



Papillary cystadenoma of epididymis: Is there a need for further investigation in unilateral cases?



Chrysovalantis Toutziaris^a, Spyridon Kampantais^{a,*}, Ioannis Perdikis^a, Victoras Gourvas^b, Leonidas Laskaridis^a, Konstantinos Gkagkalidis^a, Sotiris Lakis^b, Stavros Ioannidis^a

^a 1st Department of Urology, Aristotle University of Thessaloniki, Thessaloniki 54635, Greece

^b Department of Pathology, "G.Gennimatas" General Hospital, Thessaloniki 54635, Greece

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ABSTRACT

INTRODUCTION: The presence of a mass in the epididymis is not a common entity. The papillary cystadenoma of epididymis is a benign tumor which may occur sporadically or as a characteristic of von Hippel–Lindau disease.

PRESENTATION OF CASE: We present a case of a 27-year-old man with a right scrotal mass who was treated with surgical excision. Histopathological examination revealed a clear cell epididymal papillary cystadenoma. A computed tomography scan that was performed later showed no other abnormality or any signs of von Hippel–Lindau disease.

DISCUSSION: In this report, a case of a young man suffering from this rare tumor is discussed, focusing on the need of further evaluation in order to determinate if it occurs as a feature of VHL disease or as a sporadic form.

CONCLUSION: In unilateral cases of papillary cystadenoma of epididymis such as our patient's, literature advocates that no further examinations and expensive genetic testing is required.

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1. Introduction

The most common neoplasm of the epididymis is a benign mass called "adenomatoid tumor".¹ The papillary cystadenoma (PCE) is the second most common benign neoplasm² while leiomyomas³ and lipomas⁴ follow in frequency and it may occur sporadically or as a characteristic of von Hippel–Lindau disease (VHLD).⁵ PCE was first described in 1956 by Sherrick in a 21-year old patient²; since then, approximately 60 reports of such tumors have been published.⁵ We discuss a case of a young man suffering from this rare tumor, focusing on the need of further evaluation in order to determinate if it occurs as a feature of VHL disease or as a sporadic form.

2. Case presentation

A 27-year-old man presented to our department complaining of a mild pain in his right scrotum. According to the patient's history, a small enlargement of the right epididymal had been noticed 3 months ago. The first clinical diagnosis was suggestive of epididymitis so he was treated initially with antibiotics for 3 weeks. However, one week after the conclusion of the initial therapy, no improvement was mentioned.

A scrotal ultrasound was performed revealing a well-circumscribed mass with a complex echo pattern, contiguous to the head of the right epididymis. Power Doppler indicated increased tumor vascularity (Fig. 1). Unfortunately, no definite diagnosis could be reached through imaging, so diagnostic surgery was mandatory.

Under general anesthesia, a 3 cm well-circumscribed tumor was excised along with the right epididymis (Fig. 2). Macroscopically, the tumor was hemorrhagic with microcystic consistency and it had a golden yellow hue (Fig. 3). The patient's recovery was uneventful. Histopathological examination revealed a clear cell papillary cystadenoma consisted of clear cells in a papillary–tubular pattern, mimicking a clear cell renal carcinoma (Fig. 4). The tumor's morphology, its close relationship with the epididymis, the presence of a fibrous capsule and the immunohistochemical results which were positive for Vimentin, Cytokeratin AE1/AE3, Cytokeratins 7 and 20, while it was negative for CD-10, CEA and p53, determined the final diagnosis.

An abdominal CT scan was performed one month after the surgery and a second one, twelve months later. Neither of them revealed any abnormality or any signs of VHLD.

3. Discussion

PCE may occur as a manifestation of VHLD or sporadically (60%), mimicking a clear cell renal carcinoma (RCC).⁵ VHLD is a dominant autosomal neoplasia syndrome, resulting from a germline mutation

* Corresponding author at: 12 Gennimata Street, Thessaloniki 55132, Greece.

Tel.: +30 2314011161; fax: +30 2310992543.

E-mail address: kabspir@hotmail.com (S. Kampantais).

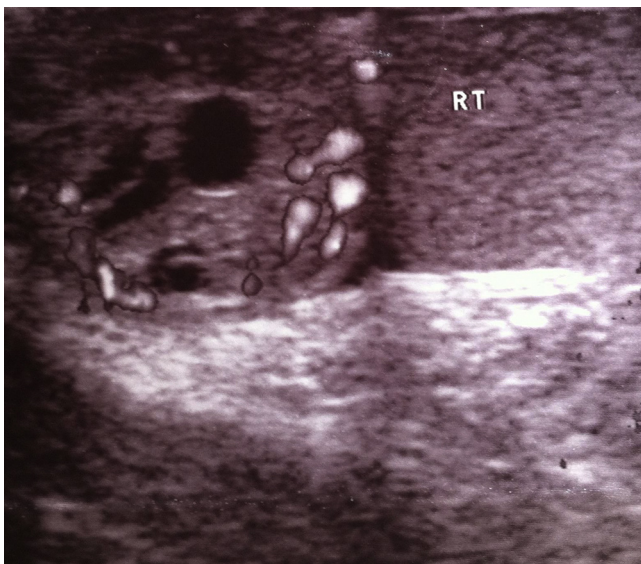


Fig. 1. Scrotum ultrasound revealing a tumor with a complex echo pattern.

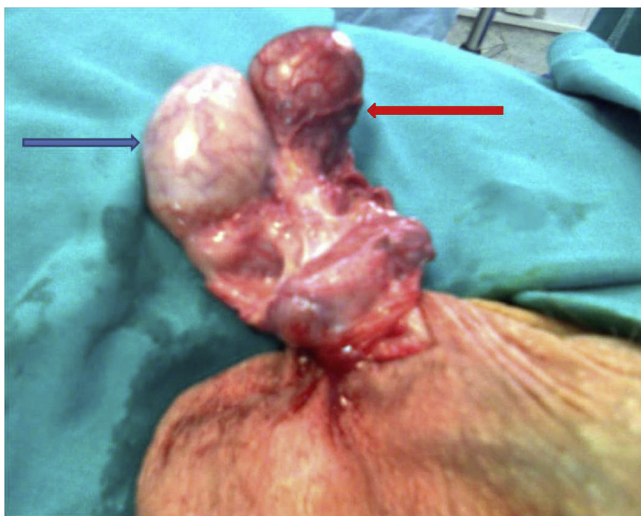


Fig. 2. Intraoperative findings revealing the epididymal tumor (marked by red arrow) contiguous to the right testicle (marked by blue arrow).

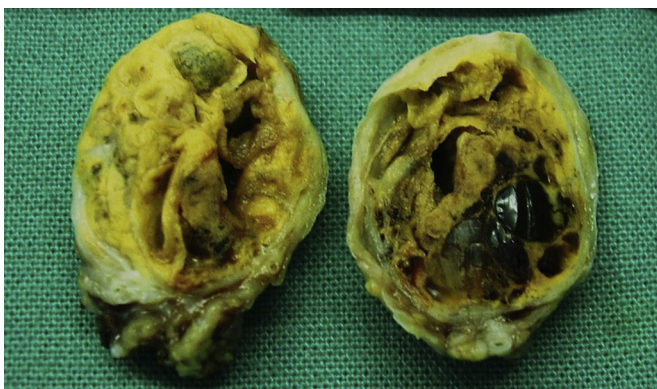


Fig. 3. Macroscopic appearance of the tumor.

in the VHL gene.⁶ Patients suffering from this syndrome are at risk of developing various benign and malignant tumors of the central nervous system, adrenal glands, pancreas, reproductive adnexal organs and kidneys. The most common histological type of RCC is

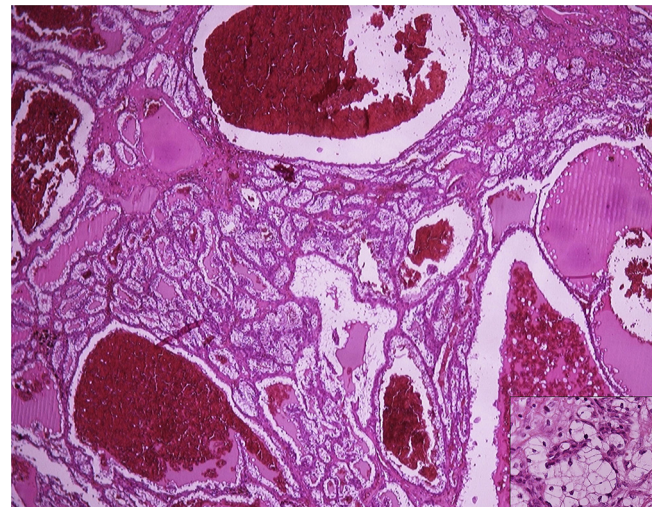


Fig. 4. Histopathological examination.

the clear cell type and is reported to develop in 24–45% of patients with VHLD. The mean age of patients with RCC associated with the VHLD is 37 years, an age at which both RCC and clear cell papillary cystadenoma are viable considerations in the differential diagnosis of an epididymal or mesosalpingeal clear cell tumor.

In the majority of cases, PCE develops within the efferent ductules of the head of the epididymis as a partially or completely cystic or solid lesion measuring about 1–3 cm in diameter and is usually asymptomatic.^{6,7} However, in symptomatic patients the most common presentation is a painless, slowly growing, scrotal swelling. In rare occasions, they may present with pain or tenderness in the scrotum or are found to have an epididymal nodule during an examination for infertility. The ages of occurrence are 16–65 with a mean age of 36.⁸ In females, the counterpart of papillary cystadenoma of the epididymis is represented by papillary tumors of the broad ligament and peritoneum most of whom are usually solid, although they may have distinct cystic spaces. Distinctive microscopic features were described by Price.¹³ Allelic loss of the VHL gene, located on the short arm of chromosome,¹³ has been demonstrated in all benign papillary tumors developing in VHL patients (papillary cystadenoma of the broad ligament, endometrioid cystadenoma of the broad ligament, papillary cystadenomas of the epididymis, papillary tumor of the retroperitoneum).¹⁴ Several hypoxia-inducible genes are regulated by protein encoded by the VHL gene, including platelet-derived growth factor (PDGF), basic fibroblast growth factor (bFGF), erythropoietin, and vascular endothelial growth factor (VEGF). VEGF overexpression has been demonstrated in VHL-associated tumors and may explain the cyst formation and vascularized stroma present in these tumors.¹¹ Odrzywolski and Mukhopadhyay analyzed in a review 59 cases of PCE reported in the literature. They found that bilateral PCE is highly associated with VHLD. Two thirds of patients with bilateral tumor had stigmata or were found to be VHLD positive. On the other hand, the association of unilateral PCE with VHLD is weaker (20.3%).⁵

A dilemma arises at this point concerning the patients with unilateral PCE tumors. Should we investigate the chance they have an undiscovered VHLD or stop any further examination? Price et al. studied 8 patients which were followed up for a long period, with intervals ranging from 18 months to 15 years. Among them no one developed VHLD.⁹ Furthermore, unilateral PCE has never been reported as the initial presentation of VHLD.⁵ The above data advocate that no further examinations and expensive genetic testing is required in the treatment of unilateral PCE tumors.

Interestingly, the histological differentiation between PCE and metastatic renal cell carcinoma in epididymis can be difficult.¹⁰

Both are known to develop in von Hippel–Lindau syndrome; they both have similar origin from meso-metanephric tissue and they are both related to VHL protein function which may disrupt tumor suppression through hypoxia-inducible factor (HIF) stimulation of angiogenesis.⁶ This may be a possible explanation of the high vascularity of the VHLD-associated tumors.¹¹ Lectin histochemistry studies are helpful in distinguishing between papillary cystadenoma and metastatic renal cell carcinoma in epididymis thus a routine examination of kidneys is not always necessary.¹²

4. Conclusion

The discovery of a benign lesion in epididymis, like a papillary cystadenoma, although rare, is still possible. It may occur sporadically or as a manifestation of VHLD; however, in the case of VHDL, the PCE is usually bilateral. In unilateral cases of PCE such as our patient's, literature reviews provide evidence against extensive and expensive genetic testing for VHLD.

Conflict of interest

None declared.

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None.

Ethical approval

Written informed consent was obtained from the patient for publication of 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.

Author's contributions

Chrysovalantis Toutziaris: drafting the article, critical revision of the article and final approval of the version to be published.

Spyridon Kampantais: conception and design, acquisition of data, analysis and interpretation of data. Ioannis Perdikis: acquisition of data. Victoras Gourvas: acquisition of data. Leonidas Laskaridis: analysis and interpretation of data. Konstantinos Gkagkalidis: critical revision of the article. Sotiris Lakis: acquisition of data. Stavros Ioannidis: final approval of the version to be published.

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