International Journal of Clinical and Experimental Medical Sciences
2024, Vol. 10, No. 2, pp. 25-28
https://doi.org/10.11648/j.ijcems.20241002.12

Case Report

Pure Metastatic Papillary Renal Cell Carcinoma Without Renal Mass: A Case Report and Literature Review

Pay Enes*, Ibrahim Hacibey, Serhat Yentur, Salih Zeki Sonmez, Atilla Semercioz

Bagcilar Training and Research Hospital, Istanbul, Turkey

Abstract

Renal cell carcinoma (RCC) is the most common solid lesion in the kidney and accounts for approximately 90% of all kidney malignancies. Metastasis usually occurs a few years after the diagnosis of RCC, but metastases can be seen at first presentation in some patients. Pure metastasis of RCC without kidney lesions is an extremely rare seen entity. Herein, we aimed to present a pure metastatic RCC (mRCC) in several lymph nodes without a kidney mass. A 41-year-old male was diagnosed with multiple lymphadenopathies based on imaging conducted after a work accident. No other lesion was detected. An excisional biopsy was performed on the supraclavicular lymph node. Histopathological examination of sample revealed a Type 2 papillary RCC metastasis. No primary lesion was observed in both kidneys in CT/MRI imaging. As a result, the patient was diagnosed as a pure metastatic papillary RCC and sunitinib treatment was started. After the treatment, metastatic lesions regressed, however, patient died due to COVID-19. In the literature, mRCC of unknown primary represents an aggressive metastatic malignancy and can be considered a poor prognostic factor in itself. However, in some cases as such in our patient, appropriate treatment could be beneficial in terms of metastatic regression. Pure metastatic RCC has been reported with only case reports and series. The treatment and prognosis in these patients are heterogeneous.

Keywords

Pure Metastasis, Renal Cell Carcinoma, RCC

1. Introduction

Kidney cancers constitute approximately 3% of all cancers and the highest incidence is seen in Western countries [1, 2]. Renal cell carcinoma (RCC) is the most common solid lesion in the kidney and accounts for approximately 90% of all kidney malignancies. The highest incidence is seen at the age of 60-70 years and there is a 1.5:1 dominance in men compared to women [3]. RCC includes different subtypes with specific histopathological and genetic features [4]. With approximately 99,200 new RCC cases and 39,100 kidney cancer-related deaths in the EU in 2018, there has been a 2% annual increase in the incidence of RCC over the past 20 years, both worldwide and in Europe [1]. The etiology of RCC includes lifestyle factors such as smoking, obesity, and hypertension [5].

Computed tomography (CT), ultrasound (US), and magnetic resonance imaging (MRI) are imaging modalities used to detect and characterize renal masses as solid or cystic [6]. Positron emission tomography (PET) is increasingly used in papillary RCC (pRCC), but PET is not currently a standard investigation in clear cell RCC (ccRCC) patients [7, 8].

*Corresponding author: enespay8964@gmail.com (Pay Enes)

Received: 20 December 2023; **Accepted:** 2 January 2024; **Published:** 27 August 2024

Due to the mutation in the von Hippel-Lindau gene, high amounts of VEGF (vascular endothelial growth factor) are produced. This results in increased angiogenesis, cell growth, metabolism, and immunosuppression [9].

There are three main types of RCC: ccRCC (70-80%), pRCC (%10-15) and chromophobic RCC (4-5%). The remaining 10% are renal pelvis carcinomas and unclassified groups [4]. In general, 60% of RCC patients, 87% of patients with stage T1a, and 36% of patients with stage 3 or 4 disease were diagnosed incidentally [10]. There are differences in prognosis between RCC subtypes in terms of tumor stage and grade and cancer-specific survival. When comparing different RCC subtypes, pRCC type I has a significantly lower risk of death compared to non-metastatic ccRCC and pRCC type II [11].

Metastasis usually occurs a few years after the diagnosis of renal primary cancer, but metastases can be seen at first presentation in up to 30% of patients [12]. The most common targets for metastases are the lung, bone, lymph nodes, adrenal glands, brain, liver, and contralateral kidney [13, 14]. However, pure metastasis of RCC without kidney lesions is an extremely rare seen entity. Herein, we aimed to present a pure metastatic RCC (mRCC) in several lymph nodes without a kidney mass.

2. Case Presentation

In December 2020, a 41-year-old male was diagnosed with right hilar, paraaortic and supraclavicular lymphadenopathy on imaging performed after a work accident in Germany. No other lesion was detected.

The patient was admitted to our clinic and an excisional biopsy was performed on the supraclavicular lymph node lesion. In samples consulted to pathology departments in 4 different centers, histopathological examination revealed a Type 2 papillary RCC metastasis. No primary lesion was observed in both kidneys in CT or MRI imaging. As a result, the patient was diagnosed as a pure metastatic papillary RCC patient and sunitinib treatment was started. After the treatment, metastatic lesions regressed, however, the patient died due to COVID-19 disease during the treatment phase.

3. Discussion

In the literature, pure metastatic RCC (mRCC) without a primary kidney mass is extremely rare and has been reported with only case reports and series. In patients without an identifiable kidney primary, tissue removal from the metastatic site is critical for diagnosis. The prognosis in these patients is heterogeneous.

When the literature is reviewed, there are 29 patients with pure mRCC cases without primary lesions, including our case [15-32]. The mean age of the patients was 61, 80 (from 34 to 83). 22 of them were male (75.8%) and the remainings were female (24.2%). Histological patterns of metastatic lesions were reported as ccRCC in 15 patients (51.7%), pRCC in 6 patients (20.7%), and unclassified in 8 patients (27.6%) [15]. Metastastatic localisations were the lung/pleura (n:6), lymph nodes (n:17), bone tissues (n:6), liver (n:5), soft tissues (n:6), adrenals (n:3), pancreas, epidural, parotid gland and pericardium (n:1 for each).

Out of 29 patients, 20 patients had metastasis on at least two different localisations. 22 patients were treated with chemotherapeutic agents including pazopanib, sunitinib, sorafenib, temsirolimus and everolimus, except that 7 patients did not receive any chemotherapeutic treatment. Surgical excision of the metastatic lesion was performed in seven patients as a treatment option for patients not receiving chemotherapeutic treatment.

4. Conclusion

Cancers of unknown primary location constitute 3% to 5% of all malignancies [31]. Cancers of unknown primary locations usually have poor outcomes and the average life expectancy is between 4-12 months [32]. In the literature, mRCC of unknown primary represents an aggressive metastatic malignancy and can be considered a poor prognostic factor in itself. However, in some cases as such in our patient, appropriate treatment could be beneficial in terms of metastatic regression.

There are opinions that they are very small tumors that metastasized early for mRCC of unknown primary. In 2 patients with mRCC detected without a primer, the primary tumor became visible on follow-up scans. However, a primary tumor was never seen in other patients who followed up. This also raises the hypothesis that the detected metastatic lesion may actually originate from immature embryological mesonephric remnants [17]. Another view is that these are ectopic kidney tissue [18]. We also see this embryological explanation in GCT (germ cell tumor) cancers from the extragonadal testis.

The number of non-primary mRCC cases is increasing with the developing technology and diagnostic methods. When sufficient data and analysis are available, treatment and follow-up protocols that can be applied to such patients will have a place in subgroups in urology and oncology guidelines.

Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] J. Ferlay, M. Colombet, I. Soerjomataram, et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries and 25 major cancers in 2018. Eur J Cancer, 103 (2018), pp. 356-387.

[2] Barajas-Ochoa Z, Suero-Abreu GA, Barajas-Ochoa A: Orbit and sinonasal metastasis as presenting sign of renal cell carcinoma. BMJ Case Rep. 2021, 14: https://doi.org/10.1136/bcr-2020-240588

[3] A. Thorstenson, M. Bergman, A. H. Scherman-Plogell, et al. Tumour characteristics and surgical treatment of renal cell carcinoma in Sweden 2005–2010: a population-based study from the national Swedish kidney cancer register. Scand J Urol, 48 (2014), pp. 231-238.

[4] H. Moch, A. L. Cubilla, P. A. Humphrey, V. E. Reuter, T. M. Ulbright. The 2016 WHO classification of tumours of the urinary system and male genital organs—part A: renal, penile, and testicular tumours. Eur Urol, 70 (2016), pp. 93-105.

[5] R. Tahbaz, M. Schmid, A. S. Merseburger. Prevention of kidney cancer incidence and recurrence: lifestyle, medication and nutrition. Curr Opin Urol, 28 (2018), pp. 62-79.

[6] C. Vogel, B. Ziegelmuller, B. Ljungberg, et al. Imaging in suspected renal-cell carcinoma: systematic review. Clin Genitourin Cancer, 17 (2019), pp. e345-e355.

[7] H. Ma, G. Shen, B. Liu, Y. Yang, P. Ren, A. Kuang. Diagnostic performance of 18F-FDG PET or PET/CT in restaging renal cell carcinoma: a systematic review and meta-analysis. Nucl Med Commun, 38 (2017), s. 156–163.

[8] R. Jena, T. A. Narain, U. P. Singh, A. Srivastava. Role of positron emission tomography/computed tomography in the evaluation of renal cell carcinoma. Indian J Urol, 37 (2021), pp. 125-132.

[9] Kaelin WG Jr. The von Hippel-Lindau tumour suppressor protein: O_2 sensing and cancer. Nat Rev Cancer 2008; 8: 865-73.

[10] N. S. Vasudev, M. Wilson, G. D. Stewart, et al. Challenges of early renal cancer detection: symptom patterns and incidental diagnosis rate in a multicentre prospective UK cohort of patients presenting with suspected renal cancer. BMJ Open, 10 (2020), p. e035938.

[11] N. Wagener, D. Edelmann, A. Benner, et al. Outcome of papillary versus clear cell renal cell carcinoma varies significantly in non-metastatic disease. PLoS ONE, 12 (2017), p. e0184173.

[12] Motzer RJ, Bander NH, Nanus DM. Renal-cell carcinoma. N Engl J Med 1996; 335(12): 865-75.

[13] Saitoh H, Hida M, Nakamura K, Shimbo T, Shiramizu T, Satoh T. Metastatic Processes and a Potential Indication of Treatment for Metastatic Lesions of Renal Adenocarcinoma. J Urol. 1982; 128 (5): 916–8.

[14] Bianchi M, Sun M, Jeldres C, Shariat SF, Trinh QD, Briganti A et al. Distribution of metastatic sites in renal cell carcinoma: a population-based analysis. Ann Oncol. 2012; 23(4): 973-80.

[15] A. Overby, L. Duval, M. Ladekarl, B. E. Laursen, F. Donskov. Carcinoma of unknown primary site with metastatic renal-cell carcinoma histologic and immunohistochemical characteristics: results from consecutive patients treated with targeted therapy and review of literature. Clin Genitourin Cancer, 17 (1) (2019), pp. e32-e37.

[16] Choi YR, Han HS, Lee OJ, et al. Metastatic renal cell carcinoma in a supraclavicular lymph node with no known primary: a case report. Cancer Res Treat 2012; 44: 215-8.

[17] Terada T. Extra-renal clear cell renal cell carcinoma probably arising from mesodermal embryonic remnants. Pathol Int 2012; 62: 291-3.

[18] Akkad T, Sergi C, Gozzi C, et al. Metastasizing renal cell carcinoma developing in a congenital ectopic and dysplastic kidney. Urol Int 2008; 81: 477-9.

[19] S. Bhatia, S. Ng, S. C. Hodder. Metastatic cutaneous head and neck renal cell carcinoma with no known primary: case report. Br J Oral Maxillofac Surg, 48 (3) (2010), pp. 214-215.

[20] Kumar RM, Aziz T, Jamshaid H, Gill J, Kapoor A. Metastatic renal cell carcinoma without evidence of a primary renal tumour. Curr Oncol 2014; 21: e521-4.

[21] Wayne M, Wang W, Bratcher J, Cumani B, Kasmin F, Cooperman A. Renal cell cancer without a renal primary. World J Surg Oncol 2010; 8: 18.

[22] Costantino C, Thomas GV, Ryan C, Coakley FV, Troxell ML. Metastatic renal cell carcinoma without evidence of a renal primary. Int Urol Nephrol 2016; 48: 73-7.

[23] Heary RF, Agarwal N, Barrese JC, Barry MT, Baisre A. Metastatic renal cell carcinoma, with a radiographically occult primary tumor, presenting in the operative site of a thoracic meningioma: long-term follow-up: case report. J Neurosurg Spine 2014; 21: 628-33.

[24] Wei EY, Chen YB, Hsieh JJ. Genomic characterisation of two cancers of unknown primary cases supports a kidney cancer origin. BMJ Case Rep 2015; 2015.

[25] Sorscher SM, Greco FA. Papillary renal carcinoma presenting as a cancer of unknown primary (CUP) and diagnosed through gene expression profiling. Case Rep Oncol 2012; 5 (2): 229-32. https://doi.org/10.1159/000339130

[26] Fayaz MS, Al-Qaderi AE, El-Sherify MS. Metastatic renal cell carcinoma with undetectable renal mass presenting as lymphadenopathy. CEN Case Rep 2017; 6: 36-8.

[27] Johnson MT, Bahnson RR, Zynger DL. Metastatic clear cell renal cell carcinoma to the adrenal gland without an identifiable primary tumor. Int J Urol 2012; 19: 92-3.

[28] Thamcharoen N, Chaiwiriyawong W. Papillary renal cell carcinoma presented with supraclavicular lymph node metastasis without renal primary lesion. World J Oncol 2013; 4: 50-3.

[29] Nagasaka M, Kukreja G, Abdulfatah E, Vaishampayan U, Sukari A. Role of molecular profiling in diagnosis of papillary renal-cell cancer presenting as cancer of unknown primary site. Clin Genitourin Cancer 2017; 15: e713-7.

[30] J Walton, J. Li, M. M. Clifton, R. L. Mori, A. M. Park, J. M. Sumfest. Metastatic clear cell renal cell carcinoma to the forearm without identifiable primary renal mass. Urology case reports, volume27 (2019) 100989.

[31] Fizazi K, Greco FA, Pavlidis N, Daugaard G, Oien K, Pentheroudakis G. Cancers of unknown primary site: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2015; 26(suppl 5): v133-8.

[32] Culine S, Kramar A, Saghatchian M, et al. Development and validation of a prognostic model to predict the length of survival in patients with carcinomas of an unknown primary site. J Clin Oncol 2002; 20: 4679-83.