12-15-2021

Abdominal paraganglioma in a patient with fever of unknown origin

Samantha Sokoloff
Thomas Jefferson University

Barbara Simon
Thomas Jefferson University

Journal of Clinical and Translational Endocrinology: Case Reports 23 (2022) 100105

Contents lists available at ScienceDirect

Journal of Clinical and Translational Endocrinology: Case Reports

journal homepage: www.elsevier.com/locate/jctecasereports.com

Abdominal paraganglioma in a patient with fever of unknown origin

Samantha R. Sokoloff [a,*], Barbara Simon [b]

[a] Thomas Jefferson University Hospital, 833 Chestnut Street, Suite 220, Philadelphia, PA, 19107, USA
[b] Thomas Jefferson University Hospital, Philadelphia, PA, USA

ARTICLE INFO

Keywords:
Paraganglioma
Abdominal mass
Endocrinology

ABSTRACT

Introduction: Paragangliomas have a wide range of clinical presentations. A significant portion of these tumors are discovered as abdominal masses on imaging or palpation in patients without typical symptoms of catecholamine excess [1]. This case reports a 28-year-old female who presented with fever of unknown origin and was found to have an abdominal mass on CT imaging. This mass was biopsied prior to a complete evaluation and confirmed to be a paraganglioma.

Case report: We discuss the case of a 28 year-old-female who presented to the Endocrinology office after she was diagnosed with a paraganglioma on retroperitoneal biopsy. The patient had initially presented to her primary care provider with fever of unknown origin. She was found to have a large retroperitoneal mass on a non-contrast CT scan done for infectious work-up, which prompted referrals to Medical Oncology and Surgery. A contrast-enhanced CT scan was ordered to assess for metastatic disease and re-demonstrated the retroperitoneal mass. It also provided further information, specifying that the mass was most suspicious for a paraganglioma. Despite this, the patient underwent a biopsy that confirmed this diagnosis without further evaluation prior. She was then referred to Endocrinology and biochemical testing showed mildly elevated normetanephrine on urine and blood analyses. Successful surgical excision of the mass was completed with preceding alpha-blockade. Genetic testing was negative.

Discussion: Paragangliomas have diverse clinical presentations, which can make diagnosis challenging. Fever of unknown origin, as seen in this case, represents a rare manifestation [2,3]. The accuracy of CT scans for identifying paragangliomas has increased significantly over the last decade [4]. Biopsy of these massesis associated with significant morbidity. It is important that clinicians are aware that paragangliomas may be present in the absence of hypertension or classic symptoms associated with pheochromocytomas.

Conclusion: Paragangliomas can be discovered as abdominal masses on imaging in patients without typical symptoms of catecholamine hyper-secretion. If a radiology report suggests a high likelihood of a paraganglioma it is critical to delay a potentially high-risk biopsy until further evaluation can be completed.

1. Introduction

Paragangliomas are rare neuroendocrine tumors that form from extra-adrenal autonomic chromaffin cells. The majority of sympathetic paragangliomas are located along the sympathetic chain in the abdomen. Some are functional and present with typical symptoms of catecholamine hyper-secretion. However, with rising use and advances in imaging modalities a significant percentage of these tumors are diagnosed incidentally [5]. Fever of unknown origin, as seen in this case, represents a rare presentation [2,3]. Biopsy of these tumors has a high complication rate [6]. Complications include hypertensive crisis, life threatening hemorrhage, and capsular disruption with tumor implantation [6]. This case reports a 28-year-old female found to have an abdominal mass on work-up for fever of unknown origin, which was ultimately confirmed to be a paraganglioma on ultrasound-guided biopsy.

2. Case

A 28-year-old female with no past medical history presented to the Endocrinology office after a retroperitoneal mass was confirmed to be a paraganglioma on biopsy. She had presented to her family physician two months prior. At that time, she reported two weeks of fevers, with temperatures reaching 103–104 degrees Fahrenheit on a daily basis.

* Corresponding author.
E-mail addresses: Samantha.Sokoloff@jefferson.edu (S.R. Sokoloff), Barbara.Simon@jefferson.edu (B. Simon).

https://doi.org/10.1016/j.jecr.2021.100105
Received 16 June 2021; Received in revised form 17 November 2021; Accepted 13 December 2021
Available online 15 December 2021

During that time, she had presented to two separate emergency departments. Similar infectious workups were completed during both encounters. Laboratory workup included negative testing for COVID-19, negative blood cultures, and negative urinalyses. Imaging included chest x-rays at both ER visits, which were within normal limits. She was suspected to have a viral syndrome during both encounters and discharged home. She continued to experience daily fevers, prompting her to present to her primary care physician. Laboratory evaluation included a BMP which was unremarkable; CBC with differential, which showed a white blood cell count of 6.9, platelet count of 731, and hemoglobin of 8.6 with MCV 68; urinalysis, which was negative for white blood cells and had trace leukocyte esterase; and urine culture, which was negative for bacterial growth. A non-contrast CT abdomen and pelvis was then completed. This showed a large mildly heterogeneous intermediate density lesion in the left retroperitoneum measuring 9.0 cm × 9.1 cm x 9.4 cm, read as sarcoma vs. duodenal tumor such as gastrointestinal stromal tumor vs. non-neoplastic lesion and further workup was recommended with MRI of the abdomen. The patient had spontaneous resolution of her fevers about one week later with a total duration of daily fevers of approximately three weeks. MRI with and without contrast re-demonstrated the mass and was read as nonspecific, but most suspicious for a neoplasm such as sarcoma. The patient was referred to Medical Oncology for further evaluation. Medical Oncology referred the patient to a surgeon specializing in soft tissue sarcoma for biopsy. During the initial surgery appointment, a CT chest/abdomen/pelvis with contrast (Fig. 1) was ordered for further evaluation of the mass. The radiology report described an enhancing left retroperitoneal mass with cystic components, concerning for an extra-adrenal paraganglioma/pheochromocytoma with differential diagnosis also including sarcoma. Despite this, the patient underwent an ultrasound-guided biopsy without further evaluation or testing for pheochromocytoma or paraganglioma prior. The biopsy was uncomplicated and pathology was interpreted as a neuroendocrine neoplasm, most consistent with paraganglioma, with diffuse and strong positivity for synaptophysin and chromogranin, foci of necrosis, and negative for AE1/AE3, ASMA, desmin, and PAX8. At this point, the patient's primary care physician referred her to Endocrinology. Review of systems was confirmed negative for sweats, palpitations, headaches, or syncope and she had no prior history of hypertension. Family history was negative for abdominal tumors or genetic syndromes. She was afebrile with a blood pressure of 99/70 and a heart rate of 88. Physical exam was unremarkable. Biochemical testing completed included plasma normetanephrine 140 [0.0–107.7 pg/mL], metanephrine 15.4 [0.0–88.0 pg/mL]; 24-h urine catecholamines and fractionated metanephrines: epinephrine 4 [0–20 μg/24 hr], norepinephrine 29 [0–135 μg/24 hr], dopamine 270 [0–510 μg/24 hr], normetanephrine 487 [95–449 μg/24 hr], and metanephrine 62 [36–209 μg/L]. Chromogranin A testing was not performed. MIBG (Fig. 2) showed a large left abdominal mass, compatible with a catecholamine producing tumor without other areas of abnormal uptake.

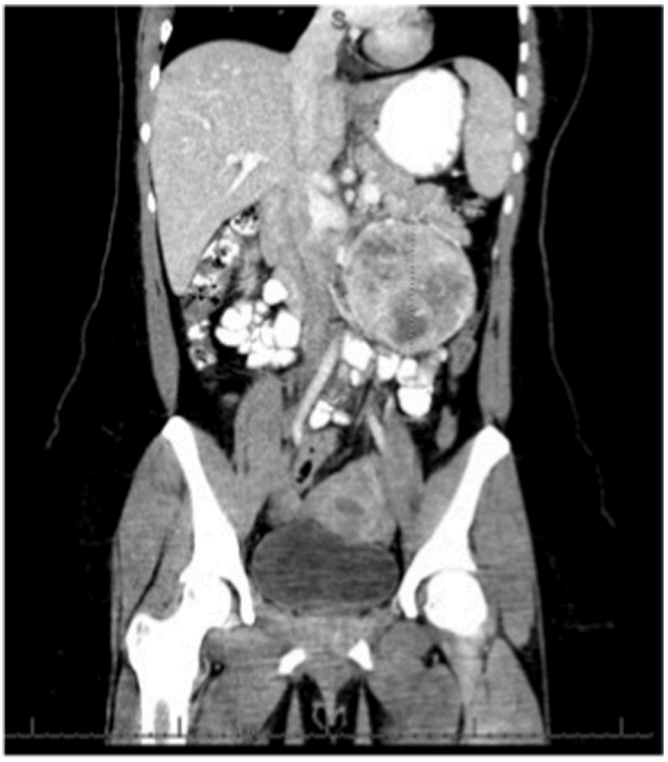

Fig. 1. Coronal image from contrast CT chest abdomen and pelvis showing large, enhancing retroperitoneal mass with cystic components.

The patient underwent uncomplicated surgical excision of the tumor after 2 weeks of preparation with alpha blockade. Pathology confirmed the diagnosis and showed tumor cells positive for synaptophysin and chromogranin with patchy positivity for S-100 in sustentacular cells. The tumor was grossly encapsulated without evidence of invasion into surrounding structures and was negative for Sox-10, Cam5.2, and AE1/AE3. Genetic testing was also performed. MEN2 RET Sequencing and Deletion/Duplication panel (Labcorp, RTP NC) showed no mutation and no clinically significant sequence changes. A VistaSeq Endocrine Panel (Integrated Genetics, LabCorp Specialty Testing, RTP NC) which included gene testing for MAX, NF1, RET, VHL, MEN1, PTEN, SDHB, SDHC, SDHD, TP53, CDC73, PRKAR1A, and TMEM127 was also negative, with no clinically significant sequence or copy number variance detected and no pathogenic or variance of uncertain clinical significance detected.

3. Discussion

Paragangliomas have a wide range of clinical presentations. A recent retrospective study of clinical characteristics of retroperitoneal paragangliomas showed that the most common presenting symptom (50%) was that of an unexplained abdominal mass identified either incidentally on imaging or on palpation, followed by hypertension (32%) and abdominal pain (24%) [1]. Fever of unknown origin, as seen in this case, is a rare initial presentation [2,3].

Previous case reports have described other rare initial presentations of retroperitoneal paragangliomas. However, often in these reports the patient also demonstrates symptoms more commonly associated with this tumor type. One case reported a 16-year-old male who presented with seizures, but who had also been noted to have a history of hypertension along with paroxysmal headaches, palpitations, and diaphoresis [7]. In another case, a 69-year-old female presented with pre-syncope, but also had a history of uncontrolled hypertension [8]. A third case reported a 19-year-old female with a primary symptom of severe headaches for six months, but who also had severe hypertension over the same time frame [9]. Additionally, in other cases of paragangliomas in which patients presented with fever of unknown origin, they often had at least one symptom more commonly associated with this tumor type. For example, one case reported a 38-year-old female who had presented with fevers and abdominal pain [2]. In our case, the patient was normotensive. The daily fevers were her chief complaint during her two presentations to the emergency department and she did not present with any additional symptoms more typically associated with this tumor type.

The diversity of symptoms at presentation often makes the diagnosis of paragangliomas challenging. Thus, it is crucial that practitioners be aware of all potential diagnostic clues. In this case, the radiology read on the contrast enhanced CT chest, abdomen and pelvis reported paraganglioma as the most likely diagnosis. The diagnostic accuracy for identification of paragangliomas on abdominal CT scan with contrast has increased significantly in the last decade, with common radiologic

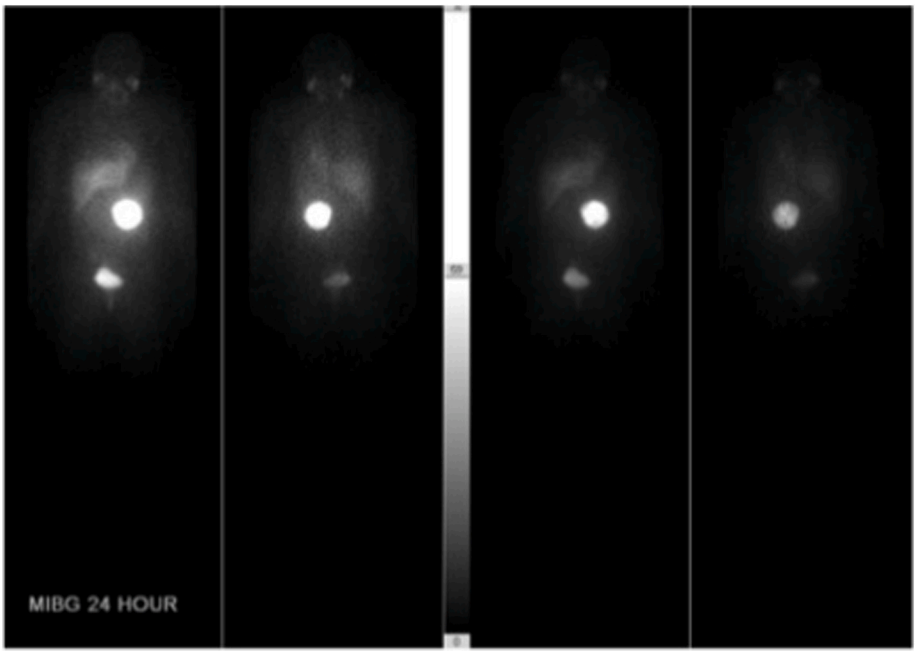

Fig. 2. Images from MIBG showing avid MIBG uptake in left abdominal mass.

findings including increased contrast enhancement, delayed washout, cystic changes, necrosis and internal calcification [4]. Whether this tumor type is discovered initially as an incidental abdominal mass, or later on a CT scan done for further workup of symptoms, it is important that providers avoid biopsy and pursue further evaluation if imaging findings are suggestive of a paraganglioma.

This case highlights the importance of awareness that paragangliomas often do not present with symptoms typically associated with pheochromocytomas. In contrast, many of the tumors are diagnosed when found as incidental abdominal masses, and some patients, such as in our case may present with atypical symptoms [1]. Thus, a high index of suspicion can be critical in avoiding high risk biopsies.

4. Conclusion

Paragangliomas may be discovered in various clinical scenarios. The most common presentation is an abdominal mass discovered incidentally on imaging or on palpation. Many patients do not present with hypertension or classic catecholamine excess symptoms. Isolated fever of unknown origin, as seen in this case, is a rare initial manifestation. The characteristic imaging findings on contrast enhanced CT scan in our case were the biggest clue to the diagnosis; therefore, it is important for clinicians and radiologists to have an increased awareness of paragangliomas and their varied presentations in order to avoid potentially harmful biopsy without further evaluation prior.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Informed consent

Verbal consent was obtained from the patient for the publication of this case report.

Patient consent

The patient provided verbal consent for the production and publication of this manuscript.

Declaration of competing interest

No conflicts of interest.

Acknowledgements

We thank Thomas Jefferson University Hospital's Division of Endocrinology and Department of Internal Medicine for their support on this project.

References

[1] Ji XK, Zheng XW, Wu XL, Yu ZP, Shan YF, Zhang QY, Zeng QQ. Diagnosis and surgical treatment of retroperitoneal paraganglioma: a single-institution experience of 34 cases. Oncol Lett 2017;14(2):2268–80. https://doi.org/10.3892/ol.2017.6468.

[2] Davies LL, Fitchett JM, Jones D. Fever of unknown origin: a rare retroperitoneal cause. BMJ Case Rep 2012:bcr0320126122. https://doi.org/10.1136/bcr.03.2012.6122. 2012.

[3] Narechania Shraddha, Bath Amrita, Ghassemi Laleh, Lokhande Chetan, Haddad Abdo, Yousuf Ali Mir, Marquard Jessica, Gopalakrishna KV. Paraganglioma presenting as postpartum fever of unknown origin. Case Rep Endocrinol 2015;2015. https://doi.org/10.1155/2015/864719. Article ID 864719, 4 pages.

[4] Baez Juan C, et al. Pheochromocytoma and paraganglioma: nimaging characteristics. Cancer Imag 2012;12(1):153–62. https://doi.org/10.1102/1470-7330.2012.0016.

[5] Lee JA, Duh QY. Sporadic paraganglioma. World J Surg 2008;32(5):683–7. https://doi.org/10.1007/s00268-007-9360-4.

[6] Vanderveen KA, Thompson SM, Callstrom MR, Young Jr WF, Grant CS, Farley DR, Richards ML, Thompson GB. Biopsy of pheochromocytomas and paragangliomas: potential for disaster. Surgery 2009;146(6):1158–66. https://doi.org/10.1016/j.surg.2009.09.013.

[7] Nguyen Khoa, Dieu Van, et al. Laparoscopic excision of retroperitoneal paraganglioma presenting with seizures. J Pediatr Surg Case Rep 2021;72:101953. https://doi.org/10.1016/j.epsc.2021.101953.

[8] Abraham Bishoy, et al. PRE-SYNCOPE and orthostatic hypotension as a presentation of juxtarenal retroperitoneal paraganglioma. J Am Coll Cardiol 2020;75(11):2673. https://doi.org/10.1016/s0735-1097(20)33300-3.

[9] Guruchannabasavaiah B, Madabhavi IV, Avinash DB, Aravindan R, Devarabhavi P, Dakappa PH. Severe headache presenting as an early sign of retroperitoneal para aortic paraganglioma. Oral Oncol 2021;117:105199. https://doi.org/10.1016/j.oraloncology.2021.105199.