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Renal cell carcinoma, synchronous pheochromocytoma and papillary urothelial neoplasm with low Malignant Potential

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AIM: *This case report descraes a patient who was diagnosed with both clear cell renal carcinoma and pheochromocytoma of the surrenal glands.*

MATERIALS AND METODS: *Ultrasonographic imaging examination, magnetic resonance imaging and thorax computed tomography performed with IV contrast scan techniques were used to diagnose and examine the mass.*
RESULTS: *The patient was diagnosed with a mass in his kidney and clear cell renal cell carcinoma. There was a casual pheochromocytoma in the surrenal gland at the same time. In addition, histopathological examination revealed a papillary urothelial neoplasm of low malignant potential (PUNLMP).*
DISCUSSION: *It is interesting in this case that the patient did not have any other complaints other than left side pain due to the mass in the kidney. It is notable that there were no clinical or radiological findings that may be compatible with the diagnosis of pheochromocytoma in this case.*
CONCLUSION: *This study reports a significant result that there was cooccurrence of pheochromocytoma (PC) and clear cell renal cell carcinoma along with VHL disease.*

KEY WORDS: Clear cell carcinoma, Pheochromocytoma, Von Hippel-Lindau

Introduction

Pheochromocytoma is a tumor that originates from chromophobe cells of the adrenal medulla and is typically seen in women unilaterally in their 40-50s [1]. While sporadic cases tend to be unilateral, cases with MEN-2 are multicentric and bilateral. These tumors are referred to the hospital with symptoms such as hypertension, headache, excessive sweating, tachycardia and chest pain due to catecholamine secretion. Pheochromocytoma is found in 4-10% of incidental cases. The patient in the present research was of an advanced age; except for his complaints due to a renal mass, there were no other remarkable clinical findings due to pheochromocytoma found in the adrenal gland during the surgery. It was also interesting to find a premalignant lesion in the bladder in a VHL TYPE-2 case.

Material and Methods

In this case, a 61-year-old male patient was admitted to the urology service with left side pain, inability to urinate, and blood in urine. His past, personal, and family histories were unremarkable. Urinary tests were observed as erythrocytes: (+3), protein: (+1), leukocytes (+2), and urine density 1,017. Blood tests showed no significant findings other than elevated C-reactive pro-

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tein. An ultrasonographic imaging examination, magnetic resonance imaging examination, histopathological examination and thorax computed tomography were performed to detect the mass.

Results

The ultrasonographic imaging examination revealed a mass in the left kidney. The magnetic resonance imaging examination detected a solid mass with a medium size of 8.5x7x7 cm, which encompassed the upper and middle part of the left kidney and extended towards the superior region. There were no remarkable findings in the other kidney. The liver was also examined and no evidence was found other than Grade 1 hepatosteatosis. The gallbladder, pancreas, spleen, surrenal glands, testicles and attachments were normal, and there were no pathological findings. In addition, there were no abnormal lymph nodes in the free fluid in the abdomen or on pathological images. Bladder filling was found normal, and pathological lesions were not observed in the lumen (intraluminal). In the thorax computed tomography performed with IV contrast scan, no image of active infiltration or nodular lesion was observed in the lung pulmonary parenchyma.

Furthermore, no anomalies, cysts or masses were detected in the mediastinal region, in the main bronchi and veins or in the cardiac region. Pleural thickening, cyst or effusion were not monitored. With these findings, surgical operation was planned due to the renal mass in the case. Bladder biopsy was performed due to the patient's urinary complaints during left radical nephrectomy and left adrenalectomy.

Histopathological examination revealed a mass with necrotic appearance and central hemorrhage, 8.5x7x7 cm in size, including the upper and middle parts of the left kidney. A 2.3x0.5 cm black area was also observed in the adrenalectomy material. This area was located in the surrenal gland and did not spread out of the surrenal tissue. Histopathological examination showed that the tumoral mass was not outside of the renal capsule and not more than 0.1cm close to the renal hilum. Vascular and neural invasion were not observed. The tumor was not observed at the surgical boundary of the ureter, in renal artery or vein. Immunohistochemical (IHC) examination with the paraffin blocks of the tumor mass indicated that the mass was positive for EMA, CD10, and pan-cytokeratin staining and negative for synaptophysin, chromogranin, NSE and S-100 staining (Fig. 1).

Following this, IHC performed on the suspicious area in the surrenal gland showed positive for synaptophysin, chromogranin and NSE staining and negative for pan-cytokeratin staining. Sustentacular cells were also positive for S-100 staining. Histochemical examination with PAS indicated some positive accumulations. The reticular structure was disrupted with reticulin staining. These

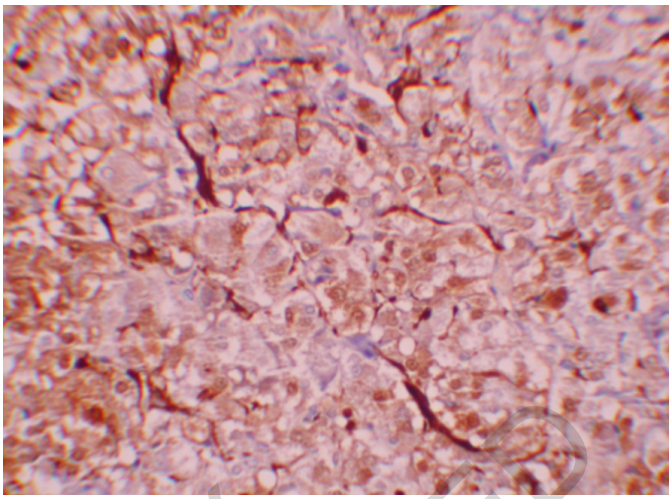

Fig. 1: Sustentacular cells S-100 staining in pheochromocytoma.

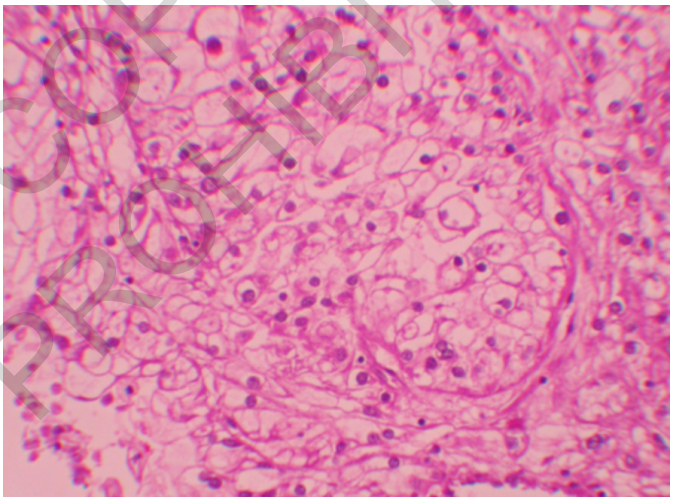

Fig. 2: Clear cell renal carcinoma Hematoxylin & Eosin 200.

histopathological, histochemical, and immunohistochemical findings indicated clear cell renal cell carcinoma and pheochromocytoma in tumoral lesions in the surrenal gland (Fig. 2).

During the histopathological examination of the bladder biopsy, a papillary urothelial neoplasm of low malignant potential (PUNLMP) was observed in the bladder. No anomalies were found in the postoperative blood and urinary tests, and no complications were filed for the patient at the 6-month and 1-year follow-ups.

Discussion

Clear cell renal cell carcinoma is considered the kidney's most common malignant tumor [2] Von Hippel Lindau syndrome (VHL) is an autosomal dominant hereditary syndrome characterized by different vascular tumors[3].

VHL is a genetic disease that remains autosomal dominant and emerges from a germline mutation of a VHL tumor suppressor gene (TSG). This gene is located on the short arm of chromosome 3. Retinal and central nervous system hemangioblastoma, clear cell renal cell carcinoma, pheochromocytoma, pancreatic islet tumors, endolymphatic sac tumors, renal and pancreatic cystadenomas, and epididymal cystadenoma are mostly diagnosed in men [3]. Previous studies showed that tumors were not found in VHL Type 1 cases but were mostly seen in Type 2 cases [4,5]. It is generally detected with clinical findings in these patients. The degree of mutation in the VHL gene determines the clinical course of pheochromocytoma.

While the overall risk of malignancy in pheochromocytoma is usually approximately 10%, the rate in VHL disease seems to be higher than this [6].

Pheochromocytoma can be observed with some clinical symptoms, such as headache, sweating, palpitations and hypertension, due to catecholamine release. It is rare to see it without clinical symptoms in patients.

Hypertension is at least observed in the patients [6,9]. In a retrospective study conducted by Mantero et al., 4.2% of the random adrenal masses were pheochromocytomas [7].

The cooccurrence of pheochromocytoma (PC) and clear cell renal cell carcinoma is not very common[8]. Previous studies have shown that renal cell carcinoma and related findings in VHL disease can determine the course of the disease and be one of the reasons for mortality[10,11]. Kidney tumors are often detected by computed tomography in VHL disease. The sizes of these tumors are 3 cm and below. The survival time of patients with this tumor can increase with tumor resection and nephron protecting surgery.

In the present study, no hypertension or cardiac problems were observed in the patient despite him being old. His side pains and urinary complaints led to urinary system-related diseases. A renal mass was first detected with USG and MRI. Histopathological examination revealed that the tumor was 8.5x7 cm. A large renal tumor is known to be a criterion of poor prognosis [12].

The additional diagnosis of pheochromocytoma with the patient in this study indicated that the patient had VHL disease. Interestingly, during the histopathological exam of the biopsy from the patient's bladder, a papillary urothelial neoplasm of low malignant potential was noted along with pheochromocytoma and clear cell carcinoma. It is known that various tumors can develop in VHL syndrome.

However, it is very rare to find a case such as this with lesions related to the bladder [13]. Two similar cases were found in previous studies. First, in a study conducted by Kinbara et al., urinary bladder carcinoma was found along with a renal tumor in a systematic evaluation of a 31-year-old patient [13]. Second, Dogra et al. reported a case of urinary bladder metastasis along with renal cell carcinoma in a patient with VHL disease [14].

Conclusion

The cooccurrence of pheochromocytoma (PC) and clear cell renal cell carcinoma is very rare. This study reports a significant result that there was cooccurrence of pheochromocytoma (PC) and clear cell renal cell carcinoma along with VHL disease. This result is important also because it supports the previous studies showing that renal cell carcinoma and related findings in VHL disease can be one of the reasons for mortality.

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