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Review Article

Renal Cell Carcinoma Presenting as Testicular Metastasis: Case Report and Review of Literature

Dr. Arsha Narayanan[1], Dr. Sanjay Kumar[2], Dr. Sant Prakash Kataria[3], Dr. Ankush[4], Dr. Rashmi Jangra[5], Dr. Sunita Singh[6]

[1]Senior Resident, [2]Professor, [3]Professor, [4]Junior Resident, [5]Junior Resident, [6]Senior Professor and Head

Department of Pathology, Pt. B. D. Sharma Post Graduate Institute of Medical Sciences, Rohtak, Haryana, India

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Corresponding author: Dr. Arsha Narayanan

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Abstract:

Renal cell carcinoma is the most common malignant tumor involving the kidney. Approximately 20-50% of RCC patients with localised tumor progress to metastases. However, testicular metastases from renal cell carcinoma are an extremely rare entity. To the best our knowledge, there have been less than 50 reported cases of RCC metastasis to the testis. Here we report a case of testicular metastasis from renal cell carcinoma in a 70-year-old man 2 years post- nephrectomy and review some of the previously reported cases. Histopathological examination after surgical removal of this testicular mass confirmed the diagnosis of metastatic RCC. This report highlights the unique diagnostic and therapeutic challenges associated with such an entity.

Keywords: Renal cell carcinoma, Testicular metastasis, Clear cell RCC, Metastatic RCC.

Introduction

Metastatic tumors to the testis are uncommon accounting for 1-2.5% of all scrotal neoplasms. The most common secondary neoplasms of testis are from prostate, lung, kidney, gastrointestinal tract and melanoma (skin). However, when they occur, they usually present as unilateral and solitary/multiple nodules. Most published cases are with unilateral testicular metastases. These tumors simulate primary testicular tumors and that make the diagnosis very challenging. Awareness of the features of these tumors, consideration of the possibility of metastasis and appropriate immunohistochemical studies are inevitable for the accurate diagnosis of these cases. The knowledge of a possibility of metastases from renal cell carcinoma helps the clinician to make an appropriate diagnosis and to provide timely adequate treatment.

Case Report

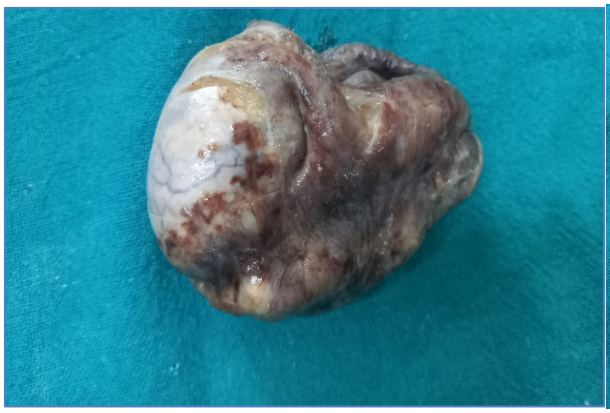
A 70 years old male patient presented in General Surgery OPD with left testicular swelling for 2.5 months. Patient developed swelling in left scrotal region which was insidious in onset and gradually progressive. He gave a history of some surgical procedure 2 years back. On examination, left testicular swelling measured 3 x 2 x 1.5 cm, firm in

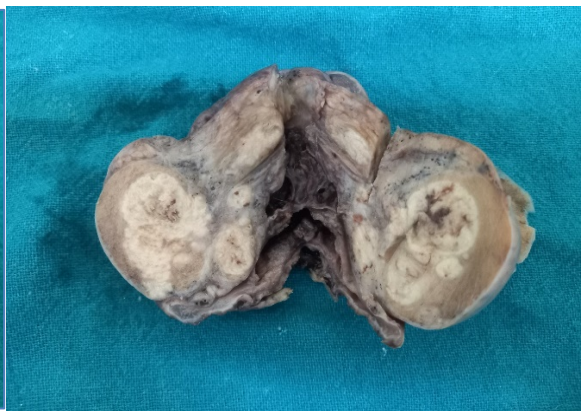
consistency. Right testis was normal. No organomegaly or lymphadenopathy were identified. On USG Scrotum, moderate to large hydrocele was noted with multiple hypoechoic lobulated mass in the left testis, largest measuring 2.8 x 1.8 cm with irregular testicular surface. Left testis was found adherent to tunica. Right testis was normal in size and echotexture with no focal lesions. Bilateral epididymis was normal in size and no evidence of hydrocele/varicocele were seen in the right side. Left high orchiectomy was performed and the sample was sent to the department of pathology.

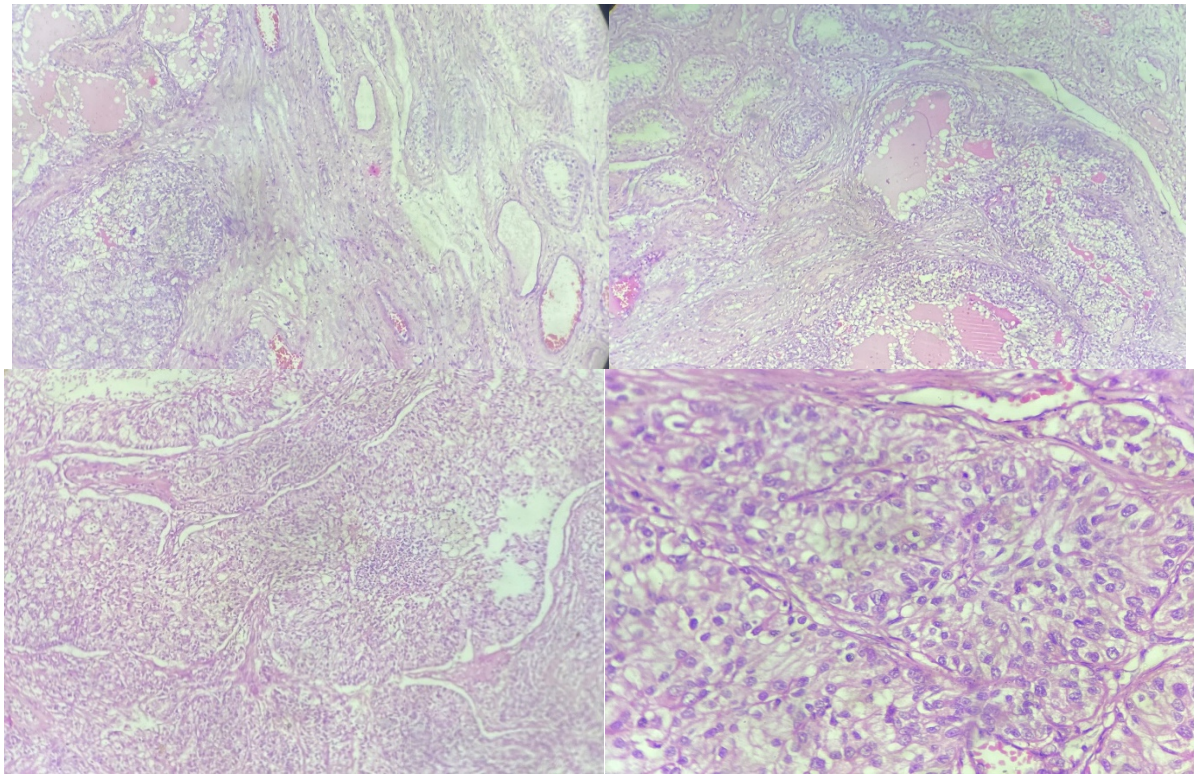
Gross examination: Left testicular specimen measured 8 x 5 x 3 cm with attached spermatic cord measuring 4 cm. External surface was irregular and congested. Serial sectioning of the specimen revealed multiple grey white areas largest measuring 3 x 2 cm in size. (Figure *a, b*). Histopathological examination revealed a tumor arranged in tubulocystic, solid as well as glandular pattern comprising of large polygonal epithelioid cells with abundant clear cytoplasm and prominent cytoplasmic membrane (Figure *c, d, e*). The nuclei were small and irregular with vesicular chromatin and inconspicuous nucleoli (Figure *f*). On Immunohistochemistry; these cells were negative for all the testicular tumor markers including PLAP, AFP, Inhibin, Calretinin, CD30, OCT3/4, CD99, AMACR, CK7 and EMA. These atypical cells were positive for PanCK, CD10, PAX8 and Vimentin. (Images attached).

On tracing back the patient's history, the details regarding previous left nephrectomy conducted 2 years back were obtained. Back then, the patient presented in urology OPD with complaints of haematuria and flank pain, and was admitted in Urology ward. USG abdomen showed a 6.7 cm lesion in the interpole region in left kidney. On CECT abdomen, a large ill-defined heterogeneous enhancing soft tissue attenuated mass lesion measuring 4.9 x 5.7 x 7.4 cm was seen at the lower and mid pole of left kidney with small exophytic component and mild left perinephric fat stranding. The lesion was involving the pelvicalyceal system and left renal pelvis with tumor thrombosis of left renal vein at renal hilum. Mild mural thickening was seen in the left upper ureter. Right kidney was normal in echotexture and size. Left nephrectomy was conducted and the case was reported as Clear cell renal cell carcinoma on histopathological examination.

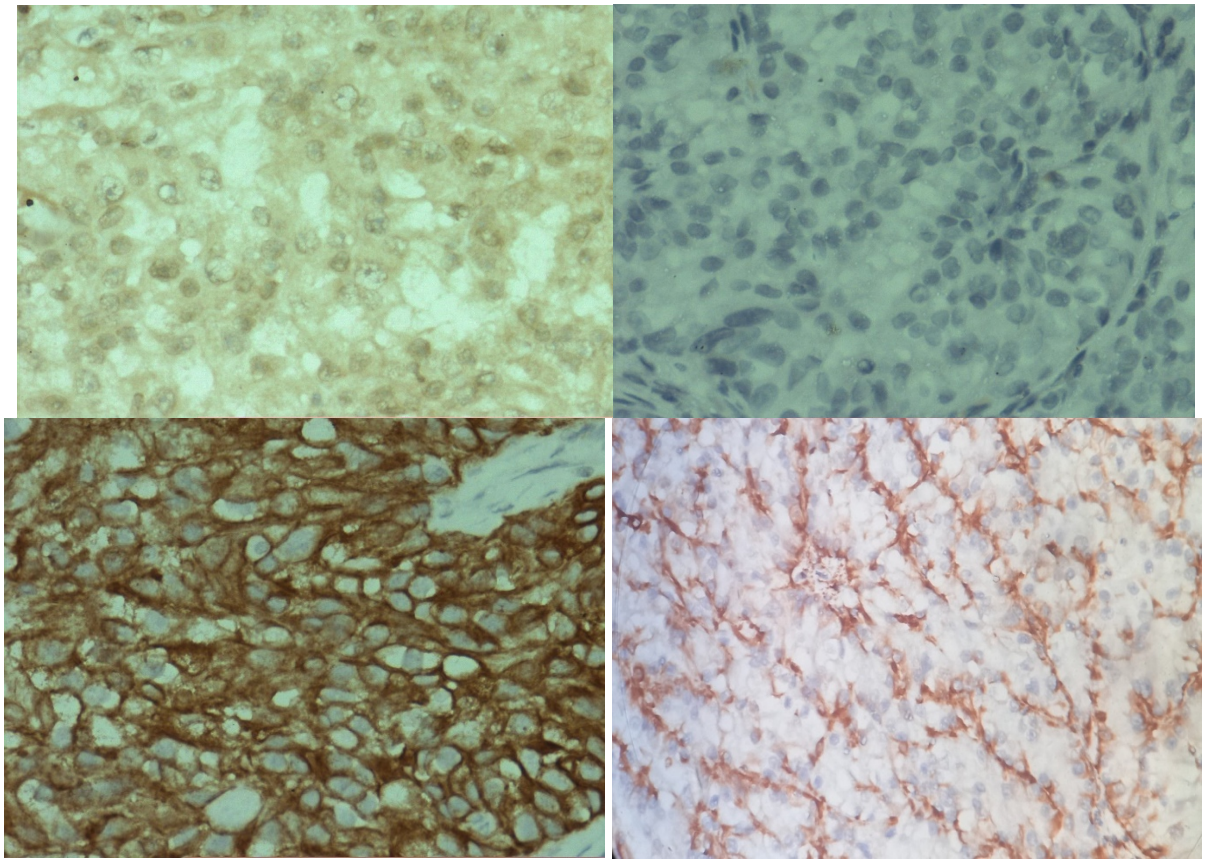
After correlating the histopathological features and the immunohistochemistry findings of the orchiectomy specimen with previous history of the patient, he was diagnosed with Clear-cell renal cell carcinoma metastasizing to left testis. After almost 15 months of follow-up from orchiectomy, the patient is currently stable and continues to undergo routine surveillance.

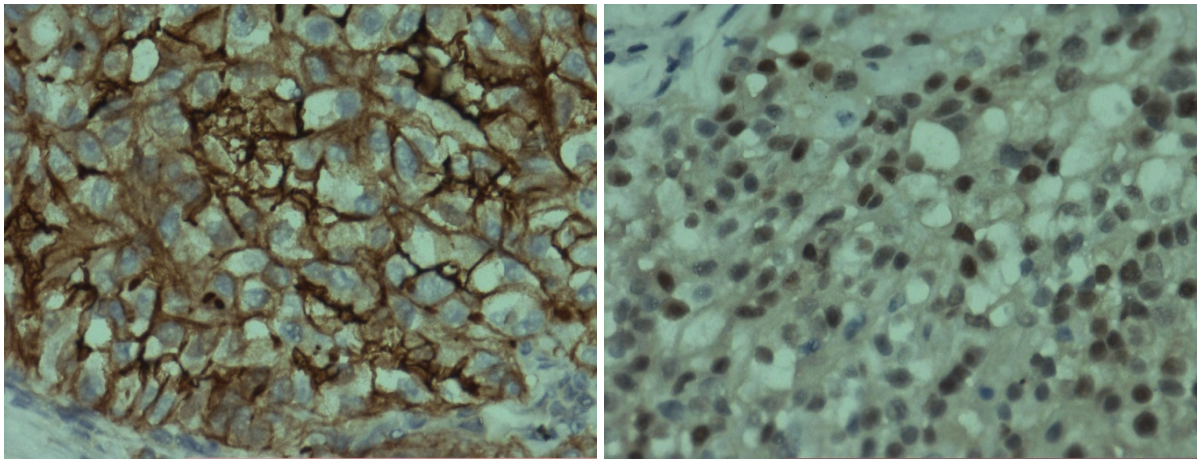






Microscopic examination of metastatic renal cell carcinoma in the testis
(a) gross appearance of specimen (b) cut surface shows multiple grey white nodules (c) low power view: normal testis separated from tumor area (d) 10x: normal testis separated from tumor area (e) the metastatic tumors with mixed patterns (f) atypical clear cells





Immunohistochemistry analysis of metastatic renal cell carcinoma in the testis
(h) metastatic renal cell carcinoma was negative for OCT3; (i) negative for Inhibin; (j) positive for cytokeratin (panCK); (k) positive for vimentin; (l) positive for CD10; (m) positive for PAX8

ANNEXURE:

VARIANTS OF RCC	CK7	VIMENTIN	AMACR	CD10	CAIX	OTHERS
Clear cell RCC	-	+	-	+	+	PAX8+
Papillary RCC	+	+	+	+	-	PAX8+
Clear cell papillary RCC	+	+	+	-	+/-	PAX8+
Chromophobe RCC	+	-	-	-	-	CD117+
Collecting duct carcinoma	-	+	-	-	-	HMWCK+
Tubulocystic carcinoma	+/-	+/-	-	+	-	PAX8+
Xp11 translocation RCC	-	+	-	-	-	TFE+

Discussion

Renal cell carcinoma is the most common malignant tumor involving the kidney. The different variants of RCC are: Clear cell carcinoma, papillary renal cell carcinoma, clear cell papillary, chromophobe, collecting duct carcinoma and translocation related RCC. Approximately 20-50% of RCC patients with localised tumor progress to metastases. RCC metastasizes to local lymph nodes, adrenals, lungs, bones, and liver. Testis is one of the most unlikely metastatic sites for renal cell carcinomas. And the majority of testicular metastasis, on microscopy, are of clear cell variant.[1]
Most of the cases of clear cell renal cell carcinoma show tumor cells arranged in mixed patterns (hollow tubules, cysts, and alveoli or well-vascularized nests). At high-power magnification, the polygonal tumor cells have lightly eosinophilic to abundant clear cytoplasm with definite cytoplasmic borders. On immunohistochemistry; these cells are positive for pan-keratin, PAX8, CD10, and CAIX. Variable positivity for vimentin and negative for CK7.

The very first case of testicular metastasis from RCC was published by Bandler and Roen in 1946. This case was diagnosed in a 47 years old man 2 years after nephrectomy.[2] Dieckman et al conducted an extensive study on testicular tumors in 1988 and reported 02 cases of testicular metastases and speculated about left lateral

dominance in unilateral testicular metastases.[3] Datta et al reported a case series with 5 cases of RCC metastasized to the testis or its adnexa, including 3 that mimicked primary testicular neoplasms. All of these patients had unilateral involvement of testis with multiple solid nodules in the involved testis. On microscopic examination all the tumors were of the clear cell type. Patterns included solid sheets, acini, cysts, alveoli, and trabeculae. Two had prominent vascular invasion. Diagnoses initially entertained in these cases included Sertoli cell tumor, Sertoli-Leydig cell tumor, and clear cell cystadenoma of the epididymis.[4]

Wang et al reported 5 cases of Metastatic renal cell carcinoma to the testis. Four of the five patients had known renal cell carcinoma. The time intervals between the partial and radical nephrectomies for the primary kidney tumors and the occurrence of testicular metastases ranged from 29 to 34 months. All of the metastatic tumors had clear cell features, microscopically concordant with the primary renal cell carcinoma subtype.[5]

A detailed study on testicular metastasis from renal cell carcinoma by Pliszka et al stated that approximately one-third of renal cell carcinoma is recognized in its metastatic stage. Review of 31 cases of testicular metastasis of RCC concluded that metastasis to testis suggests a late stage of the disease. Usually, these patients present in Urology clinic without systemic or specific symptoms, but with a suspicion of a primary testicular tumor, confirmed on ultrasound. Standard management is typically based on orchiectomy and postoperative histopathological examination, which reveals the primary tumor.[6]

The testes are generally considered as a tumor sanctuary, since the low temperature of the scrotum provide unfavourable atmosphere for metastatic tumor cells and inhibit the growth of tumors. It is also speculated that the blood testes barrier indirectly prevents testicular metastasis. There is predominance for the metastasis to occur in the ipsilateral testis, which may be attributed to the routes of spread between the kidney and the testis, including retrograde venous spread via the spermatic vein. Other modes of metastases to testis are: Vascular -via the left testicular vein and lymphatic channels. Metastases to ipsilateral testis: retrograde venous spread via a spermatic vein. Metastases to contralateral testis: through Batson's venous plexus, an avalvular venous network linking renal capsular veins and contralateral spermatic cord vessels.[8]

The review of literature of these cases suggest that ipsilateral metastases are much more common and the interval period between diagnosis or nephrectomy and diagnosis of testicular metastases varied from 2 years usually to even 6 years long. Most of the cases of metastatic renal cell carcinoma involving the testis are of clear cell type. In symptomatic patients, scrotal enlargement and presence of a testicular mass are two common symptoms. Also, the symptoms of testicular metastasis often appear in advanced stage, which makes it impossible for early disease identification and proper treatment implementation.

It should also be noted that certain primary testicular tumors morphologically resemble renal cell carcinoma. Sertoli or Sertoli-Leydig tumor can show solid nests and tubular patterns as in clear-cell RCC. Although they lack the intricate and delicate vascular network as in RCC, sometimes hyalinized vessels may be prominent. The tumor cells of Sertoli Leydig cell tumor are positive for inhibin. Classic seminoma sometimes presents with prominence of clear cells as in metastatic RCC[9]. But these patients are generally younger than those with metastatic RCC and the tumor cells are positive for PLAP. Almost all variants of RCC show immunopositivity for PAX8.[1]

Conclusion

This report highlights an interesting case of RCC metastasized to testis. RCC metastasis to the testis has similar ultrasonographic findings as primary testicular tumors and the serum tumour markers may be negative. A previous history would have been helpful to diagnose this case. Without a known history of a primary tumor, cases of metastatic carcinoma to the testis would be a great diagnostic challenge because they are usually solitary and unilateral, and may have similar patterns and cytological features with primary tumors; especially clear cell tumor or Sertoli cell tumor of the testis. The diagnosis of metastatic carcinoma should not be difficult once the pathologists are aware of this rare scenario. Due to the rarity of RCC metastasis to the testis, the clinical suspicion for it may be quite minimal and this adds to the challenges in diagnosing metastasis.

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Conflict of interest

The authors declare no potential conflicts of interest with respect to research, authorship and/or publication of this article**.**

Ethical Approval

Not applicable since it is a case report.

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