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Aggressive posterior paraganglioma presenting with generalized weakness, anemia, hypertension, and weight loss: A case report

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ABSTRACT

Paragangliomas (PGLs) are rare neuroendocrine tumors that originate from chromaffin cells in the extra-adrenal autonomic nervous system's ganglia. The diagnosis of PGL is made based on clinical characteristics, biochemical tests, imaging, functional studies, and pathology reports. Catecholamines and chromogranin A levels should be evaluated prior to biopsy or surgical excision. We present a case of aggressive PGL in a 55-year-old woman presented with weakness, blurred vision, hypertension, and weight loss.

1. Introduction

Paragangliomas (PGLs) are rare neuroendocrine tumors originating from chromaffin cells in the extra-adrenal autonomic nervous system's ganglia. These tumors arise from sympathetic or parasympathetic ganglia in the abdomen (80–95 %), thorax (10 %), pelvis, and head and neck (5 %).[1] According to endocrine society guidelines, pheochromocytomas (PCC) and PGLs are typically classified together and called pheochromocytomas and paragangliomas (PPGLs). PPGL is most prevalent between the third and fifth decades of life. In outpatient clinics, the prevalence of PPGL among patients with hypertension ranges between 0.1 % and 0.6 % in adults. PPGLs are mostly benign, with only about 10 % being malignant.[2] Here, we reported a rare case of aggressive PGL in a 55-year-old woman.

2. Case presentation

A 55-year-old woman complained of persistent weakness two months before admission. She also complained of blurred vision, nausea, and significant weight loss (15 kg in 1 year). There were no previous episodes of headache, palpitation, or excessive sweating. Her past medical history revealed a previous history of hypertension with the highest systolic blood pressure of 190 mmHg, yet she was controlled with amlodipine 5 mg orally. Her family history was remarkable for hypertension.

The physical examination showed elevated blood pressure of 130/70 mmHg, pale conjunctiva, and hepatomegaly. Laboratory examination revealed reduced hemoglobin (7.6 g/dL) with a platelet elevation 954.000. Fasting blood sugar (FBS) was mildly elevated (113 mg/dL). Thyroid hormones T3, fT4, and TSH were within normal limits, while the 1 mg dexamethasone suppression test (DST) was suppressed. Plasma metanephrines (MET) (1310 pg/mL; normal <57 pg/mL), normetanephrine (NMET) (1255 pg/mL; normal <148 pg/mL), and total metanephrines and normetanephrine (TMNMET) (2565 pg/mL; normal <205 pg/mL) were elevated. Peripheral blood morphology compatible with inflammatory anemia. Multislice computerized tomography (MSCT) of the abdomen revealed a solid mass (73 HU) with a necrotic component (Fig. 1).

A functional scan with somatostatin meta-iodobenzylguanidine (SST-MIBG) examination with I131-MIBG showed increased radioactivity over the right suprarenal region (Fig. 2).

The patient pretreated with carvedilol 25 mg/day and candesartan 8

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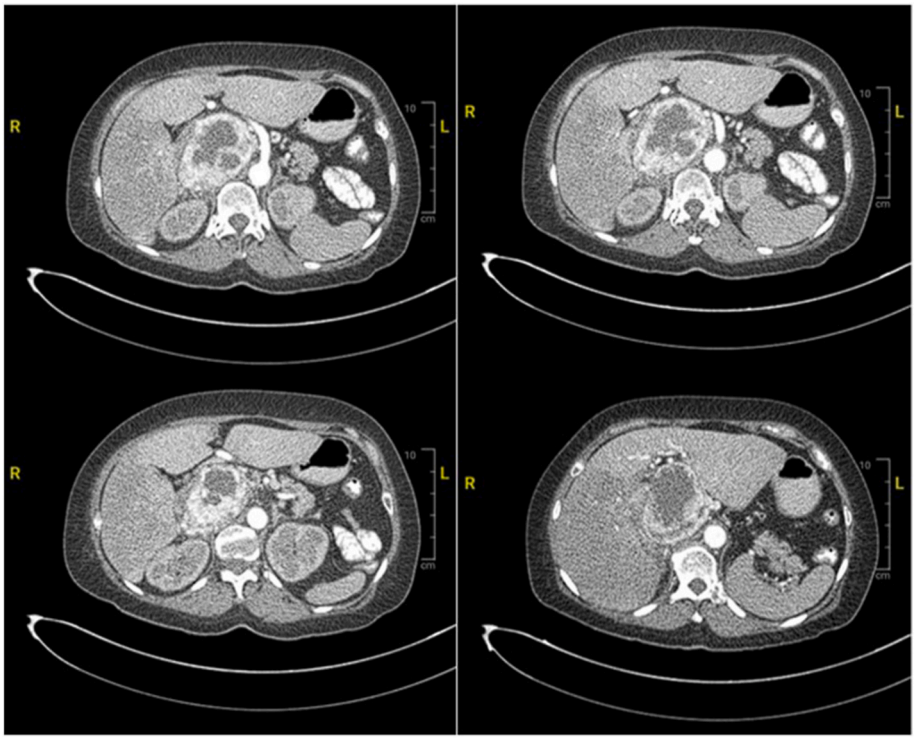

Fig. 1. Multislice computerized tomography (MSCT) of the abdomen showed a solid mass with a necrotic component bordering the liver in the posteroinferior region of the right lobe of the liver and anterosuperior to the right kidney.

mg/day. After two weeks of the perioperative period, she planned to undergo laparoscopic adrenalectomy. However, intraoperatively, an 8x6x4 cm posterior paraganglion mass was extracted. (Fig. 3). The microscopic examination revealed that the connective tissue capsule and vasculature were partially invaded by tumor cells. In the subcapsular area, there is a tumor mass consisting of round, oval cells, densely packed in groups, forming a nest of Zellballen appearance with extensive areas of necrosis and hemorrhage. Histopathologic Pheochromocytoma of the Adrenal gland Scaled Score (PASS) examination score of 8 supported for aggressive paraganglioma.

Four months post-surgery, the patient appeared asymptomatic with normal blood pressure. Postoperative evaluation of MET, NMET, and TMNMET were within normal limits of 40 pg/mL (normal: <57 pg/mL), 105 pg/mL (normal: <148 pg/mL), and 145 pg/mL (normal: <205 pg/mL) respectively. After three months, the follow-up MSCT of the abdomen and pelvis showed no residual mass.

3. Discussion

Paragangliomas are extremely hypervascular, benign, and slow-growing tumors. These tumors are frequently symptomatic and may cause fight-or-flight sympathetic symptoms such as dry mouth, flushing of the face, racing pulse, dilated pupils, constipation, fatigue, profuse sweating, headache, tremors, panic-like symptoms, and general exhaustion. In addition, blurred vision, dizziness, weight loss, excessive thirst or hunger, mood disturbances, elevated blood sugar, and weight loss are possible symptoms. Nevertheless, the most common symptoms are headache, palpitations, and profuse perspiration.[3] The clinical findings in this case were similar to those in the literature; the patient presented with weakness, blurred vision, weight loss, and hypertension.

The diagnosis of PGL is made based on clinical characteristics, biochemical tests, imaging, functional studies, and pathology reports. Biochemical testing is mandatory and performed initially to the imaging tests. Excessive synthesis of catecholamines or metanephrine should be confirmed by laboratory analysis. Many studies indicate elevation in plasma or urine metanephrine levels to diagnose PCC or PGL.[4] In this case, serum MET, NMET, and TMNMET were significantly elevated.

Extra-adrenal lesions are biopsied before biochemical evaluation due to their accessibility, broader differential diagnosis, and low likelihood of being hormonally active. However, this could be hazardous in some cases. The initial evaluation of adrenal computed tomography (CT) showed good sensitivity for PCC or PPGL.[4] In this case, multislice computerized tomography (MSCT) of the abdomen to the pelvis was performed. It showed a solid mass with a necrotic component bordering the liver in the posteroinferior region of the right lobe of the liver and anterosuperior to the right kidney, mimicking adrenal mass, adrenal metastasis, or posterior ganglion enlargement.

Radionuclide imaging agents, such as radioiodinated MIBG or 68Ga-DOTATATE, can be used to evaluate PPGL, especially tumors with a size >10 cm, to assess the extent and further metastasis. MIBG is a noradrenaline and guanethidine analog that is radiolabeled as ^{131}I-MIBG and ^{123}IMIBG with I-131/I-123.[5] This agent's sensitivity for detecting PPC or PPGL is approximately 90 %, while its specificity exceeds 95 %. In this case, we used ^{131}I-MIBG radionuclide imaging. The results showed that the mass that appeared on the right adrenal gland was a PCC with no further metastasis.

Surgery is preferred in over 90 % of patients. The Endocrine Society recommends two weeks of adequate alpha-blockade, fluid, and salt consumption for individuals having PPGL resection to avoid hemodynamic instability during tumor manipulation. If alpha-adrenergic inhibition has successfully normalized blood pressure, the beta-blocker or other antihypertensive could be delivered to maximize perioperative management.[3] Following surgery, hypotension can complicate 20–70 % of patients. The abrupt withdrawal of catecholamines after tumor removal also results in rebound hyperinsulinemia, which, combined with depleted glycogen stores, results in severe hypoglycemia during the postoperative period. Hence, postoperative monitoring of arterial pressure and blood sugar is required. In this case, we did a right adrenalectomy, and both during the surgery and afterward, there were no complications. Histopathological examination of posterior ganglion

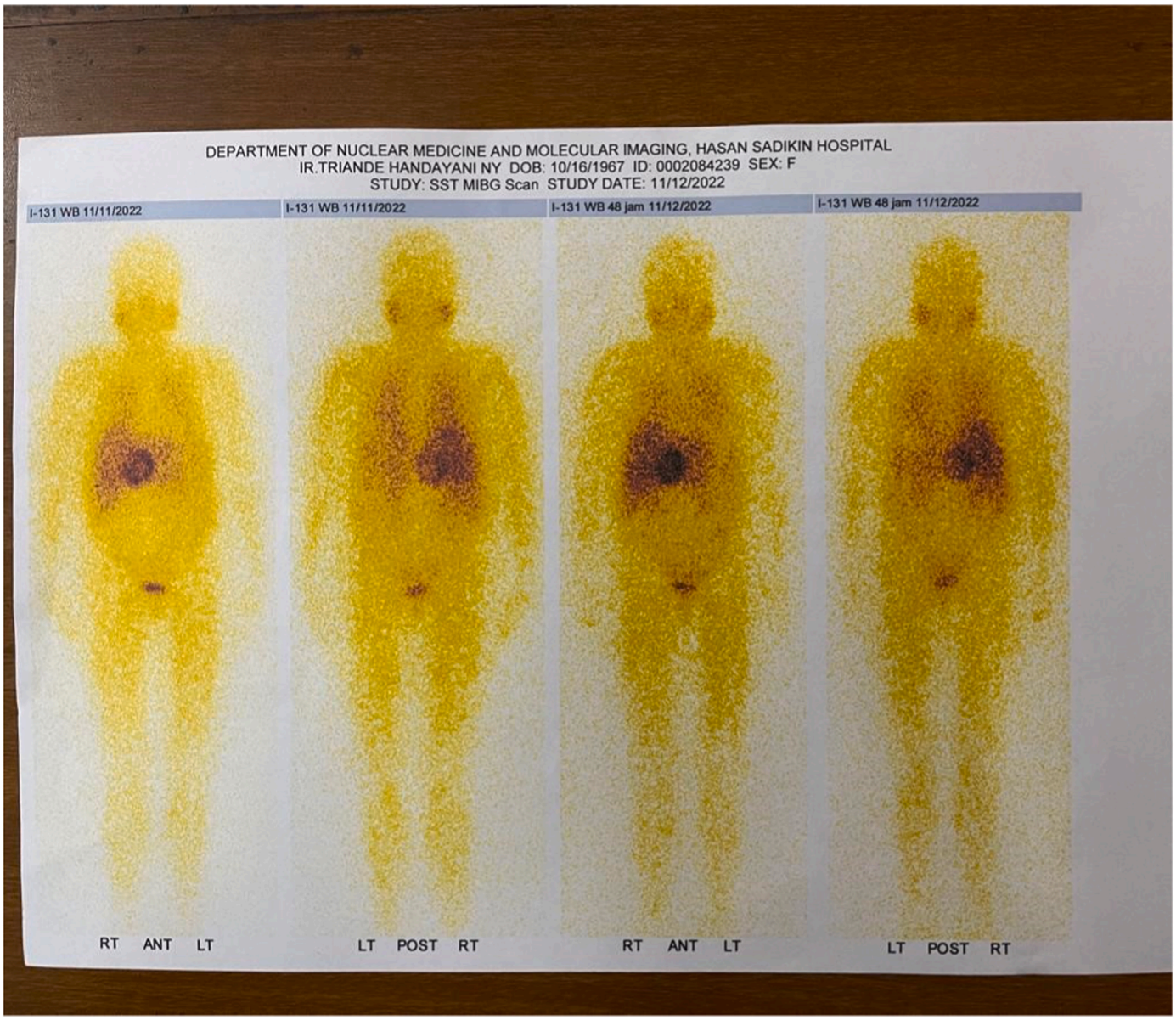

Fig. 2. Increased ^{I}131-MIBG uptake over the right supra renal region.

mass compatible with high-grade PPGL.

Patient surveillance or evaluation should be planned in PPGL for patients with certain genetic mutations or high-grade histopathology. The time for mass recurrence is low (3 %), with a recurrence time of approximately 49.4 months. In this case, clinical, biochemical, and radiologic evaluations showed no mass or active disease recurrence.

4. Conclusion

PGLs are rare norepinephrine neuroendocrine-secreting tumors in the extra-adrenal autonomic nervous system. A good clinical examination, biochemical tests, radiology examination, or radionuclide evaluation are required for disease identification. PGLs are treatable with surgery, although long-term monitoring in patients with high-grade histopathology is highly recommended.

Consent

Written informed consent was obtained from the patient to publish this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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CRediT authorship contribution statement

Hasnah Siregar: Conceptualization, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Marshell Tendean:** Investigation, Writing – original draft, Writing – review & editing. **Maya Kusumawati:** Methodology, Writing – original draft, Writing – review & editing. **Aaron Tigor Sihombing:** Methodology, Writing – original draft, Writing – review & editing. **Ria Bandiara:** Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that there is no conflict of interest.

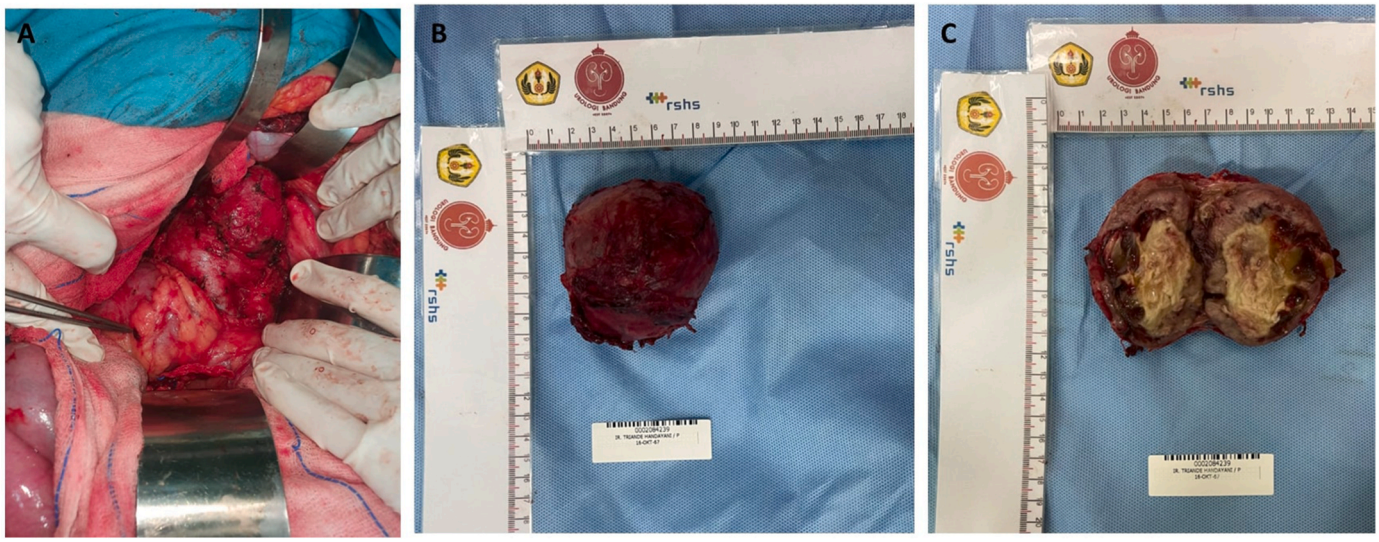

Fig. 3. A. Intraoperative view. B, C. Macroscopic examination of the posterior paraganglioma. The tissue appeared rubbery brownish yellow (8x6x4 cm), approximately 160 g. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

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