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CASE REPORT

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Paraganglioma of the spermatic cord: A rare tumor with unique imaging findings and diagnostic challenges

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Abstract: Pheochromocytomas and paragangliomas are rare endocrine neoplasms derived from neural crest cells, with spermatic cord paragangliomas being exceptionally uncommon. A 42-year-old man presented with a longstanding complaint of left scrotal enlargement. Initial imaging raised suspicion of testicular carcinoma, but contrast-enhanced computed tomography and magnetic resonance imaging revealed a well-circumscribed, hypervascular mass distinct from the testis. The tumor exhibited heterogeneous T2 signal intensity, characteristic of vascular lesions, a thick capsule, and early-phase peripheral contrast enhancement with delayed homogeneous filling. A solitary fibrous tumor was initially considered as a differential diagnosis. Surgical resection confirmed the tumor's origin in the spermatic cord. Histopathology revealed small, round neoplastic cells with a delicate sinusoidal vascular network, and immunohistochemical analysis was positive for chromogranin A and synaptophysin, confirming the diagnosis of paraganglioma, with its origin traced to the spermatic cord. The surgical margins were clear, and postoperative imaging showed no metastases. At 18 months follow-up, no recurrence was detected, and biochemical markers remained normal. This case highlights the diagnostic challenges of spermatic cord paragangliomas due to their rarity and imaging resemblance to other intra-scrotal neoplasms. Although preoperative diagnosis is crucial for appropriate management, almost all of the reported cases of spermatic cord paragangliomas have been diagnosed postoperatively. New imaging techniques, including ^{68}Ga-DOTATATE PET/CT, may change this situation. This report expands the limited literature on spermatic cord paragangliomas and underscores the importance of considering paraganglioma in the differential diagnosis of intra-scrotal masses.

***Keywords*:** pheochromocytoma, scrotum, urogenital system

Introduction

Pheochromocytomas and paragangliomas (PPGLs) are endocrine neoplasms that originate from the chromaffin cells of the adrenal medulla or from the chromaffin-like cells located within the sympathetic or parasympathetic paraganglia, all of which derive from the neural crest. PPGLs are among the most genetically predisposed tumors, with more than twenty susceptibility genes identified to date, contributing to germline mutations in about 40% of cases (*1,2*). Prominent among the syndromes associated with PPGLs are Von Hippel-Lindau disease, multiple endocrine neoplasia type 2, and neurofibromatosis type 1. The emergence of paragangliomas within the genitourinary tract, particularly those originating in the spermatic cord, is exceedingly rare.

Herein, we present a case of a paraganglioma arising in the spermatic cord and contribute to the knowledge regarding these uncommon neoplasms. This study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from the patient.

Case Report

A 42-year-old man was referred to our institution in May 2023 for evaluation of a progressive enlargement of the left scrotum which he had observed for several years but had hitherto neglected. At another facility, a presumptive diagnosis of left testicular carcinoma was considered. The patient's medical history was otherwise unremarkable, with no evidence of hypertension or tachycardia.

Physical examination revealed a palpable, elastic, hard mass approximately 5 cm in diameter within the left scrotum. Serum levels of alpha-fetoprotein and human chorionic gonadotropin were within normal parameters. Radiological assessment *via* abdominal contrast-enhanced computed tomography revealed a neoplasm measuring 6 cm in diameter, characterized by heterogeneous hypoattenuation and the presence of multiple venous proliferations surrounding the lesion (Figure 1A).

Contrast-enhanced magnetic resonance imaging demonstrated a scrotal mass with a diameter of 6 cm, featuring a relatively thick capsule exhibiting low signal intensity and a heterogeneous high signal intensity interior on T2-weighted sequences (Figure 1B) and dispersed high-signal foci within the mass on T1-weighted sequences. Serpentine dilated arterioles were observed proximal to the neoplasm, exhibiting rapid contrast enhancement from the periphery during the early phase. In the delayed phase, the enhancement appeared relatively homogeneous extending to the interior of the mass (Figures 1C and D). A solitary fibrous tumor, likely originating from the peritoneal sheath, was considered as a differential diagnosis. The mass was discerned to be anatomically distinct from the testis.

The intra-scrotal mass was surgically resected. Intraoperative observations confirmed the tumor's origin from the spermatic cord, necessitating the ligation and transection of the cord more than 2 cm proximal to the lesion due to the impracticality of testicular preservation. No perioperative complications, such as blood pressure fluctuations or tachycardia, were encountered, and the patient recovered uneventfully.

Macroscopically, the specimen revealed a substantial neoplasm measuring 50 x 45 x 35 mm on the cut surface. The lesion exhibited a yellowish-white color, interspersed with internal hemorrhage (Figure 2A). Microscopic examination identified relatively small neoplastic cells proliferating in a focal arrangement, set against a backdrop of a delicate sinusoidal vascular network. These tumor cells exhibited small, round nuclei and relatively abundant pale cytoplasm (Figure 2B).

Immunohistochemical staining demonstrated positivity for chromogranin A and synaptophysin and negativity for anti-epithelial antigen 1/anti-epithelial antigen 3 (Figure 2C and D). These findings led to the diagnosis of a paraganglioma of the spermatic cord. The surgical margins were free of tumor involvement.

Postoperative evaluation *via* 18F-fluorodeoxyglucose positron emission tomography revealed no evidence of distant metastases, confirming the localized nature of the neoplasm. At 18 months postoperatively, computed tomography revealed no evident metastatic recurrence, and plasma-free metanephrines and normetanephrines remained within normal limits.

Discussion

PPGLs are rare endocrine tumors arising from adrenal medulla or paraganglia cells, associated with a risk of metastasis. The latest guidelines and World Health Organization classification emphasize that all PPGLs have metastatic potential and define malignancy as the presence of metastases in non-chromaffin cell locations (*3*). Risk assessment for metastasis involves considering tumor size, location, the presence of a

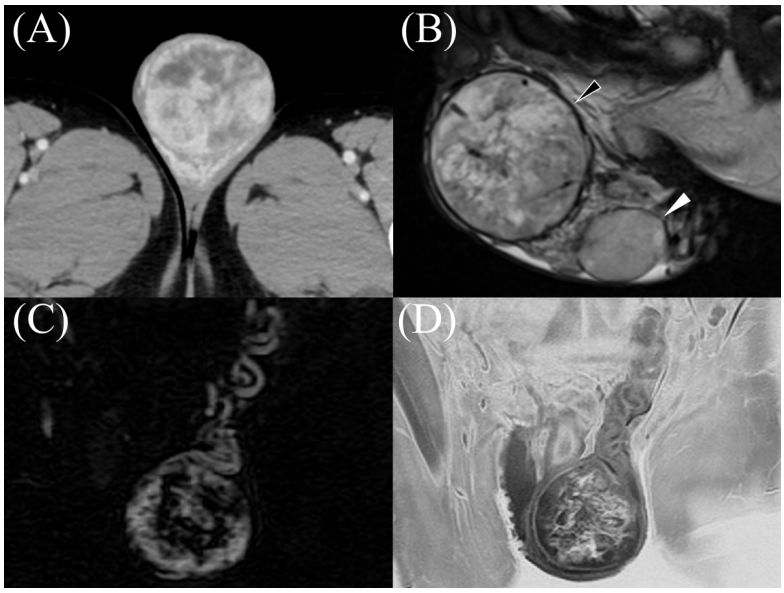

Figure 1. (A) Contrast-enhanced CT shows a 6 cm neoplasm with heterogeneous hypoattenuation and surrounding venous proliferations; **(B)** T2-weighed magnetic resonance image shows a scrotal mass with a thick capsule of low signal and a heterogeneous, high-signal interior (black arrowhead). The left testis is denoted by a white arrowhead; **(C)** The post-contrast dynamic study revealed a prominently dilated feeding artery and drainage veins, accompanied by rapid intratumoral enhancement starting from the periphery; **(D)** Fast field echo resembling a computed tomography scan using restricted echo-spacing.

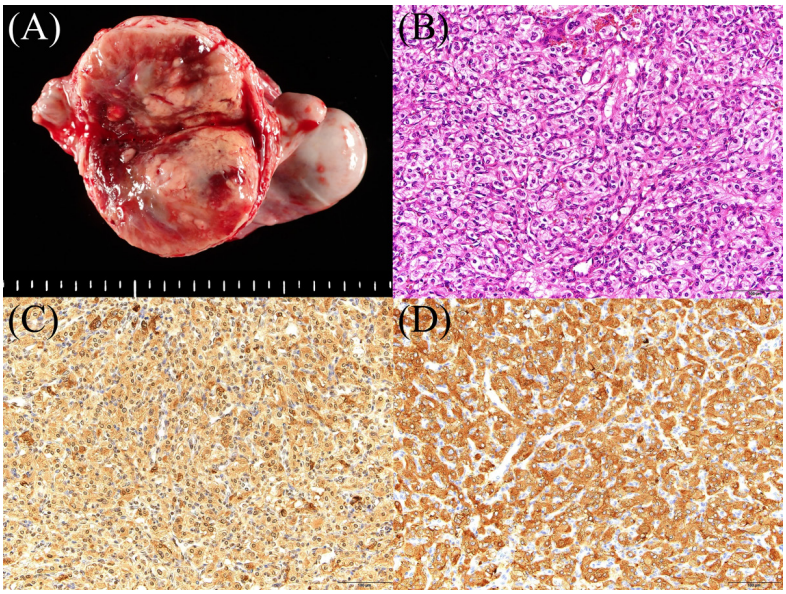

Figure 2. Pathological findings. (A) The tumor exhibits with a yellowish-white color, accompanied by mixed patterns of internal hemorrhage; **(B)** Microscopic image reveals small neoplastic cells in focal arrangements, amid a fine sinusoidal vascular network, with these cells displaying small, round nuclei and abundant pale cytoplasm; **(C)** Immunohistochemical examination reveals positive staining for chromogranin A; **(D)** Immunohistochemical examination reveals positive staining for synaptophysin.

succinate dehydrogenase subunit B (SDHB) mutation, dopaminergic phenotype, and the Ki-67 index (*1,2,4*). Immunohistochemistry for SDHB and metabolite profiling are crucial for identifying SDHB mutations and assessing metastatic risk, although genetic testing remains essential for accurate diagnosis (*5*).

The Pheochromocytoma of the Adrenal Gland Score and the Grading of Adrenal Pheochromocytoma and Paraganglioma score are the primary histological tools for risk stratification, indicating potential malignant behavior with varying sensitivity and specificity (*6,7*). Studies suggest that 10% to 15% of pheochromocytomas and 35% to 40% of paragangliomas develop metastases, with a reported median overall survival of 7 years for metastatic cases (*2,8,9*).

PPGLs are the most heritable tumor types. Considering the spectrum of known germline mutations, approximately 30% to 35% of patients with PPGL harbor germline mutations in various susceptibility genes, while an additional 35% to 40% possess somatic driver mutations (*10*). Collectively, approximately 70% of PPGL cases exhibit mutations in more than 20 identified PPGL driver genes, categorized into three principal molecular clusters: pseudohypoxia cluster 1, kinase-signaling cluster 2, and Wnt signaling cluster 3. This categorization correlates with distinct biochemical phenotypes, clinical courses, and prognostic outlooks. Moreover, genetic abnormalities affecting telomere and chromatin maintenance are implicated in further influencing the disease trajectory (*10-12*).

All patients with a history of PPGL and asymptomatic mutation carriers require lifelong follow-up tailored to their mutation status and disease characteristics. Surgical removal is the primary treatment, with chemotherapy, radionuclide therapy, and tyrosine kinase inhibitors as options for inoperable or metastatic disease (*1,2*). Future treatment strategies may include genetically driven, cluster-specific therapies, though these are not yet standard practice.

Given the rarity of paragangliomas, estimating their prevalence, particularly in the genitourinary tract, presents significant challenges. These neoplasms have been identified in various genitourinary locations, including the kidney and renal pelvis, ureters, urethra, prostate gland, and notably, the bladder, which is the most common site of occurrence (*13*). A retrospective observational analysis of the Surveillance, Epidemiology, and End Results database identified 299 instances of paragangliomas, of which 20 (6.7%) originated from the genitourinary tract. Among these, the majority occurred in the bladder (83%), followed by the kidney and renal pelvis (17%), with a minor proportion arising from the spermatic cord (2%) (*13*). A literature search was conducted using PubMed, Embase, and Google Scholar to identify previously reported cases of spermatic cord paraganglioma. This case represents the eighteenth reported instance of a paraganglioma in the spermatic cord in medical literature, thereby expanding our understanding of such rare occurrences. Due to the lack of distinct imaging characteristics, almost all cases of spermatic cord paraganglioma are diagnosed intraoperatively through frozen section analysis or postoperatively. However, a recent report described a case of spermatic cord paraganglioma in which a preoperative diagnosis was successfully made using ^{68}Ga-DOTATATE PET/CT (*14*). This was possible because PPGLs overexpress somatostatin receptors, and recent studies have demonstrated the excellent utility of

^{68}Ga-DOTATATE PET/CT in localizing both primary and metastatic PPGLs (*15*).

In conclusion, this report details a case of an uncommon paraganglioma associated with spermatogenic tissue. It underscores the necessity of considering paraganglioma in the differential diagnosis of challenging intra-scrotal neoplasms.

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Conflict of Interest: The authors have no conflicts of interest to disclose.

References

1. Lenders JWM, Kerstens MN, Amar L, *et al.* Genetics, diagnosis, management and future directions of research of phaeochromocytoma and paraganglioma: A position statement and consensus of the Working Group on Endocrine Hypertension of the European Society of Hypertension. J Hypertens. 2020; 38:1443-1456.
2. Nölting S, Bechmann N, Taieb D, Beuschlein F, Fassnacht M, Kroiss M, Eisenhofer G, Grossman A, Pacak K. Personalized management of pheochromocytoma and paraganglioma. Endocr Rev. 2022; 43:199-239.
3. Lam AK. Update on adrenal tumours in 2017 World Health Organization (WHO) of endocrine tumours. Endocr Pathol. 2017; 28:213-227.
4. Fassnacht M, Assie G, Baudin E, Eisenhofer G, de la Fouchardiere C, Haak HR, de Krijger R, Porpiglia F, Terzolo M, Berruti A; ESMO Guidelines Committee. Adrenocortical carcinomas and malignant phaeochromocytomas: ESMO-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2020; 31:1476-1490.
5. Van Nederveen FH, Gaal J, Favier J, *et al.* An immunohistochemical procedure to detect patients with paraganglioma and phaeochromocytoma with germline SDHB, SDHC, or SDHD gene mutations: A retrospective and prospective analysis. Lancet Oncol. 2009; 10:764-771.
6. Thompson LD. Pheochromocytoma of the Adrenal gland Scaled Score (PASS) to separate benign from malignant neoplasms: A clinicopathologic and immunophenotypic study of 100 cases. Am J Surg Pathol. 2002; 26:551-566.
7. Kimura N, Takayanagi R, Takizawa N, Itagaki E, Katabami T, Kakoi N, Rakugi H, Ikeda Y, Tanabe A, Nigawara T, Ito S, Kimura I, Naruse M; Phaeochromocytoma Study Group in Japan. Pathological grading for predicting metastasis in phaeochromocytoma and paraganglioma. Endocr Relat Cancer. 2014; 21:405-414.
8. Eisenhofer G, Lenders JW, Siegert G, Bornstein SR, Friberg P, Milosevic D, Mannelli M, Linehan WM, Adams K, Timmers HJ, Pacak K. Plasma methoxytyramine: A novel biomarker of metastatic pheochromocytoma and paraganglioma in relation to established risk factors of tumour size, location and SDHB mutation status. Eur J Cancer. 2012; 48:1739-1749.
9. Hescot S, Curras-Freixes M, Deutschbein T, *et al.* Prognosis of malignant pheochromocytoma and paraganglioma (MAPP-Prono Study): A European network for the study of adrenal tumors retrospective study. J Clin Endocrinol Metab. 2019; 104:2367-2374.
10. Fishbein L, Leshchiner I, Walter V, *et al.* Comprehensive molecular characterization of pheochromocytoma and paraganglioma. Cancer Cell. 2017; 31:181-193.
11. Fishbein L, Khare S, Wubbenhorst B, DeSloover D, D'Andrea K, Merrill S, Cho NW, Greenberg RA, Else T, Montone K, LiVolsi V, Fraker D, Daber R, Cohen DL, Nathanson KL. Whole-exome sequencing identifies somatic ATRX mutations in pheochromocytomas and paragangliomas. Nat Commun. 2015; 6:6140.
12. Job S, Draskovic I, Burnichon N, *et al.* Telomerase activation and ATRX mutations are independent risk factors for metastatic pheochromocytoma and paraganglioma. Clin Cancer Res. 2019; 25:760-770.
13. Purnell S, Sidana A, Maruf M, Grant C, Agarwal PK. Genitourinary paraganglioma: Demographic, pathologic, and clinical characteristics in the Surveillance, Epidemiology, and End Results database (2000-2012). Urol Oncol. 2017; 35:457.e9-457.e14.
14. Hao Y, Li X, Xie J, He W, Wang C, Sun F. Case report: Rare case of a preoperatively diagnosed spermatic cord paraganglioma and literature review. Front Oncol. 2024; 14:1373727.
15. Archier A, Varoquaux A, Garrigue P, *et al.* Prospective comparison of (68)Ga-DOTATATE and (18)F-FDOPA PET/CT in patients with various pheochromocytomas and paragangliomas with emphasis on sporadic cases. Eur J Nucl Med Mol Imaging. 2016; 43:1248-1257.

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