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PARATESTICULAR PARAGANGLIOMA: CASE REPORT AND LITERATURE REVIEW

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INTRODUCTION

Paratesticular paragangliomas are rare scrotal neoplasms related to neural crest tissue(1). Considering the related origin, main sites related to paragangliomas are abdomen (about 85%, mainly at adrenal glands), thorax (12%) and neck (3%)(2). Up to 30% of the tumors harbors malignant cell degeneration(3). Paragangliomas usually present as slow growing silent masses (4), symptoms are related to catecholaminergic stimulation when there is hormonal secretion (25 – 79% of non-adrenal masses)(5). Minor group of paragangliomas are ectopic from previous main sites. Places of note are kidney, bladder, urethra, uterus, prostate, vagina, spermatic chord(2). Scrotal occurrences are rare, being described only in case reports, first dated in 1971(5).

Vast majority of paragangliomas are sporadic, however some are related tumoral syndromes such as multiple endocrine neoplasia (NEM 1 and 2) Von Hippel-Lindau and Carney syndrome(6,7). This paper's objective is to present a rare case report of scrotal paraganglioma presented as asymptomatic paratesticular mass and review all the reports on actual medical literature.

METHODS

Evidence Aquisition and Syntesis

To identify relevant articles pertaining to ectopic paragangliomas full literature review was made using Medline® through PubMed®, "Virtual Health library" (BVS) and Scholar Google databases to access papers with the search terms: paratesticular, paraganglioma and spermatic chord. Full written consent was obtained with the patient and all the relevant data and imagens were collected.

CASE REPORT

A 43-year-old male presented to urologic medical appointment at "Luiz Roberto Barradas Barata" State ambulatory with a scrotal mass noted at age of 22. Three years before this medical evaluation started to present high blood pressure, headache, facial blush and flutter. Without other past health issues of note, started treating primary idiopathic hypertension with Losartan 50 mg BID. Later after, because of size progression, the scrotal mass was evaluated with

scrotum Doppler ultrasound showing 4,0 x 2,8 cm solid mass and no testicular tumoral marker was elevated after blood tests. At that time (2020) there was no suspicion of paraganglioma and so no collection of blood and urine tests for serum metanephrines (8). After about 2 years of lost follow up due to COVID-19 pandemic he presented again for surgery in July 2022 when an inguinal approach nodulectomy with testicular preservation was made without any complications at a day-hospital regimen. Histopathologic evaluation showed 4,4 x 3,3 × 2,5 cm yellow, smooth and shinny surface tumor with firm, elastic and brown cut surface. No lympho-vascular invasion or tumor necrosis was found and imunohistochemistry evaluation showed CD31, CD34, S-100 positivity on sustentacular cells and CD56, cromogranina-A and synaptophysin on tumoral cells (typical paraganglioma findings). No distant disease was found in further analysis and arterial pressure got regulated without need of antihypertensives.

DISCUSSION

Paratesticular tumors are rare scrotal masses, mostly benign (up to 70%) and mainly from epididymal origin (90%)(9). In terms of histological findings, literature shows soft tissue benign tumors as the most frequent, of note lipomatous, dermoid cysts, neurofibroma, hemangioma are most relevant ones(10). Malignant lesions represent less than a third of scrotal paratesticular tumors, histology findings in this cases generally depict rabdomiosarcoma, leiomiosarcoma, fibrosarcomas, mesothelioma, linfoma and metastatic carcinoma lesions. Considering the vast number of different histologies histopathology is a main step on diagnosing and treatment planning for this rare findings(9).

Behind testicular tumors, paratesticular masses are the second most common origin of scrotal tumors(11). Previous presented case report turned to figure out rare histology on scrotal site, a neuroendocrine tumor (Paraganglioma). Reports discuss about the possible origin of this neural crest cells at scrotum and the most believed one is spermatic chord cell dysgenesis during embryonal development(5,12). Hematoxilin & eosin findings of mitotic activity, tumoral necrosis and linfovascular embolysm are associated with bad prognosis and possible malignant behavior on genitourinary paragangliomas (mostly related on

literature on vesical site however)(13). It is consensual on medical literature related to the topic that malignant lesions can only be defined with the advent of metastatic lesions(2).

Typical histology of paragangliomas present with Zellballen nests (small nest of chromaffin cells with pale eosinophilic staining, segmented bands of fibrovascular stroma and surrounded by supporting sustentacular cells). Imunohistochemistry is key to definitive diagnosis, presenting with positivity for CD56 and synaptophysin in tumor cells and S100 protein straining on sustentacular cells(14). Tumor size is important characteristic to note When one is defining malignant potential. Makris et al. described malignant behavior on paratesticular paraganglioma sized as 17,5cm showing subpleural limphonode and pulmonar metastatic lesions(15). This report presents 4,4 cm lesion without metastatic findings aligned to the small size benign tumor belief as presented elsewhere.

Catecholaminergic secretion divide functional and non-functional paragangliomas. Parasympathetic origin lesions tend to be unfunctional whereas sympathetic ones tend to produce metanefrines driving to typical clinical findings described above. Clinical preparation is desirable when facing a functional paraganglioma before surgical resection to prevent high systolic blood pressure when manipulating the lesion and refractory hypotension after removal(16). Challenge comes to suspect on hormonal production considering rare sites of paraganglioma (as this cases presented). Urinary metanephrines as well as blood samples on serum epinephrine are mandatory to plan surgical excision of suspect lesions allowing preparation with alfa adrenergic block two weeks prior to surgery and beta adrenergic block ever since tachycardia is a positive clinical finding (17). The only appropriated treatment at the moment is surgical resection (8).

Clinical staging on suspected malignant paraganglioma includes computed tomography (cervical, thoracic and abdominal) and with the suspicion on maintenance of catecholaminergic stimuli, whole body mibg scintigraphy is helpful tool to investigate other sites of neuroendocrine chromaffin cells tumor(14). After more than 1 year of follow-up the Young male maintain good arterial pressure control without any drugs and no evidence of distant metastasis.

CONCLUSION

A rare case of paratesticular benign hormonal producer tumor (Paraganglioma) was presented with brief literature review of other rare case reports (less than 10 cases were found in our research). Cautious observation of paratesticular scrotal masses may include possible neuroendocrine functional lesions as previous case reports presented elsewhere. Rare diseases research is challenging, and this article contribution is relevant to bring attention on secondary hypertension investigation on the field of catecholaminergic producing lesions.

REFERENCES

1. Erickson D, Kudva YC, Ebersold MJ, Thompson GB, Grant CS, Van Heerden JA, et al. Benign paragangliomas: Clinical presentation and treatment outcomes in 236 patients. Vol. 86, The Journal of Clinical Endocrinology & Metabolism. 2001. Available from: https://academic.oup.com/jcem/article/86/11/5210/2849297
2. Lack EE. Tumors of the Adrenal Glands and Extraadrenal Paraganglia. 3rd ed. Vol. 8. American Registry of Pathology Washington, DC; 2007. 269–284.
3. Lee JA, Duh QY. Sporadic Paraganglioma. World Journal Surgery. 2008 May 27;32(5):683–687.
4. DeVita VT, Hellman SJR. Principles and Practice of Oncology. 10th ed. 2003. 841–847.
5. Eusebi V, Massarelli G. Phaeochromocytoma of the spermatic cord: report of a case. 1971; 105 (4); 283-284.
6. Castinetti F, Waguespack SG, Machens A, Uchino S, Hasse-Lazar K, Sanso G, et al. Natural history, treatment, and long-term follow up of patients with multiple endocrine neoplasia type 2B: an international, multicentre, retrospective study. Lancet Diabetes Endocrinol. 2019 Mar;7(3):213–220.

7. Castinetti F, Qi XP, Walz MK, Maia AL, Sansó G, Peczkowska M, et al. Outcomes of adrenal-sparing surgery or total adrenalectomy in phaeochromocytoma associated with multiple endocrine neoplasia type 2: an international retrospective population-based study. Lancet Oncol. 2014 May;15(6):648–655.
8. Neumann HPH, Young WF, Eng C. Pheochromocytoma and Paraganglioma. New England Journal of Medicine. 2019 Aug 8;381(6):552–565.
9. Richie JP: Neoplasms of testis. In Walsh Pc Ravena etc. Campbells' Urology. 7th ed. WB Saunders, editor. Vol. III. Philadelphia; 1998 3(78); 2411–2452.
10. Lioe TF, Biggart JD. Tumours of the Spermatic Cord and Paratesticular Tissue. A Clinicopathological Study. Br J Urol. 1993 May;71(5):600–606.
11. Khoubehi B, Mishra V, Ali M, Motiwala H, Karim O. Adult paratesticular tumours. BJU Int. 2002 Sep 19;90(7):707–715.
12. George G. Glenner, Philip M. Grimley. Tumors of the extra-adrenal paraganglion system (including chemoreceptors). 2nd ed. Washington DC: Armed Forces Institute of Pathology (U.S.); 1974. 81–82.
13. Cheng L, Leibovich BC, Cheville JC, Ramnani DM, Sebo TJ, Neumann RM, et al. Paraganglioma of the urinary bladder. Cancer. 2000 Feb 15;88(4):844–852.
14. Gupta R, Howell RS, Amin MB. Paratesticular Paraganglioma A Rare Cause of an Intrascrotal Mass. Vol. 133, Arch Pathol Lab Med. 2009; 133; 811-813.
15. Makris MC, Koumarelas KC, Mitrousias AS, Psathas GG, Mantzioros A, Sakellariou SP, et al. A 'giant' paraganglioma in the testis. Endocrinol Diabetes Metab Case Rep. 2014 Aug;2014.
16. Simpson LN, Hughes BD, Karikari IO, Mehta AI, Hodges TR, Cummings TJ, et al. Catecholamine-Secreting Paraganglioma of the Thoracic Spinal Column. Neurosurgery. 2012 Apr;70(4):E1049–1052.
17. Srivastava SK, Marathe N, Bhosale S, Purohit S, Raj A, Manghwani J. Learning Point of the Article: Paratesticular Paraganglioma with Metastasis to D1 Vertebra-A Case Report and Review of Literature. Journal of Orthopaedic. 2018;8(6):92–93.