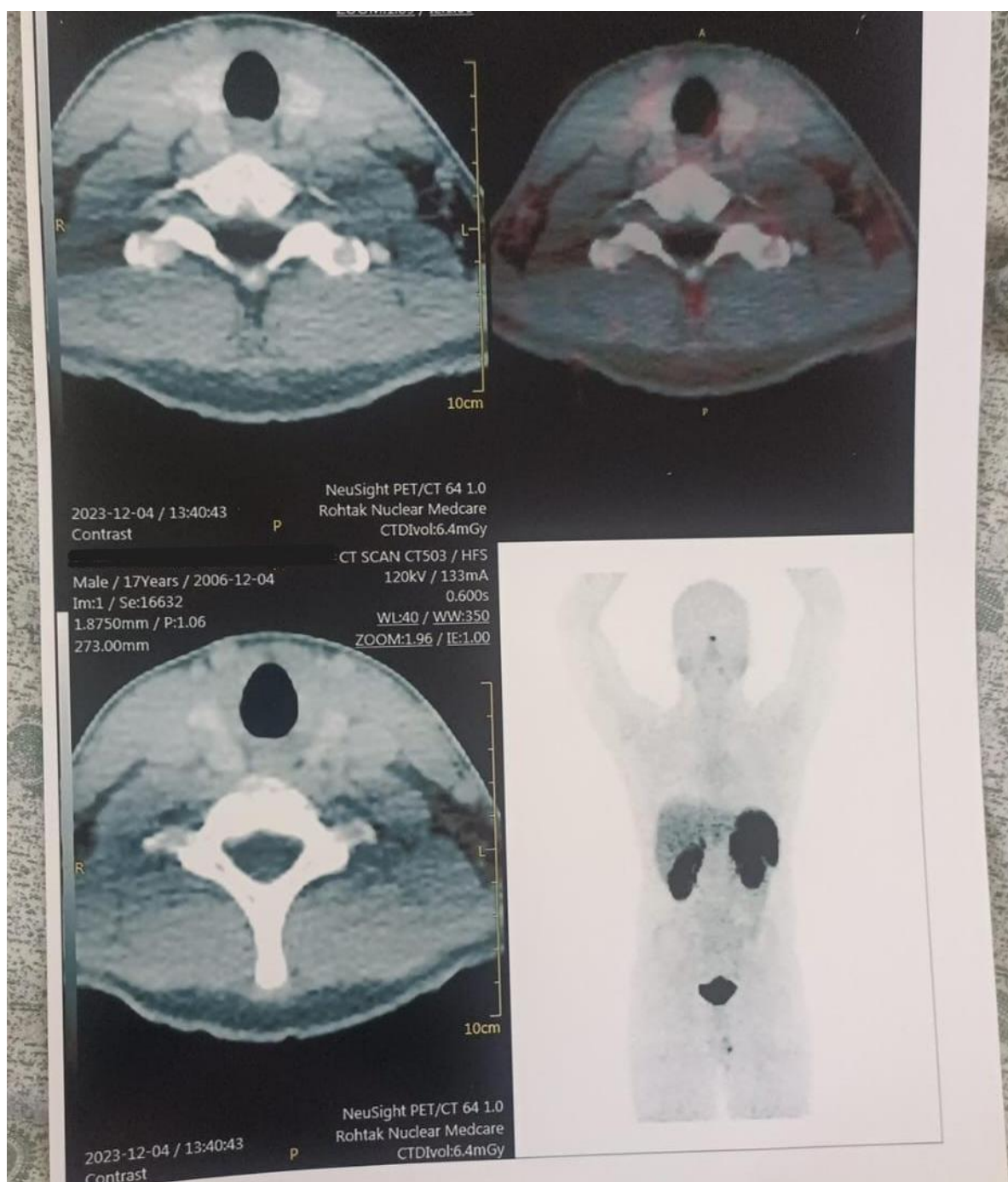


Fig 2: PET/CT Imaging of the Cervical Spine and Thoracic Region in a 17-Year-Old Male

There were lesions in the neck that showed no bright uptake in the PET component, this could mean that they are less metabolically active. Nevertheless, since the lesions were localized in the neck and the vicinity of the carotid vessels and were bilateral the diagnosis of a neuroendocrine tumor such as paraganglioma could not be ruled out. There was no tracer uptake in other distant sites and this was a good sign because at this time there was no sign of metastases. Of these, the study highlighted a localized malignant disease that impacted surgical choices.

PET-CT also provided information about the metabolic status of the lesions and the position of the tumors. It was therefore the surgery of the case that the patient had lesions in the neck and no metastases in other organs. The imaging studies in conjunction with other clinical features were useful in the diagnosis of paraganglioma and in planning the management which involves surgical removal of the localized tumor and follow-up for metastatic disease.

3. Discussion

This case of a 17-year-old male with hypertension, palpitations, and panic attacks is a good example of the diagnostic difficulty of paraganglioma. Other such case reports in the medical literature have also pointed out that paragangliomas though rare should be suspected in patients with unexplained secondary hypertension and elevated catecholamine metabolites (Pacak, 2022). The majority of paragangliomas are hypertensive because of the secretion of catecholamines as seen in the patient's history of recurrent hypertension and tachycardia. In comparison with other reported cases, their high normetanephrine level and the fact that the symptoms are not constant make this patient's catecholamine secretion profile typical of paraganglioma (Young & Wen, 2023). This case also has the peculiarity of the patient's young age and the symptoms such as panic attacks and unprovoked severe panic, which are not typical for most of the other paragangliomas cases. Since panic attacks and palpitations are presented as episodic phenomena, it means that catecholamines are released on and off, and this creates a diagnostic problem because these symptoms could be of psychogenic origin. These variations of blood pressure during the day, and normal values in some biochemical tests such as the second plasma-free metanephrine test also support the observation that catecholamine secretion in paragangliomas is intermittent (Eisenhofer & Peitzsch, 2014). This means that biochemical tests and imaging studies may have to be done more elaborately, or repeated when working with patients who are suspected to be paragangliomas. A significant clinical application can be interpreted from this study, especially in the diagnosis of paragangliomas in young people with secondary hypertension. Biochemical testing is crucial in the first step since the delayed diagnosis results in a hypertensive crisis, cardiovascular events, or metastases in case the tumor is not treated. The management in this case which involved imaging and biochemical workup is in agreement with the guidelines on diagnosing catecholamine-secreting tumors as described by Lenders and his team (2014). This case affirms that paraganglioma should be considered in differential diagnosis of hypertension in young people especially those who do not have a family history of cardiovascular or neuroendocrine diseases as in this patient. The following recommendations for future clinical practice are made: A high index of suspicion of paragangliomas in patients with unexplained hypertension and repeated or multiple tests because of the intermittent secretion of catecholamines. MRI and PET-CT scans both had their applications in the case in that they helped to establish the position of the tumor and its metabolic rate to help with the surgery. The lack of metastatic features in the localized tumor also alerts the need to diagnose and treat the disease at early stages to improve the survival of the patient (Buffet et al., 2019).

4. Conclusion

This case illustrates the diagnostic challenge in paragangliomas especially in young patients with features of hypertension, palpitations, and panic attacks. This is made worse by the fact that catecholamines are periodic since the fluctuating blood pressure and plasma metanephrine levels show. The symptoms of severe panic attacks and episodic hypertension of this patient resembled more common diseases like primary hypertension and anxiety disorders and thus the correct diagnosis was

delayed. However, the inability to explain unexplained hypertension in the absence of a family history of cardiovascular disease, biochemical, and imaging examination revealed high normetanephrine levels and bilateral neck lesions. MRI and PET-CT scans were useful in determining the position of the tumors and in ruling out metastasis. Paragangliomas may lead to life-threatening conditions such as hypertensive crises or metastases if not diagnosed early and that is why diagnosis is very crucial. This case shows that paragangliomas should be considered in the list of differential diagnoses of young patients with secondary hypertension and episodes. In such cases, biochemical evaluation and imaging studies have to be done, and early intervention to prevent cardiovascular events and improve patients' outcomes.

5. Recommendations

- Further Testing: Confirm the diagnosis with a 24-hour urine metanephrine test.
- Follow-up: Regular monitoring of blood pressure and symptoms is essential.
- Referral: Consult with an endocrinologist and surgical oncologist for potential surgical intervention.

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Supplementary data

Table: Blood Pressure Monitoring Table

Date	Morning	Evening
14/05	134/78	148/94
15/05	129/82	135/78
16/05	125/84	141/83
17/05	129/76	139/93

18/05	135/73	141/84
19/05	134/69	138/89
20/05	138/90	155/102
21/05	155/100	149/92
22/05	136/83	146/90
23/05	145/90	150/88
24/05	135/84	144/86
25/05	135/73	142/87
26/05	134/81	134/73
27/05	149/73	156/89
28/05	141/81	146/77
29/05	126/79	135/80
30/05	144/84	151/96
31/05	133/80	137/77
01/06	134/70	144/87
02/06	145/80	143/91
03/06	136/73	139/88
04/06	140/82	145/74
05/06	132/74	136/84
06/06	145/74	133/73
07/06	147/73	141/81
08/06	141/81	140/86
09/06	133/89	128/88
10/06	128/80	136/77
11/06	121/79	

This table records blood pressure readings taken in the morning and evening over nearly a month (14/05 to 11/06). The following key points can be observed from the data:

1. General Trend

- The systolic blood pressure (the first number) ranges from 121 to 155 mmHg, while the diastolic blood pressure (the second number) ranges from 69 to 102 mmHg.
- Higher blood pressure readings tend to occur in the evening compared to the morning, suggesting a circadian variation in blood pressure. This is a known phenomenon, where blood pressure rises in the late afternoon and evening and is generally lower in the morning.

2. Hypertensive Episodes

- On 20/05, the evening reading is 155/102 mmHg, indicating stage 2 hypertension according to American Heart Association (AHA) guidelines. Another high reading occurred on 21/05 (morning: 155/100 mmHg), signaling the need for urgent investigation or treatment adjustment.
- Other days with high systolic and diastolic readings (such as 30/05 with 151/96 mmHg) also suggest intermittent hypertensive episodes, which could be linked to stress, diet, or other factors.

3. Normal and Lower Ranges

- Normal systolic readings are noted on several days, such as 10/06 (128/80 mmHg in the morning) and 11/06 (121/79 mmHg in the morning), which fall within the AHA's ideal blood pressure range (<120/80 mmHg).
- Lower diastolic readings are observed on some days, such as 19/05 (134/69 mmHg in the morning), which suggests good vascular health during the morning, although evening readings often show a slight increase in diastolic pressure.

4. Variability

- The patient's blood pressure fluctuates throughout the day and over the observation period, a pattern that could indicate labile or borderline hypertension. This variability could be influenced by physical activity, diet, medication adherence, and stress levels.

5. Possible Risk Factors

- The persistent readings above normal (140/90 mmHg) over multiple days suggest that hypertension could be present, potentially requiring pharmacological intervention if lifestyle modifications alone do not suffice.
- The patient should be monitored for symptoms of secondary hypertension, particularly given prior suspicion of a paraganglioma.