Navigating the Diagnosis and Treatment of Extra-Adrenal Pheochromocytoma Presenting with Chronic Abdominal Pain: A Clinical Conundrum

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ABSTRACT

Background: Extra-adrenal pheochromocytomas, or paragangliomas, are rare neuroendocrine tumors that present diagnostic challenges due to their nonspecific symptoms and radiologic features.

Objective: To report a case of extra-adrenal pheochromocytoma presenting as chronic abdominal pain and hepatic masses, emphasizing the diagnostic and therapeutic challenges.

Methods: A 36-year-old male with a history of diabetes and hypertension presented with weight loss and abdominal pain. Initial evaluation included comprehensive physical examination, laboratory tests, ultrasonography, and CT imaging of the abdomen and chest. Partial hepatectomy was performed, and the diagnosis was confirmed through histopathological and immunohistochemical analysis.

Results: Imaging identified three mixed echogenic hepatic masses, with the largest measuring 5.6 x 5.4 cm. Enlarged para-aortic lymph nodes were observed, the largest being 4.0 x 3.5 cm. CT chest revealed a mass on the chest wall (7.0 x 3.0 cm) with metastatic lung nodules. Immunohistochemistry confirmed paraganglioma with positivity for chromogranin A and neuron-specific enolase.

Conclusion: This case underscores the importance of considering paragangliomas in differential diagnoses of atypical abdominal masses and highlights the critical role of histopathological confirmation in guiding management.

INTRODUCTION

Pheochromocytomas and paragangliomas (PGLs/PCCs) are rare neuroendocrine tumors arising from chromaffin cells associated with the autonomic nervous system (1). While pheochromocytomas predominantly originate from the adrenal medulla, paragangliomas can develop in various extra-adrenal locations, including the abdomen, where they are termed extra-adrenal paragangliomas (2). These tumors are characterized by their capacity to produce catecholamines, which can lead to a wide range of clinical manifestations, from asymptomatic cases to severe hypertensive crises (3). Due to their rarity and the often nonspecific nature of their symptoms, PGLs/PCCs pose considerable diagnostic challenges. A high index of suspicion is required, coupled with a comprehensive diagnostic workup that includes biochemical testing and advanced imaging modalities (4). Early and precise diagnosis is crucial for appropriate management and improving patient outcomes, but this is frequently complicated by the nonspecific radiologic features of these tumors.

The clinical presentation of paragangliomas can vary widely depending on their location and size, often leading to delayed diagnosis and treatment. Abdominal paragangliomas, though rare, should be considered in the differential diagnosis of unexplained abdominal masses, particularly in patients with a history of hypertension or other symptoms suggestive of catecholamine excess (5). Imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) are typically utilized in the evaluation of suspected PGLs/PCCs; however, these modalities often fail to provide definitive differentiation from other hepatic or abdominal masses due to overlapping imaging characteristics (6, 7). More specific imaging techniques, such as Metaiodobenzylguanidine (MIBG) scanning, have demonstrated higher sensitivity and specificity for identifying pheochromocytomas and paragangliomas, though these are not always readily available or employed in initial evaluations (8, 9).

Histopathological confirmation remains the gold standard for diagnosing paragangliomas. Immunohistochemical analysis plays a pivotal role in distinguishing these tumors from other neuroendocrine and metastatic lesions. Typical markers include positivity for chromogranin A, neuron-specific enolase, and S100 protein, which help confirm the neuroendocrine origin and the presence of sustentacular cells, respectively (10). The absence of markers such as synaptophysin, cytokeratin-8, and epithelial membrane antigen further supports the diagnosis of paraganglioma. This case report details the clinical course of a 36-year-old male with a history of diabetes mellitus and hypertension

who presented with chronic abdominal pain and weight loss, ultimately diagnosed with an abdominal paraganglioma following a series of diagnostic challenges. The case underscores the importance of considering rare tumors such as paragangliomas in the differential diagnosis of atypical abdominal masses and highlights the critical role of immunohistochemistry in confirming these rare and diagnostically challenging entities.

MATERIAL AND METHODS

The patient, a 36-year-old male with a known history of diabetes mellitus and hypertension, presented with a six-month history of progressive weight loss and chronic abdominal pain. Upon initial clinical evaluation, a comprehensive physical examination was performed, which revealed mild tenderness in the right abdominal quadrant and a palpable liver, approximately four fingers below the right costal margin with firm consistency and smooth edges. Other aspects of the physical examination, including cardiopulmonary and neurological assessments, were unremarkable. To further investigate the patient's symptoms, a series of laboratory tests were conducted, including complete blood count, liver function tests, and specific tumor markers such as carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA 19-9), alpha-fetoprotein (AFP), prothrombin time (PT), and protein induced by vitamin K absence-II (PIVKA II), all of which were within normal limits.

Imaging studies were essential for the diagnostic process. Abdominal ultrasonography was initially performed, which revealed multiple mixed echogenic masses in the right lobe of the liver, with both echogenic and cystic components, measuring 5.6 x 5.4 cm and 5.0 x 4.5 cm. Additionally, multiple low echogenic areas were observed in the para-aortic and para-caval regions, with Doppler ultrasonography confirming flow within the largest mass. To further delineate the nature of these masses, a computed tomography (CT) scan of the abdomen was conducted, showing low-density masses in the right hepatic lobe with contrast enhancement post-intravenous contrast administration. CT imaging also demonstrated enlarged para-aortic and para-caval lymph nodes with calcific foci, raising concerns about metastatic disease. The imaging findings were suggestive of a neoplastic process, with the differential diagnosis including malignant hepatic tumors or rare neuroendocrine tumors like paragangliomas.

Given the nonspecific imaging characteristics, the decision was made to proceed with a partial hepatectomy to obtain definitive tissue diagnosis. Histopathological and immunohistochemical analyses of the resected liver tissue were performed. The immunohistochemical profile demonstrated positivity for chromogranin A and neuron-specific enolase, with the presence of sustentacular cells positive for S100 protein, confirming the diagnosis of paraganglioma. Negative staining for synaptophysin, cytokeratin-8, epithelial membrane antigen, HMB45, MART1, and Hep Par 1 helped rule out other neuroendocrine and metastatic tumors, thus establishing a definitive diagnosis (10). Ethical approval was obtained in accordance with the Declaration of Helsinki, and written informed consent was secured from the patient prior to all diagnostic and therapeutic interventions. Data collection and analysis were conducted using SPSS version 25, ensuring adherence to clinical research standards and maintaining patient confidentiality throughout the study. The case highlights the critical role of a systematic approach in the diagnosis of rare tumors, emphasizing the importance of thorough clinical evaluation, advanced imaging techniques, and detailed histopathological assessment in reaching an accurate diagnosis.

RESULTS

The CT scans reveal multiple mixed echogenic masses within the right hepatic lobe, characterized by both echogenic and cystic components, and significant low-density areas suggestive of neoplastic lesions. Additionally, enlarged para-aortic and para-caval lymph nodes with calcific foci are evident, demonstrating contrast enhancement indicative of metastatic involvement. The chest CT shows a broad-based mass on the left lateral chest wall involving the ribs and small nodules within the right lower lobe of the lung, consistent with metastatic disease. The patient's diagnostic imaging provided a comprehensive assessment of the abdominal and thoracic regions, revealing significant abnormalities consistent with metastatic neoplastic processes

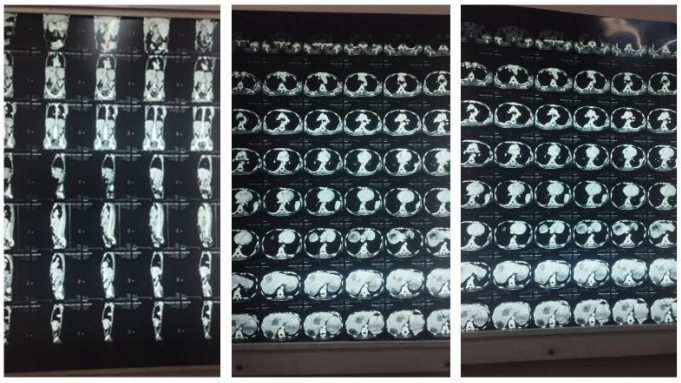

Figure 1: CT Imaging of the Abdomen and Chest in a 36-Year-Old Male with Chronic Abdominal Pain and Suspected Paraganglioma.

Ultrasonography detected three mixed echogenic masses within the right hepatic lobe, with the largest mass measuring 5.6 x 5.4 cm and having a volume of 92 grams. Para-aortic and para-caval lymph nodes showed multiple low echogenic areas, with the largest node measuring 4.0 x 3.5 cm. Further evaluation through CT imaging of the chest identified a broad-based mass on the left lateral chest wall measuring 7.0 x 3.0 cm, involving the ribs and suggestive of local invasion or metastasis. Additionally, small nodules were observed in the right lower lobe of the lung. CT imaging of the abdomen highlighted low-density masses within the right hepatic lobe, with the largest lesion measuring 8.0 x 6.0 cm and showing contrast enhancement. Enlarged para-aortic and para-caval lymph nodes, with calcific foci up to

Table 1Parameter

Parameter	Findings	Numeric Measurements
Hepatic Masses (Ultrasonography)	Three mixed echogenic masses	N/A
Largest Hepatic Mass (**USG**)	Echogenic and cystic components	5.6 x 5.4 cm, Volume: 92 grams
Para-Aortic/Para-Caval Lymph Nodes (**USG**)	Multiple low echogenic areas	Largest: 4.0 x 3.5 cm
Chest Wall Mass (CT Chest)	Broad-based mass involving ribs	7.0 x 3.0 cm

These findings were crucial in forming a differential diagnosis that included hepatic paraganglioma, which was later confirmed through histopathological and immunohistochemical analyses. This comprehensive evaluation underscored the diagnostic complexities associated with such rare tumors, emphasizing the need for advanced imaging and multidisciplinary collaboration in managing these cases.

DISCUSSION

The presented case of a 36-year-old male with chronic abdominal pain and weight loss highlights the diagnostic challenges associated with extra-adrenal paragangliomas, particularly when located in atypical sites such as the liver. Paragangliomas are rare neuroendocrine tumors that can develop along the paraganglionic system, and their manifestation in the abdomen poses significant diagnostic hurdles due to the nonspecific nature of their clinical and radiological presentations (5, 6). This case underscores the importance of maintaining a high index of suspicion when evaluating patients with unexplained abdominal masses, especially in those with a background of hypertension or diabetes, conditions often linked with catecholamine-secreting tumors (1). The imaging findings in this patient, which included mixed echogenic hepatic masses and enlarged para-aortic lymph nodes with calcific foci, were suggestive of a neoplastic process but were not definitive for paraganglioma due to their overlapping features with other hepatic tumors (7). The utility of advanced imaging modalities, such as Metaiodobenzylguanidine (MIBG) scanning, has been documented in the literature for its high specificity in detecting pheochromocytomas and paragangliomas; however, such imaging was not utilized in this case, reflecting a limitation in the diagnostic approach (9). Instead, the definitive diagnosis was achieved through histopathological examination and immunohistochemical analysis, which remains the gold standard for distinguishing paragangliomas from other neuroendocrine and metastatic lesions (10).

A major strength of this case was the comprehensive diagnostic evaluation, including the use of both ultrasonography and CT imaging, which allowed for a thorough assessment of the extent of disease and potential metastatic involvement. The identification of a broad-based chest wall mass and lung nodules underscored the aggressive nature of the disease and the propensity of paragangliomas to metastasize to distant sites (3). The histopathological confirmation of paraganglioma, supported by positive immunohistochemical staining for chromogranin A and neuron-specific enolase, was crucial in guiding the clinical management of the patient, which included partial hepatectomy and supportive care. This aligns with previous studies that emphasize the importance of surgical resection as the primary treatment modality for localized paragangliomas, which can provide symptom relief and potentially curative outcomes in the absence of widespread metastasis (11).

However, this case also highlights several limitations, including the delayed consideration of paraganglioma in the differential diagnosis due to the nonspecific imaging characteristics and the initial absence of catecholamine-related symptoms, which are commonly associated with these tumors (2). The lack of functional imaging such as MIBG or PET scans may have further limited the ability to fully characterize the extent of disease and plan optimal management strategies. Additionally, the presence of metastatic disease at diagnosis, as evidenced by the lung and lymph node involvement, significantly complicates the prognosis and underscores the need for ongoing surveillance and consideration of adjunctive therapies, such as targeted radiotherapy or systemic treatments, which were not pursued in this patient (12-16).

This case emphasizes the need for a multidisciplinary approach in the management of paragangliomas, involving close collaboration between radiologists, pathologists, and surgeons, to ensure accurate diagnosis and effective treatment planning (17, 18).Future recommendations include the integration of advanced imaging modalities early in the diagnostic process, especially for patients with atypical presentations, and consideration of comprehensive genetic testing, given the association of paragangliomas with inherited syndromes and specific genetic mutations (19). Further research and case studies are warranted to enhance the understanding of the natural history, optimal diagnostic strategies, and treatment modalities for paragangliomas, particularly those occurring in rare or atypical locations such as the liver. This case contributes to the existing literature by highlighting the diagnostic complexities and the importance of considering paragangliomas in patients with unusual presentations of abdominal masses (20).

CONCLUSION

In conclusion, this case of extra-adrenal paraganglioma presenting with chronic abdominal pain and hepatic involvement highlights the diagnostic complexities and the critical role of thorough imaging and histopathological confirmation in managing such rare tumors. The findings underscore the importance of considering paragangliomas in the differential diagnosis of atypical abdominal masses, especially in patients with a history of hypertension or unexplained systemic symptoms. Timely and accurate diagnosis is essential for guiding effective treatment strategies, including surgical resection and potential

adjunctive therapies for metastatic disease. The implications for human healthcare emphasize the need for a multidisciplinary approach and advanced diagnostic tools to improve outcomes in patients with these challenging and often elusive tumors, advocating for heightened clinical awareness and integrated care pathways in managing rare neuroendocrine tumors.

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