

Clear cell Papillary Cystadenoma of Epididymis, a Mimic of Metastatic Renal Cell Carcinoma

Nausheen Yaqoob, Aamir Ahsan, Zubair Ahmad, Ambreen Nasir Khan
Department of Pathology & Microbiology, The Aga Khan University, Karachi.

Abstract

We discuss a case of 25 year old male who was evaluated for primary infertility following marriage. He had no previous history of urogenital complaints or abnormalities. Infact, his past medical history was unremarkable. On examination epididymal masses were found. Semen analysis showed azoospermia. Right epididymal mass was surgically excised. Histopathology showed an epididymal neoplasm composed of simple and complex papillary processes lining and filling the ducts. The tumor cells were clear and positive for cytoplasmic glycogen. Immunohistochemistry was also supportive. Diagnosis of clear cell papillary cystadenoma was made based on histopathological and immunohistochemical features.

Introduction

Papillary Cystadenoma of the epididymis is the second commonest benign neoplasm of this organ following adenomatoid tumor.¹ Its is a rare epithelial tumour which is thought to develop within the efferent ductules.² It was first described in 1956.³ It may occur sporadically or as a manifestation of von Hippel-Lindau disease (VHL). Two thirds of patients with this neoplasms have von Hippel-Lindau disease.⁴ Metastatic renal cell carcinoma (RCC) is a close histologic mimic of this neoplasm and both are related to von Hippel-Lindau disease. It is important to differentiate between these two entities for the proper management of the patient.

Case Report

A 25 years old Asian male was evaluated for primary infertility. He was married since one year. There was no

history of any urogenital complaints or abnormalities. His past medical and surgical history was unremarkable. On examination he was found to have bilateral painless epididymal masses. Right epididymal mass was 2 X 2 cm in size and was firm, mobile and non-tender. Spermatic cord and adnexae were unremarkable on palpation. Left sided testis also showed a small mass. Semen analysis revealed azoospermia. Serum Leutinizing hormone (LH) and Follicle stimulating hormone (FSH) levels were within normal ranges. Urinalysis and blood tests were normal. Fundoscopic examination and CT scan of brain showed no abnormality. Right epididymal mass was removed and sent for histopathological examination. Grossly the tumor was grey white in colour and measured 2 X 1.5 cm in size. Cut surface showed multiple cysts filled with yellowish serous fluid. Histologically, sections showed predominantly

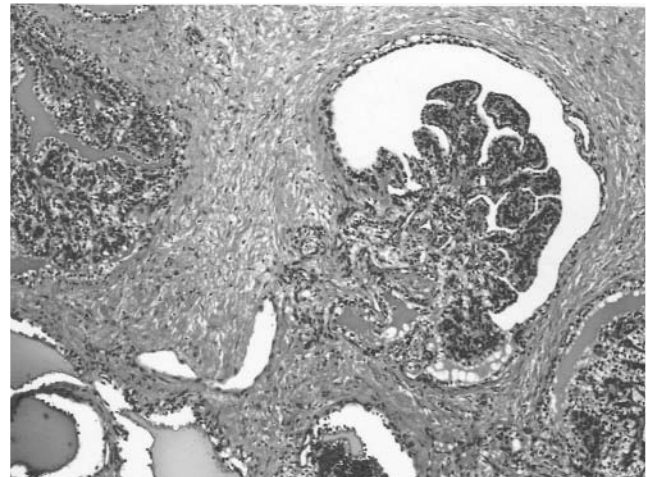


Figure 1. Ducts showing papillary formations. H & E X 20.

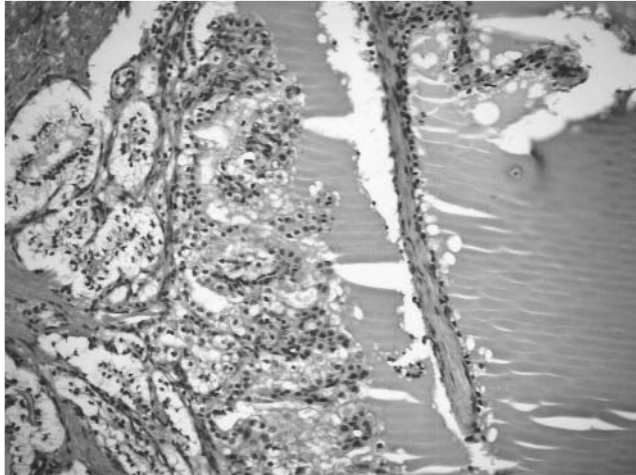


Figure 2. Papillae lined by cuboidal and columnar cells with clear to vacuolated cytoplasm H&EX20.

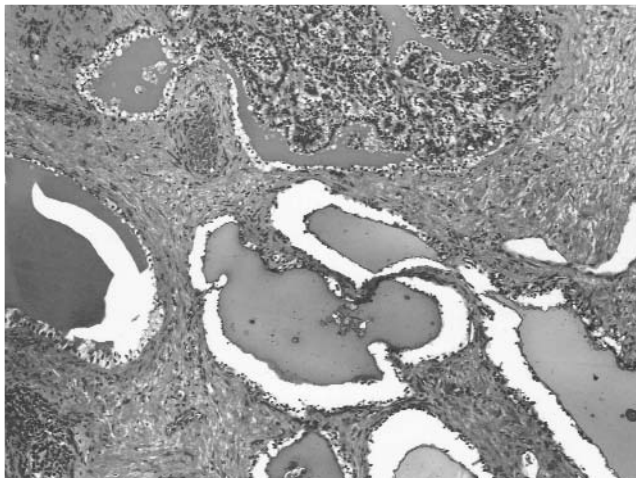


Figure 3. Ducts focally filled with eosinophilic colloid like secretions.

epididymal tissue with ectasia of the afferent ducts with eosinophilic secretions. There were areas showing ducts with papillary formations (Figure 1) which were lined by cuboidal and columnar cells with clear to vacuolated cytoplasm (Figure 2) and focally they were filled with colloid like eosinophilic secretions (Figure 3). Simple and complex papillary processes were seen in a few ducts completely filling the cystic spaces. Nuclei were small and round and showed no atypia. Mitoses were not identified. Glycogen positivity was noted on PAS +/- diastase special stain. Immunohistochemical profile showed positivity for Cytokeratin AE1/AE3, Cytokeratin (CK7), Cytokeratin Cam 5.2, Epithelial Membrane Antigen (EMA) and Vimentin. The tumour cells were negative for Cytokeratin 20 (CK 20), Alpha fetoprotein (AFP), CD 68, S-100, inhibin and CD 10.

The diagnosis of clear cell papillary cystadenoma was made based on morphological and immunohistochemical

features.

Discussion

Tumours of the epididymis comprise only 5% of intrascrotal neoplasms and most are benign. Papillary cystadenoma of the epididymis is the second most common benign tumour following adenomatoid tumour. Other benign tumours of epididymis include leiomyoma, lipoma, melanotic neuroectodermal tumour of infancy, mixed gonadal stromal tumour and cavernous haemangioma.¹

Clear cell papillary cystadenoma is a rare epithelial tumor that is thought to develop within the efferent ductules.² It was first described by Sherrick in 1956 in a 21-year old man.³ It occurs in post pubertal males of 16-65 years, with a mean age of 36 years. Most common location is the head of epididymis. It may occur sporadically or as a manifestation of von-Hippel Lindau disease. Two thirds of patients have risk of developing benign cysts in kidney, pancreas and tumours of the central nervous system, kidneys, adrenals, pancreas and reproductive adnexal organs. The risk of developing papillary cystadenoma of epididymis with von Hippel-Lindau disease (VHL) is high in bilateral cases. In up to 40% of patients having VHL these tumours can be bilateral. Tsuda et al described a familial pattern of occurrence with three siblings having this tumour, one of whom was suspicious for having VHL.⁵ Gaffey et al⁶ has described a solitary case of benign adnexal papillary tumour of probable mesonephric origin in the broad ligament seen in association with VHL.

Price⁷ reported on 5 patients with bilateral papillary cystadenoma, four of whom had lesions in other organs consistent with an incomplete form of von Hippel-Lindau's syndrome. Elevated levels of Vascular endothelial growth factor have been shown with in situ hybridization techniques in a patient with von Hippel-lindau disease with bilateral epididymal clear cell papillary cystadenomas.⁸

Metastatic renal cell carcinoma may appear to be histologically similar to papillary cystadenoma and both may be seen in patients with VHL. To differentiate between these two entities is most important and may present as a diagnostic challenge. Possible explanations for the histologic similarity between papillary cystadenoma and RCC include similar origin of renal tubules and the ductuli efferentes of globus majus of the epididymis from mesonephric tissue. Another explanation is that both are related to VHL protein function, which may disrupt tumour suppression through Hypoxia-inducible factor (HIF) stimulation of angiogenesis. This link might explain the high vascular nature of tumours associated with VHL, which is one of the notable similarities between clear cell RCC and clear cell papillary cystadenoma.⁹ Kragel et al

demonstrated positive staining with soybean agglutinin in two of three cases of clear cell papillary cystadenoma and was not observed in renal cell carcinoma.¹⁰ Lectin histochemical staining may also provide a means to differentiate papillary cystadenoma from renal cell carcinoma.

Ayedini et al² compared the immunohistochemical profile of this tumour with RCC and described that papillary cystadenomas are positive for cytokeratin AE1/AE3 and EMA, CK7 and negative for CK20 and RCC immunostain. Four of 5 cases were negative for CD10. This staining profile contrasts with that reported for clear cell RCC, which are typically negative for CK7 and are immunoreactive for RCC and CD 10 immunostain.

There is a possibility of discovering an epididymal neoplasm in patients presenting with epididymal enlargement and azoospermia. The recognition of this entity is important so that unnecessary radical surgical procedures in these patients may be avoided; and they should be further investigated for von Hippel-Lindau syndrome and its other associated lesions.

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