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Sporadic renal cell carcinoma with widespread metastasis in young patient: A rare case report

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ABSTRACT

Renal cell carcinoma occurrence is increasing from time to time and known as one of the most common cancers worldwide. RCC usually found in older age and common acquired risk factors for RCC including obesity, hypertension, diabetes, smoking and long-term use of NSAIDs. As for genetic risk, it is noted that Von Hippel–Lindau gene involved in the pathogenesis of RCC. Many treatment strategies were developed for RCC with various outcome. Here, we present a sporadic clear cell renal carcinoma in young male without VHL gene mutation and survive for long term period despite progressivity of treatment.

1. Introduction

Renal cell carcinoma (RCC) is commonly found in elderly and also considered as highly resistant to chemotherapy. Early age of onset might be a sign of hereditary RCC. Even in the absence of clinical manifestations and personal/family history, an age of onset of 46 years or younger should be considerate for genetic counseling/germline mutation testing.[1]

Most patients present with localized disease amendable to surgical treatment with definitive intent. However, approximately one third of patients treated with curative intent will develop metastatic disease recurrence.

Here, we report sporadic renal cell carcinoma in young patient who experience disease progression after multiple lines therapy, including sequential monotherapy and combination therapy, like pazopanib, sunitinib, everolimus, pembrolizumab and lenvatinib, resulting in 31 months' survival.

2. Case presentation

A 30-year-old male presented with a painful mass in left temporal lobe 5 × 6 cm for 2 months and difficult to control by analgesics. Head magnetic resonance imaging (MRI) showed solid inhomogeneous mass, irregular margins originating from the left temporal lobe, suggestive metastases. No mutation of Von Hippel-Lindau (VHL) gene was found during gene analysis. He has hypertension for past six years with irregular consumption of amlodipine. He had no history of diabetes mellitus (DM), no smoking and no history of tumor in the family.

Two years ago, he had left flank mass and hematuria. Imaging examination showed mass at lower left kidney sized 11 × 10 cm, neither nodule enlargement and nor distant metastases (T3AN0M0/stage III). He underwent left radical nephrectomy. Histopathologic examination revealed clear cell renal carcinoma International Society of Urologic Pathologists (ISUP) grade 2 which had infiltrated the renal pelvis, and perirenal fat (Fig. 1). PD-L1 expression was not examined in this patient. Four months after surgery, chest multi slice computer tomography (MSCT) scan showed intrapulmonary metastases. He was treated with pazopanib 800 mg/day for 6 months, but the pulmonary nodules increased in number and size. Pazopanib was changed to sunitinib 50 mg/day, but he had no improvement. Everolimus 10 mg/day was administered to substitute sunitinib.

While on everolimus for 1 month, he experienced shortness of breath

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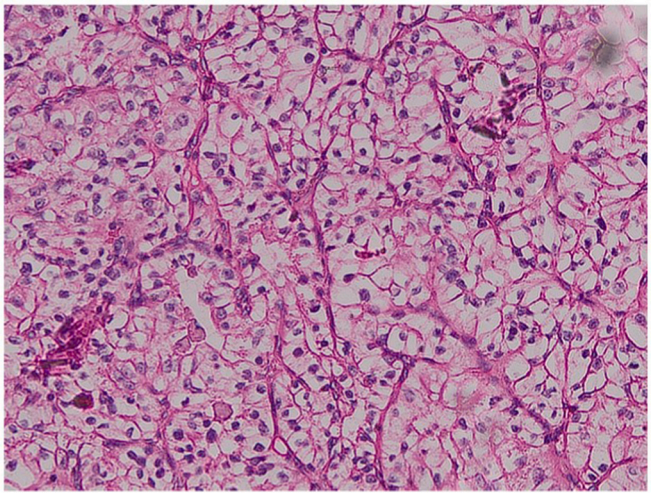

Fig. 1. Histopathologic slide: Clear cell carcinoma from nephrectomy (2 September 2020).

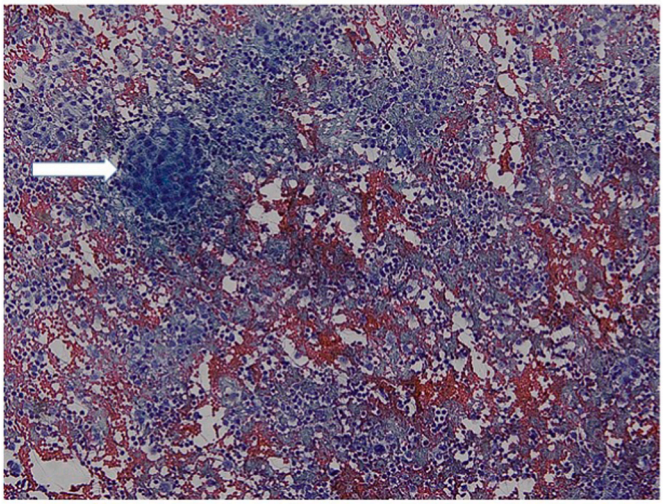

Fig. 3. Histopathologic slide: malignant cell from pleural fluid (8 February 2022): white arrow.

and hospitalized for pleural effusion (Fig. 2). Chest MSCT showed localized multiloculated left pleural effusion and multiple nodules enlargement at superior lobe right lung. Multiple lymph nodes enlargement was also found at paratracheal. Patient underwent chest tube insertion, followed by pleurodesis. Pleural fluid citology was analyzed (Fig. 3). Everolimus was stopped and changed to pembrolizumab 200 mg every 3 weeks and Lenvatinib 20 mg/day.

After 7 months treated with pembrolizumab and lenvatinib, he complained of bone pain in pelvic and right upper quadrant abdominal pain. MSCT revealed pulmonary nodule, intrahepatic enhancement nodule and lytic sclerotic lesion with pathologic fracture on left coxae and right pubic bone, which indicates pulmonary, pleural, hepatic and bone metastases. Bone scan revealed osteoblastic and osteolytic metastatic processes on the left temporal bone, left zygomaticus, left sphenoid bone, left coxae III, VI, VII, VII, IX, bilateral iliac bones and bilateral pubic bones. The latest lumbosacral X-ray showed sclerotic lesion on left iliac bone (Fig. 4). The treatment was changed to lenvatinib 18 mg/day and everolimus 5 mg/day. Zolendronic acid 4 mg infusion monthly was added to the treatment. Unfortunately, the patient eventually died on March 23rd, 2023 after 31 months of survival.

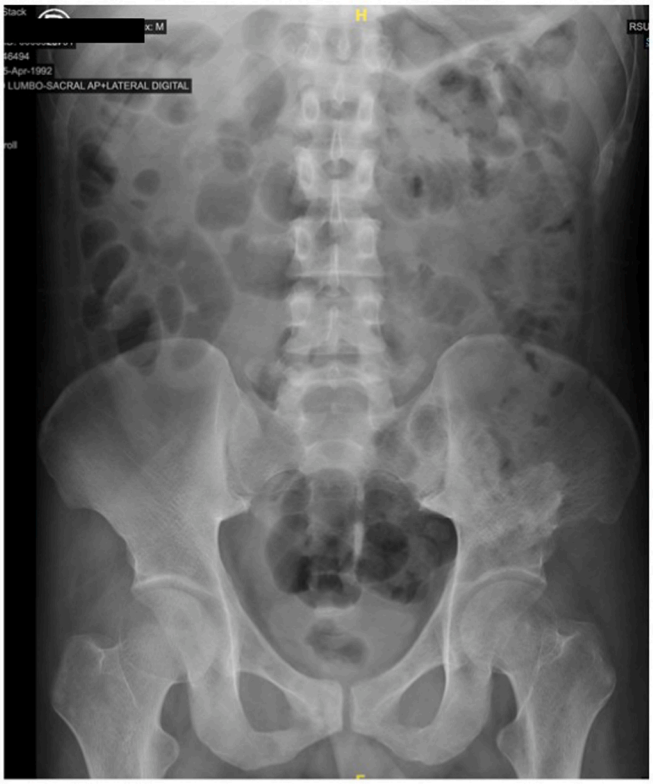

Fig. 4. Bone X-Ray 14 February 2022: sclerotic lesion on left iliac bone.

3. Discussions

We highlighted unusual sporadic renal cell carcinoma occurred in young age with hypertension as risk factor. After various therapies, starting from left radical nephrectomy continued by multiple lined therapies, the treatment showed poor response and keep progressing. However, the patient has survived for 31 months.

According to International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) our patient was stratified into intermediate risk with prognostic factor less than one year from time diagnosis to systemic

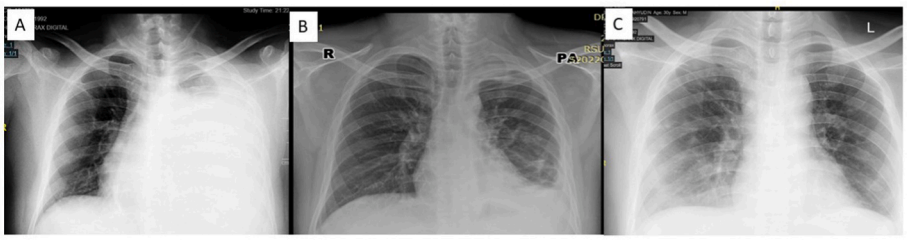

Fig. 2. Chest X-Ray:
A. 17 February 2022, B. 19 May 2022 (after Pleurodesis, Pembrolizumab + Lenvatinib), C. 11 February 2023.

therapy. Our patient was also categorized to intermediate risk group according to Memorial Sloan Kettering Cancer Center (MSKCC) with interval from diagnosis to treatment less than one year as prognostic factors. Nevertheless, patient can survive until 31 months, longer than in previous study that reported median overall survival (OS) of. 18 (95% CI 14 to 22) months in intermediate risk group.[2]

Clear cell was found on our patient's histopathologic examination, which Matteo et al. revealed that clear-cell was correlated with a longer survival compared with other histologic types (18 months' vs 12 months). Our patient had no disability in daily living and had zero score for Easter cooperative oncology group-performance status (ECOG-PS). Low ECOG-PS at time of diagnosis of metastatic disease was associated to patients' survival.

Our patient developed bone metastases later (24 months after diagnosis) than previous study that revealed median time occurrence for bone metastatic (BMs) was 16 months (range 0–44).[3]

Patient was diagnosed with RCC at age of 28 with poor outcome treatment. Multiple risk factors for RCC along with their pathophysiologic mechanisms have been described. These include both genetic and acquired risk factors. In our case, patient has been diagnosed with hypertension six years' prior kidney cancer was found that might support the incidence of RCC.

The most common gene involved in the pathogenesis of RCC is the VHL gene. Despite the absence of VHL mutation the patient still survived for 31 months. Nevertheless, recent meta-analysis indicated that VHL gene alteration has no prognostic or predictive value in patients with clear cell RCC.[4]

Our patient seemed to develop resistant along with treatment: VEGFR tyrosine kinase inhibitor and immunotherapy, either as single agent or in combination. Resistance to targeted therapeutics can be classified into intrinsic (primary) and acquired (secondary) resistance. Intrinsic resistance can be attributed to the presence of resistant tumor clones prior to therapy due to inherited resistance or evolutionary clonal selection. Acquired resistance is characterized by tumor growth after initial tumor regression while the patient is still receiving therapeutic treatment. Resistance to VEGFR TKIs often develop alongside continued target inhibition.[5]

4. Conclusion

Our case indicated that sporadic RCC without VHL mutation could occur in young age. Even though our patient had intermediate risk clear cell RCC he developed pulmonary, pleural, bone and hepatic metastases longer than usually reported. Despite poor treatment response, the patient survived for 31 months.

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Ethical approval

Not applicable.

Consent

Written informed consent was obtained from the patients for publication. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Conceptualization: Kartikasari A, Oehadian A Writing-original draft preparation: Kartikasari, A. Writing review and editing: Kartikasari A, Oehadian A, Mardia A, Safriadi F, Suryanti S, Usman A. Approval of final manuscript: All authors.

Declaration of competing interest

The authors report no conflicts of interest.

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