Clinical and Experimental Health Sciences

Review / *Derleme*

Juxtaglomerular Cell Tumor (Reninoma): A Case Report and Mini-Review

Jukstaglomerüler Hücreli Tümör (Reninoma): Vaka Sunumu ve Literatür Derlemesi

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Abstract

Reninomas are rare tumors derived from juxtaglomerular cells. Here, we report a case of a 17-year-old male patient who presented to our outpatient clinic with secondary hypertension and flank pain. Initial work-up revealed hypokalemia, and magnetic resonance imaging (MRI) revealed a solid lesion as a 4.8×4.8-cm contrast-enhanced exophytic mass. He underwent open nephron-sparing surgery, and the lesion was excised. The pathological study revealed a juxtaglomerular cell tumor (reninoma). Shortly after the surgery, all medications were withdrawn, and his blood pressure and hypokalemia normalized. This case can lead physicians to better understand the importance of the management of reninomas as a curable cause of secondary hypertension and also points out the importance of diagnostic care.

Keywords: Reninoma, secondary hypertension, nephron-sparing surgery, diagnostics

Öz

Reninoma, jukstaglomerüler hücrelerden köken alan nadir bir tümördür. Bu çalışmamızda sekonder hipertansiyon ve yan ağrısı ile üroloji polikliniğine başvuran 17 yaşında bir erkek hastayı ve ardından literatürde reninoma ile ilgili bilgileri sunmayı amaçladık. Hastanın yapılan değerlendirmesinde hipokalemik olduğu görüldü ve çekilen batın manyetik rezonans (MR) görüntülemesinde sağ böbrekte 4.8x4.8 cm'lik kontrast tutan ekzofitik lezyon saptandı. Hastaya açık nefron koruyucu cerrahi operasyon uygulandı ve patolojik inceleme ile eksize edilen lezyonun jukstaglomerüler hücreli tümör (reninoma) olduğu saptandı. Operasyondan kısa bir süre sonra hastanın hipertansiyon tedavisi amacıyla aldığı tüm ilaçlar kesildi ve kan basıncının normal seyrettiği ve hipokaleminin ortadan kalktığı görüldü. Bu vaka, sekonder hipertansiyonun sebeplerinden biri olan reninoma tedavisinin önemini ve tanısal yaklaşımın tedavinin temeli olduğunu gösteren, klinisyenlere yön verebilecek önemli bir vakadır.

Anahtar kelimeler: Reninoma, sekonder hipertansiyon, nefron koruyucu cerrahi, tanısal inceleme

INTRODUCTION

Reninomas are rare tumors derived from juxtaglomerular cells. They are generally discovered during the work-up for secondary hypertension and hypokalemia. We report a case of reninoma diagnosed after presentation with secondary hypertension and afterwards treated with nephron-sparing surgery, along with a mini-review of the literature focusing on the diagnostic work-up and treatment outcomes.

CLINICAL RESEARCH and CONSEQUENCES

A 17-year-old male patient presented to our outpatient clinic with secondary hypertension and flank pain. He was already on anti-hypertensive medication that kept his blood pressure under control, but he was not evaluated for etiological causes of secondary hypertension. On initial work-up, he was hypokalemic with a potassium value of 2.9 mEq/L. Ultrasonographic examination revealed a 4-cm solid lesion in his right kidney. MRI confirmed the solid lesion as a 4.8×4.8-cm contrast-enhanced exophytic mass (Figure 1). On May 2015, he underwent open nephron-sparing surgery, and the lesion was excised with clear surgical margins (Figure 2). The pathological study revealed a juxtaglomerular cell tumor (reninoma). Shortly after the surgery, all medications were withdrawn; his blood pressure normalized, and his potassium levels increased to 3.9 mEq/L. After an uneventful follow-up, he was fully recovered and discharged on post-operative day 3.

Macroscopically, the size of the mass and the tumor was 6×6×5.5 cm and 5×4.5×4.4 cm, respectively. The tumor originated from juxtaglomerular cells and exhibited the vascular cell surface marker CD34. The tumor consisted of confluent cultures of elongated smooth muscle actin (SMA)-positive cells producing high amounts of renin (Figure 3, 4).

Secondary hypertension is one of the interesting topics for the urologists due to potentially treatable causes. Refractory hypertension before 20 or after 50 years of age should be evaluated for underlying causes. Approximately 5% or these patients have an underlying cause, and with detailed investigation, these causes can be identified and treated accordingly (1). Among the possible underlying causes,

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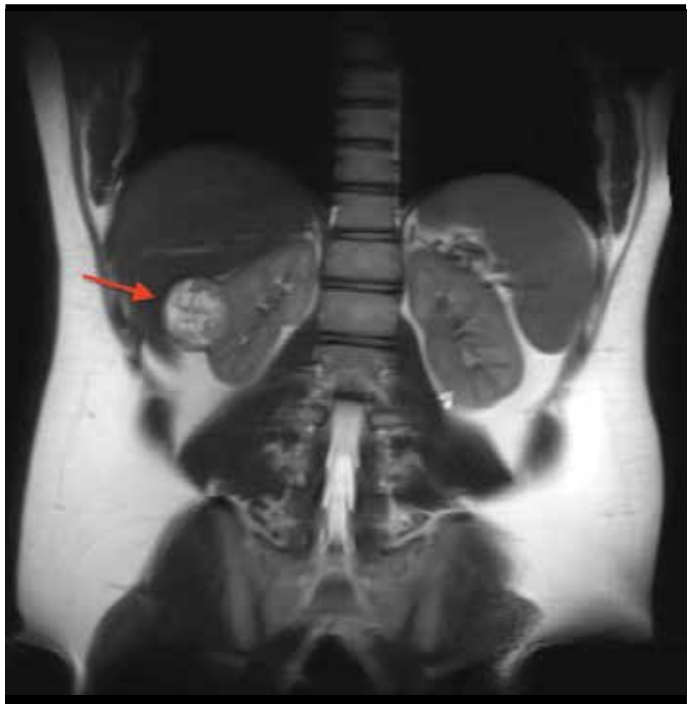

Figure 1. Contrast-enhanced MRI of the patient prior to surgery

Figure 2. Macroscopic view of the excised tumor

renovascular hypertension, primary hyperaldosteronism, and pheochromocytoma are the most encountered; but less frequent causes such as chronic pyelonephritis, nephroblastoma, renin-producing tumors, and renal cell carcinomas should be kept in mind (2-5).

Here, we report the case of a 17-year-old boy with hypertension and hypokalemia who was eventually diagnosed to have a renin-secreting tumor and was treated successfully with nephron-sparing surgery and recovered without complications. The importance of this case is the diagnosis of reninoma, a rare tumor worldwide, and its potential of curability with appropriate treatment.

Reninomas are rare juxtaglomerular tumors that produce considerable amounts of renin and cause hypertension and hypokalemia. The first reninoma case was identified by Robertson et al. (6) in 1967.

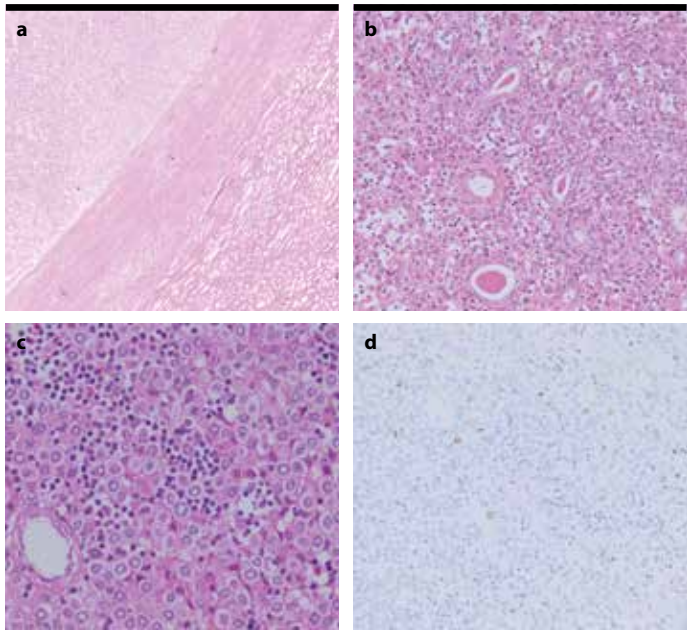

Figure 3. a-d. Microscopic appearance of the pathology specimen. (a) Well-encapsulated tumor nodule on x4 magnification (normal renal parenchyma on the right); (b) Well-developed tubules lined by cuboidal cells, similar to collecting duct epithelium on ×20 magnification; (c) Classic glomoid appearance of round-polygonal tumor cells with slightly eosinophilic cytoplasm and distinct borders on ×40 magnification, stroma exhibits focal areas of lymphoplasmacytic infiltrate; (d) Low proliferation index seen with Ki-67 labeling on x20 magnification (3%)

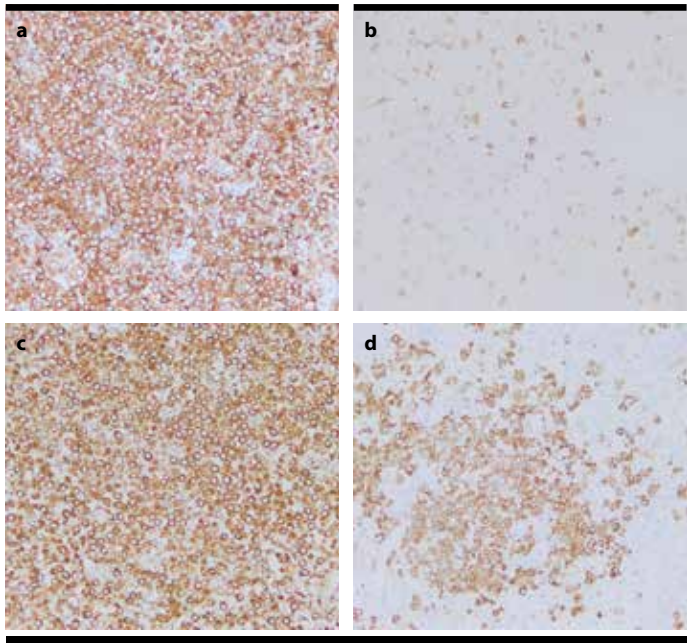

Figure 4. a-d. Microscopic appearance of the pathology specimen. (a) Tumor cells showing diffuse and strong immunoreactivity with CD34 on ×20 magnification; (b) Scattered tumor cells stained positive with CD117; (c) Tumor cells showing diffuse and strong immunoreactivity with vimentin on ×20 magnification; (d) Focal positive areas with smooth muscle actin (SMA) on ×20 magnification)

Since then, approximately 100 cases have been identified in the literature (7-9). This case report is the second case of a reninoma reported in Turkey, the first being reported by Karaosmanoglu et al. (10)

in 2015. The diagnosis is generally delayed because patients usually present with non-specific symptoms such as headache due to hypertension, malaise, nausea, and fatigue (7, 11). Our patient was an adolescent boy similar to most of the cases in the literature (7, 8, 12). He had controlled hypertension with one anti-hypertensive medication, and unlike the symptoms reported in the literature, he had flank pain, which was hypothesized to be a cause of renal capsule stretching due to the large tumor mass.

Gottardo et al. (8) and Mete et al. (12) reported in their case reports similar results with 14- and 16-year-old adolescents with hypertension who were subsequently diagnosed with reninomas. Both patients underwent nephron-sparing surgeries and recovered without further symptoms.

With high amounts of persistent renin secretion by the juxtaglomerular cells of reninoma, angiotensin activation and aldosterone secretion is stimulated. As a result of renin–angiotensin–aldosterone system activation, peripheral vasoconstriction and salt retention occurs, and this situation leads to systemic hypertension. High amounts of aldosterone causes high amounts of potassium loss in urine due to sodium–potassium exchange by the principal cells of collecting duct; consequently, potassium stores in the body are depleted, and as a result, hypokalemia ensues (13). In cases of hypertension and hypokalemia, renin-mediated causes should be kept in mind and the choice of anti-hypertensive medication should be either renin inhibitors (aliskiren), angiotensin-converting enzyme (ACE) inhibitors (ACEI), or angiotensin II receptor blockers (ARB). ACEIs and ARBs are the most commonly used medications in clinical practice (13). Our patient was taking an ARB, which successfully controlled his blood pressure.

Diagnosis of renin-secreting juxtaglomerular cell tumors should be established systematically in a young patient with secondary hypertension along with hypokalemia. The diagnosis of high renin secretion is based on very high plasma renin activity following acute administration of ACEI treatment, and with an ACEI, the activity shows inconsistency of the autonomy of the tumor. The primary role of the kidney in terms of regulating the arterial pressure via renin secretion is of high importance, and in cases of secondary hypertension, the involvement of renin secretion should be determined to reach a final diagnosis. Therefore, the discovery of a renin-secreting tumor is a life-saving diagnosis. CT scan is very useful in establishing the localization of the tumor (14).

A carefully taken medical history combined with a good clinical evaluation and appropriate laboratory work-up is generally enough to establish a diagnosis of a renin-mediated cause. In these cases, MRI and contrast-enhanced CT are usually able to identify reninomas with detection rates approaching 100% in some series (7, 15). However, small lesions can be difficult to diagnose in some cases. Dong et al. (16) reported in their small series that CT failed to detect the tumor in 2 patients before and 1 patient after contrast enhancement.

Measurement of renin and aldosterone blood levels is crucial in diagnosis of renin-mediated hypertension. High levels combined with a normal renin/aldosterone ratio are suggestive of renal causes as the cause of hypertension. A high aldosterone level with a suppressed renin level points to an adrenal cause in which autonomous hypersecretion of aldosterone suppresses renin secretion by the kidneys, (13) whereas in renin secreting tumors, the plasma renin activity is very high. Blockage with beta-adrenergic blockers, ARBs, and ACEIs should be routinely performed to see if plasma renin activity is diminished. The persistence of high plasma renin activity despite appropriate blockage is suggestive of the diagnosis of extrarenal renin secretion (17).

An additional information is that in some cases, functional study of renal vein renin ratios (RVRR) can also assist in diagnosing and also lateralizing the lesion. Wong et al. (7) demonstrated in their review that RVRR has a sensitivity of 56% and specificity of 94% for confirming the correct side of reninoma. Wolley et al. (18) summarized in their study that even when the lesion is not visible on imaging modalities, RVRR can correctly localize the reninomas. In our patient, the lesion was a round lesion with a diameter of 4.8 cm and was easily localized on MRI. Also, we prefer not to perform selective venous sampling as this procedure is a more invasive technique. However, there is good evidence that it can help in diagnosis when all other diagnostic modalities are performed, and there is still doubt regarding the cause of secondary hypertension.

CONCLUSION

Secondary hypertension is a condition that should be evaluated thoroughly. Approximately 5% of the patients have specific conditions, and a careful and detailed investigation can identify these causes. Furthermore, these cases can be treated and cured successfully. This case can lead physicians to better understand the importance of the management of reninomas as a curable cause of secondary hypertension and also points out the importance of diagnostic care.

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REFERENCES

1. Viera AJ, Neutze DM. Diagnosis of secondary hypertension: an age-based approach. Am Fam Physician 2010; 82: 1471-8.
2. Baglivo HP, Sánchez RA. Secondary arterial hypertension: improvements in diagnosis and management in the last 10 years. Am J Ther 2011; 18: 403-15. [CrossRef]

3. Giacchetti G, Ronconi V, Lucarelli G, Boscaro M, Mantero F. Analysis of screening and confirmatory tests in the diagnosis of primary aldosteronism: need for a standardized protocol. J Hypertens 2006 24: 737-45. [CrossRef]
4. Espiner EA, Ross DG, Yandle TG, Richards AM, Hunt PJ. Predicting surgically remedial primary aldosteronism: role of adrenal scanning, posture testing, and adrenal vein sampling. J Clin Endocrinol Metab 2006; 88: 3637-44. [CrossRef]
5. Khorram-Manesh A, Ahlman H, Nilsson O, Friberg P, Odén A, Stenström G, et al. Long-term outcome of a large series of patients surgically treated for pheochromocytoma. J Intern Med 2005; 258: 55-66. [CrossRef]
6. Robertson PW, Klidjian A, Harding LK, Walters G, Lee MR, Robb-Smith AH. Robb-Smith, Hypertension due to a renin-secreting renal tumour. Am J Med 1967; 43: 963-76. [CrossRef]
7. Wong L, Hsu TH, Perlroth MG, Hofmann LV, Haynes CM, Katznelson L. Reninoma: case report and literature review. J Hypertens 2008; 26: 368-73. [CrossRef]
8. Gottardo F, Cesari M, Morra A, Gardiman M, Fassina A, Dal Bianco M. A kidney tumor in an adolescent with severe hypertension and hypokalemia: an uncommon case--case report and review of the literature on reninoma. Urol Int 2010; 85: 121-4. [CrossRef]
9. Kuroda N, Maris S, Monzon FA, Tan PH, Thomas A, Petersson FB, et al. Juxtaglomerular cell tumor: a morphological, immunohistochemical and genetic study of six cases. Hum Pathol 2013; 44: 47-54. [CrossRef]
10. Karaosmanoğlu AD, Onur MR, Shirkhoda A, Ozmen M, Hahn PF. Unusual benign solid neoplasms of the kidney: cross-sectional imaging findings. Diagn Interv Radiol 2015; 21: 376-81. [CrossRef]
11. Martin SA, Mynderse LA, Lager DJ, Cheville JC. Juxtaglomerular cell tumor: a clinicopathologic study of four cases and review of the literature. Am J Clin Pathol 2001; 116: 854-63. [CrossRef]
12. Mete UK, Niranjan J, Kusum J, Rajesh LS, Goswami AK, Sharma SK. Reninoma treated with nephron-sparing surgery. Urology 2003; 6: 1259. [CrossRef]
13. Trnka P, Orellana L, Walsh M, Pool L, Borzi P. Reninoma: an uncommon cause of Renin-mediated hypertension. Front Pediatr 2014; 2: 89. [CrossRef]
14. Torricelli FC, Marchini GS, Colombo JR Jr, Coelho RF, Nahas WC, Srougi M. Nephron-sparing surgery for treatment of reninoma: a rare renin secreting tumor causing secondary hypertension. Int Braz J Urol 2015; 41: 172-6. [CrossRef]
15. Kang SK, Chandarana H. Contemporary imaging of the renal mass. Urol Clin North Am 2012; 39: 161-70. [CrossRef]
16. Dong D, Li H, Yan W, Xu W. Juxtaglomerular cell tumor of the kidney--a new classification scheme. Urol Oncol 2010; 28: 34-8. [CrossRef]
17. Baruch D, Corvol P, Alhenc-Gelas F, Dufloux MA, Guyenne TT, Gaux JC, et al., Diagnosis and treatment of renin-secreting tumors. Report of three cases. Hypertension, 1984; 6: 760-6. [CrossRef]
18. Wolley M, Gordon RD, Stowasser M. Reninoma: the importance of renal vein renin ratios for lateralisation and diagnosis. Am J Nephrol 2014; 39: 16-9. [CrossRef]