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Synchronous adrenal myelolipoma with renal cell carcinoma: A case report

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Abstract

Synchronous adrenal myelolipoma and Renal Cell Carcinoma (RCC) have been rarely reported in the literature. Cases occurring on the ipsilateral side are even rarer. We report a case of a 65-year-old male who presented with hematuria, lithuria, and suprapubic pain. On radiological evaluation, he was found to have a mass in the right kidney and in the right adrenal gland, respectively. He underwent radical nephrectomy, which revealed the masses to be clear-cell RCC and adrenal myelolipoma of the right kidney and adrenal gland, respectively. The patient was followed up. He is fine without any signs of tumor recurrence or distant metastasis. The case emphasizes that a rare scenario of synchronous adrenal myelolipoma and RCC can occur, and such patients can be managed with concurrent laparoscopic removal of both masses. Hence, both pathologists and surgeons should be mindful of the same for the proper diagnosis and management of such cases.

Keywords: Myelolipoma; Adrenal cortex neoplasm; Carcinoma; Renal cell.

Abbreviations: CCRCC: Clear-Cell Renal Cell Carcinoma; CECT: Contrast-Enhanced Computerized Tomography; HU: Hounsfield Density; ML: Myelolipoma; Mpmri: Multiparametric Magnetic Resonance Imaging; RCC: Renal Cell Carcinoma; WHO/ISUP: World Health Organisation/International Society of Urological Pathology.

Introduction

Adrenal Myelolipoma (ML) is the second most common adreno-cortical neoplasm composed of adipose tissue and hematopoietic elements. It forms 2.6% of all primary adrenal neoplasms [1].

Synchronous adrenal ML with Renal Cell Carcinoma (RCC) is very rare. Moreover, this combination occurring on the ipsilateral side is even rarer. We searched the literature since 1993 to look for well documented cases of co-existing adrenal MLs with RCC and found eight such cases. Out of these eight cases, only four were found to involve the ipsilateral kidney. We hereby report an additional case of this rare association of adrenal ML with Clear Cell RCC (CCRCC) occurring synchronously in the same kidney and managed concurrently.

Case report

A 65-year-old male presented with complaints of a single episode of gross, painless hematuria and spontaneous lithuria associated with severe suprapubic pain. He was evaluated for the same in other health-care facilities and was found to have a mass in the right kidney along with another mass in the right adrenal gland. He was thus referred to the Urology Department of our tertiary care institute for further management. There was no history of fever, lower urinary tract symptoms, or any other urological or systemic complaints. He was diabetic for the past

Table 1: Summary of case reports of adrenal gland myelolipoma presenting with renal cell carcinoma.

S.No.	Article	Age/Sex	Symptom	Associations	Laterality	Side of adr ML	Size of adr ML[a]	Side of RCC	Size of RCC[a]	Type & Grade of RCC	Stage of RCC	Management	Concurrent Surgery / different surgeries	Complications	Follow-up
Ipsilateral															
1.	Bahrami et al., 2009 Annals of Diagnostic Pathology [10]	NS	NS	NS	I/P	NS	6.5 cm	NS	2.5 cm	CCRCC	NS	Radical nephrect	NS	NS	NS
2.	Lewitowicz et al, 2014 Romanian Journal of Morphology & Embryology [11]	69 yr/M	Flank pain and abdominal pain for four months	None	I/P	Left	6.5 cm	Left	3.5 cm	CCRCC (Furhman Grade 4) with undifferentiated cell component, Sarcomatoid component and ganglioneuroma	pT1b	Trans-abd nephrect	Concurrent	None	NR
3.	Senthil K et al, 2015Case Reports in Urology [12]	60 yr/M	No specific symptom. Diagnosed incidentally on USG	None	I/P	Right	4 cm	Right	4 cm	CCRCC (Fuhrman Grade 2	pT1b	Lapros right nephrect with adrenalect	Concurrent	None	NS
4.	**Our case**	65 yr/M	Hematuria and spontaneous lithuria associated with severe suprapubic pain	Diabetes Mellitus & H/O hydrocoele 15 years back	I/P	Right	2.5 cm	Right	6.5 cm	CCRCC (WHO/ISUP Grade 1)	pT1b	Laparos right radical nephrect with adrenalect	Concurrent	None	NR (6m)
Contralateral															
5.	Matsumoto et al., 1993, Hinyokika Kiyo [13]	4 yr/M	Left flank mass	None	C/L	Right	6 cm	Left	11 cm	CCRCC (Fuhrman Grade 2)	pT2b	Left nephrect with right adrenalect	Concurrent	None	NS
6.	Hofmockel et al., 1995, The Journal of Urology [4]	59 yr/M	Hypertensive crisis	Hypertension	C/L	Right	11 cm	Left	5 cm	CCRCC (Fuhrman Grade 2)	pT2b	Left nephrect followed by right adrenalect 2 months later	Two surgeries	None	NS
7.	J. Padilla-Pineapple et al., 2015, Mexican Journal of Urology [7]	44 yr/M	Gross hematuria and left flank pain	None	C/L	Right	6 cm	Left	7 cm, lower pole	CCRCC (Fuhrman Grade 2)	pT3	Lapros left nephrect with right adrenalect	Concurrent	None	NS
8.	Jindal et al., 2022, Asian Journal of Urology [2]	54 yr/M	Discomfort in the right hypochondrium for 1 month	Hypertension	C/L	Right	1.2 cm	Left	6.1 cm	CCRCC (Fuhrman Grade ,2)	pT1b	Lapros left nephrect with right adrenalect	Concurrent	None	NS
Side of not specified															
9.	Sharma MC et al., 1997 Urologica Internationalis [9]	56/M	Hematuria	NS	NS	NS	2 cm	NS	NS	CCRCC	NS	Radical nephrect	Concurrent	None	NR

Symbols: a: Maximum dimension

Abbreviations: Adr.: Adrenal; ML: Myelolipoma; RCC: Renal Cell Carcinoma; NS: Not Specified; I/P: Ipsilateral; CCRCC: Clear Cell RCC; Trans-Abd: Trans-Abdominal; Nephrect: Nephrectomy; USG: Ultrasonography; Lapros: Laproscopic; Adrenalect: Adrenalectomy; NSTEMI: Non-ST Elevated Myocardial Infarction; DAPT: Dual Antiplatelet Therapy; M: Months; H/O: History of; WHO/ISUP: World Health Organization/ International Society of Urological Pathology; C/L: Contralateral; NR: No Recurrence.

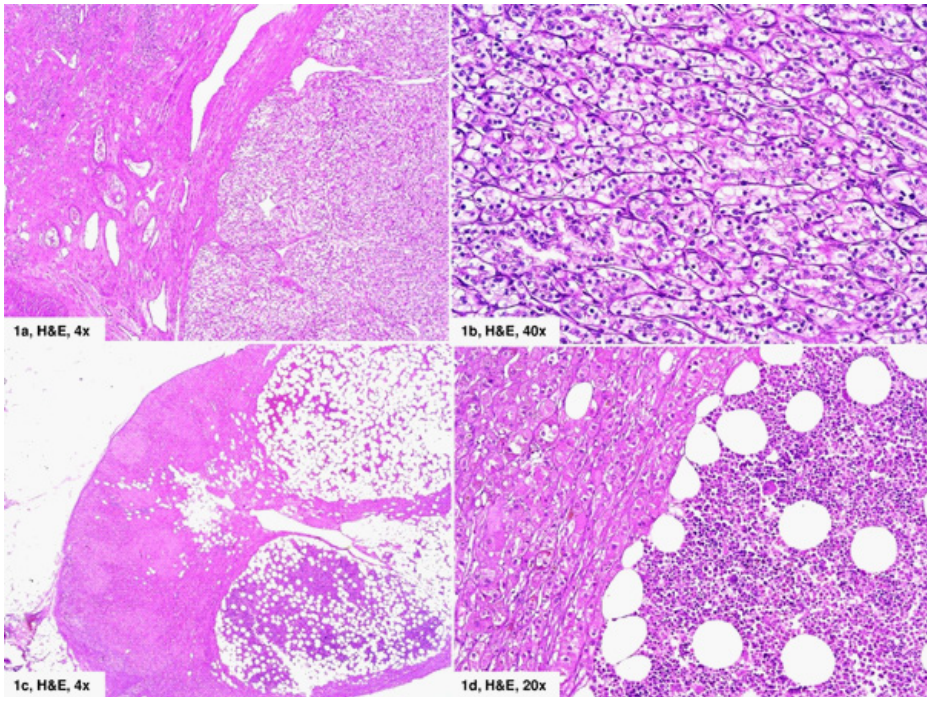

Figure 1: Photomicrographs of the Adrenal Myelolipoma (ML) and Clear Cell Renal Cell Carcinoma (CCRCC). A-ML with adjacent adrenal gland parenchyma (H&E, 4x); B-ML is composed of hemotopoietic elements and interspersed mature adipose tissue; adjacent adrenal gland parenchyma is also seen (H&E, 20x); C-CCRCC with adjacent renal parenchyma (H&E, 4x); and D-CCRCC disposed of in sheets, nests, and vague nodules. Tumor cells display WHO/ISUP grade 1 nuclear features and clear to pale eosinophilic cytoplasm (H&E, 40x).

15 years. He also gave a history of having undergone surgery for hydrocoele 15 years ago. His general and systemic examinations were within normal limits. His haematological parameters and urine analysis at our institute were normal.

The abdominal Contrast-Enhanced Computerized Tomography (CECT) revealed an ill-defined heterogeneously enhancing hypo-dense lesion measuring 5.6 x 6.3 cm in the mid and upper pole of the right kidney with peri-nephric fat stranding, along with a 5 mm calculus of 231 Hounsfield density (HU) in a mildly dilated pelvi-calyceal system. In addition, the right adrenal gland showed a well-defined hypodense lesion measuring 2.1 x 1.7 cm. No significant lymphadenopathy or any other abnormality was detected. Multiparametric magnetic resonance imaging (mpMRI) revealed similar-sized T1-hypointense and T2-hypointense exophytic lesion displaying contrast enhancement in the right kidney, along with T1/T2 hyper-intense lesion exhibiting a signal drop on fat suppressed images located in the body of right adrenal gland. Radiological differential diagnoses included adrenal adenoma and myelolipoma.

In view of the adrenal nodule, an endocrine consultation was taken to evaluate its functionality, which revealed it to be non-functional. Other laboratory parameters were within normal limits. The patient underwent laparoscopic right radical nephrectomy. The post-operative period was uneventful, and the patient was discharged in stable condition.

Grossly, the right radical nephrectomy specimen measured 17 x 7.5 x 7 cm. The cut surface showed a firm and solid tumor occupying the upper pole and mid-region of the right kidney, measuring 6.5 x 5.5 cm. The tumor was heterogeneous, predominantly greyish-yellow, with foci of hemorrhagic areas. The right adrenal gland was received in four fragments with attached fatty tissue, largest measuring 2.5 x 2 cm. The cut surface was glistening brown with fatty areas.

On microscopy, the renal tumor was disposed of in sheets, nests, and vague nodules with intervening thin fibrovascular septae (Figure 1a). The tumor cells were large, round, to polygonal, displaying moderately pleomorphic nuclei with dispersed chromatin, inconspicuous nucleoli, and moderate to abundant amount of clear to pale eosinophilic cytoplasm (Figure 1b). Intervening areas showed congested vessels, foci of hemorrhage, and lymphoplasmacytic infiltrate. Renal sinus, capsule, ureteric, and vascular resection margins were tumor-free. Uninvolved renal parenchyma showed few sclerosed glomeruli, periglomerular fibrosis, tubular atrophy, and moderate to dense mononuclear interstitial infiltrate. Adrenal tumor revealed hematopoietic elements comprising erythroid cells, myeloid cells, and a fair number of megakaryocytes, along with interspersed mature adipose tissue (Figures 1c and 1d). Foci of hemorrhage were noted. An unremarkable adrenal gland parenchyma with an overlying capsule was seen surrounding the tumor. With the above histopathological findings, the diagnosis of clear cell renal cell carcinoma, i.e., CCRCC (WHO/ISUP grade 1), in the right kidney and myelolipoma in the right adrenal gland was rendered. The pathological tumor stage was pT1b.

The patient was kept on follow-up and showed no signs of tumor recurrence, metastasis, or development of any other tumor or abnormality after 6 months post-surgery.

Discussion

Myelolipomas are uncommon benign adrenal neoplasms. They occur in a wide age group ranging from 16 months to 84 years and are seen twice as commonly on the right side than the left, as in our case [1]. It has a female predilection.

MLs are usually non-functioning. Thus, most cases are asymptomatic and are diagnosed incidentally on radiological scans for unconnected causes [2]. Adrenal MLs amount to ~6% of ad-

renal incidentalomas [3]. On autopsy, they are found in ~0.08 to 0.2% of cases [3,4]. In symptomatic patients, abdominal or flank pain is the most common manifestation [5]. Hofmockel et al [4] reported that their case got hospitalized for a hypertensive crisis. Large-sized MLs can manifest due to associated complications like retroperitoneal hemorrhage, rupture, and abscess [1]. Cases of functional MLs with hormonal hypersecretion have also been described, which can be adreno-cortical adenomas with myelolipomatous elements [1]. Our case presented with hematuria along with lithuria associated with suprapubic pain. However, this may be attributed to the co-existing RCC.

The etio-pathogenesis of MLs is still unclear and includes various hypotheses, like stress- or infection-induced metaplastic changes in mesenchymal cells of the adrenal cortex; hyperplasia or metaplasia of myeloid cells relocated during embryogenesis; degeneration of adrenocortical adenomas or hyperplastic nodules; undifferentiated stromal cell metaplasia; and abnormal hormone-induced variations in mesenchymal stem cell functions [6]. Association with chromosomal translocation t(3;21)(q25;p11) has also been reported.

The most sensitive radiological test for identifying the MLs is presumed to be a CT scan, owing to its tissue density (30-100 HU), which is equivalent to fat, and its well-circumscribed nature [7]. Radiological differentials include adrenal lipoma and liposarcoma. Calcifications can be occasionally identified [8].

Grossly, MLs are usually well-demarcated tumors located in the adrenal cortex. They are variably yellow to red-colored tumors ranging in size from 4-6 cm. Still, larger tumors also occur, and giant tumors as large as 38 cm have also been reported [1].

On histopathology, the tumor displays a variable amount of mature adipocytes along with marrow elements. Focal calcifications and metaplasia can also be identified occasionally. Histopathological differentials include adreno-cortical adenoma, lipoma/liposarcoma, teratoma, and angiomyolipoma. Immunohistochemistry or molecular studies are of no clinico-histopathological significance [8].

MLs have been documented with obesity, hypertension, hormonal disorders, chronic diseases, and benign as well as malignant neoplasms including, RCCs [4,9]. Adrenal MLs occurring synchronously with RCC have rarely been reported in the literature. They are reported to have a concurrent incidence of 0.1% [7]. Table 1 summarizes all eight cases of adrenal MLs with associated RCCs, along with ours [2,4,7,9-13]. Four out of eight cases were reported to have ML and RCC in the contralateral kidney. One of the cases didn't specify the laterality of the tumors. The remaining three cases represented tumors in the same kidney, as ours. These were reported by Bahrami et al [10], Lewitowicz et al. [11], and Senthil K. et al. [12]. In all eight cases, the RCC is of the clear cell type (CCRCC). Clear-cell RCC is the most common renal neoplasm in general. At the same time, it forms ~60% of all renal neoplasms reported with MLs as well [7]. Bahrami et al [10] reported 80 cases of RCC with co-existing adrenal gland lesions, out of which only one was that of ML, while the others were those of metastasis or adrenal adenomas.

Bilateral adrenal MLs and extra-adrenal MLs have also been reported [8,12,14]. Extra-adrenal ML can occur rarely in ~0.4% of cases [5,8]. Extra-adrenal MLs have been reported in the kidney, sacro-pelvic region, thoraco-mediastinal region, retroperitoneum, stomach, liver, and even thyroid glands [8]. About four cases of renal MLs have been reported in the literature. Of note, one of these cases reported by Bangash et al [5] had the simultaneous presence of CCRCC in the ipsilateral kidney.

MLs are considered benign, displaying no malignant transformation on observational follow-up [1]. However, chances of an increase in size, rupture, or hemorrhage always exist. Thus, if opting for expectant management, they should be strictly kept under radiological surveillance [5]. Laparoscopic surgical excision is considered to be the gold standard of management and is indicated for symptomatic tumors or those larger than 5 cm in size to avoid the risk of spontaneous hemorrhage [2].

When MLs occur along with RCC, the treatment of RCC gains the upper hand. However, when MLs are giant-sized, concurrent removal of the ML may be necessary [2]. Zografos et al. [15] advocated laparoscopic excision of the MLs in cases of favorable tumor characteristics, patient-dependent factors, and the availability of surgical experience and expertise. Laparoscopic nephrectomy with adrenalectomy is chosen over the trans-abdominal approach owing to its feasibility and safe nature [12]. Most reported cases mention concurrent removal of both the ML and RCC together, whether in the same or contralateral kidneys. Hofmockel et al. [4] excised the tumors in two subsequent surgeries.

Conclusion

Myelolipomas are rare adrenocortical tumors of uncertain origin. They may rarely occur with concurrent RCCs. To date, eight such cases have been reported. Of these, three have occurred on the ipsilateral side. Our manuscript puts forward yet another case of adrenal gland myelolipoma which presented with synchronous ipsilateral renal cell carcinoma and was managed by laparoscopic right radical nephrectomy. The case emphasizes that even though the combination of myelolipoma with renal cell carcinoma is rare, it does occur and has been reported in the literature. Thus, both surgeons and pathologists should be mindful of the same in the diagnosis and management of such cases.

Declarations

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Author contribution: Singh A was responsible for designing, literature search and manuscript preparation. Verma R was responsible for conceptualizing, manuscript editing and review. She is also the corresponding author. Mathur V was responsible for data acquisition.

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