Case Report
Coexistence of multiple myeloma and clear cell renal cell carcinoma: a case report and review of literature

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Abstract: Coexistence of multiple myeloma (MM) and renal cell carcinoma (RCC) is an extremely rare condition. Nevertheless, there is a higher than expected incidence of co-occurrence of these two malignancies. Several case series, in the recent past, have postulated an association between MM and RCC. Population-based data analyses have revealed a bi-directional association between these two malignancies. However, the cause still remains speculative up to date. Here, we aim to describe a patient with MM and clear cell renal cell carcinoma (CCRCC) one after another for the second time from China. Clinical implications are discussed with a critical review of existing literature and we expect to draw much more awareness among clinicians regarding such association.

Keywords: Multiple myeloma, clear cell renal cell carcinoma, interleukin (IL)-6, interferon-a

Case report

A 48-year-old man was presented to the neurology clinic of our hospital due to a progressive history of headache on 12-Jun, 2012. Blood routine examination showed the WBC was normal but decreased of platelet and moderate anemia. The count of platelet was 85×10^9/L and the amount of hemoglobin was 86 g/L. Blood chemistry result showed globulin was at an abnormal high concentration of 84.3 g/L and albumin was at a below normal concentration of 29.3 g/L. Immunoglobulin G (IgG) was at an abnormal concentration of 7470 mg/dl and was confirmed as a monoclonal protein by immunofixation. The concentrations of other types of Ig were below the lower normal limit, β2-microglobulin was 2799 µg/L. The concentration of Kappa-Light from blood and urine was 9350 mg/dl and 68.40 mg/dl respectively. The proportion of abnormal plasma cells in bone marrow accounted for 34%. The cell surface of these plasma cells was CD38 positive, CD138 positive. X-ray examination showed no abnormal bone damage. This patient was diagnosed with multiple myeloma (MM) IgG type (Durie-Salmon stage III and International System Stage II) and he was transferred to hematology department immediately. Subsequently, the patient underwent first cycle of VAD (Vindesine 1 mg d1-4, Epirubicin 15 mg d1-4, Dexamethasone 40 mg d1-4, 9-12, 17-20) chemotherapy from 19 Jun, 2012. After one cycle, the patient got a partial response (PR). Next, the patient received 4 cycles of VAD consolidated chemotherapy. The whole process was smoothly. When the patient came to our department for the 6th course chemotherapy, ultrasound examination indicated a hypoechoic mass in the down pole of the right kidney. Contrast enhanced CT scan revealed presence of a mild to moderate enhancing mass of size approximately 2.5×2.7 cm at down pole of the right kidney (Figure 1). After reviewed all the CT scans since the MM onset we confirmed this was the new lesion. Resection of the right kidney was done under general anesthesia on 21 Mar, 2013, after review of the literature and communication with patient. The biopsy was confirmed clear cell renal cell carcinoma (CCRCC) (Figure 2). According to 2010 AJCC 7th Edition (American Joint Committee on Cancer) staging criteria, the patient was divided into clinical stage I T1a N0 M0. Urologists and hematologists together formulated the follow-up treatment strategy for this patient:
Chemotherapy for multiple myeloma was first and the patient regularly came to urology clinic for CCRCC follow-up monitoring every 3-months after interferon-a 3 million unit biw was given to the patient for 3-months. After conducting a six cycles of VAD chemotherapy, the best response for MM is PR, so the PD (Velcade 1.3 mg/m² d1, 4, 8, 11, Dexamethasone 20 mg d1-2, 4-5, 8-9, 11-12) program was selected for this patient. The efficacy was very good partial response (VGPR), but PD regimen was stopped only after one course due to grade-3 peripheral neuropathy. Thalidomide plus dexamethasone was selected to be as a maintenance therapy. The last follow-up time was 3 Feb, 2015, VGPR state in the myeloma and no sign of recurrence of renal cell carcinoma nearly 35 months passed since the coexistence of the two malignancies.

Discussion

Hematological malignancies with renal cell carcinoma (RCC) are rarely seen. Despite coexistence of multiple myeloma (MM) and renal cell carcinoma (RCC) is an extremely rare condition. There is a higher than expected incidence of co-occurrence of these two malignancies. To the best of our knowledge, the first report of coexistence of MM and RCC was on 1977 by Dr Law IP [1]. Later, coexistence of these two malignancies gradually increased and caused clinical physician’s attention. Cooper GL et al [2] presented a case of multiple myeloma diagnosed by fine-needle aspiration (FNA) biopsy and confirmed by laboratory studies in a patient with a history of renal-cell carcinoma. Cielińska S et al [3] reported a case of 59-year old patient who simultaneously developed renal clear cell carcinoma and IgG kappa multiple myeloma. Bhandari MS [4] reported 6 cases of RCC in their institutional data base of 600 patients with plasma cell dyscrasias. Ozturk MA et al [5] reported 2 cases of synchronous RCC and MM. Sargın G et al [6] reported a 69-year-old male patient diagnosed as stage-I RCC and IgG kappa stage-IIA MM at the same time. Padhi S [7] described an elderly male patient with plasmablastic multiple myeloma (MM) (IgG λ, International System Stage II) 36 months after the diagnosis of RCC. Somanath Padhi et al [8] described two patients, aged 64 and 54 years, with RCC-MM association. These are the representative reports in the past decades on the coexistence of these two malignancies.

In the same time, the scientists committed to evaluate the association of MM and RCC. Some case reports and small case series have hypothesized an association between these two malignancies [4, 5, 9, 10]. This hypothesis has also been expounded in a large population-based study from the USA by Dr Ojha RP and his colleagues and they supposed the association was to be bidirectional and shared risk factors [11]. Their date showed MM cohort yielded 69 RCC cases during 100,804 person-years of follow up. Patients with MM had a higher relative risk of RCC than the general population (SIR=1.89, 95% CI 1.47-2.40). Their analyses also revealed a bidirectional association between RCC and MM, which typically indicates shared risk factors. Choueiri TK et al [10] also retrospectively reviewed the records of patients with MM and RCC at the Cleveland Clinic between 1990 and 2005, and identified 1100 with MM, 2704 with RCC and eight with concomitant MM and RCC. The medical records of these eight patients were reviewed. In four of the eight patients, RCC was diagnosed after the MM at 3, 8, 23 and 46 months, respectively; in the remaining four, the RCC was diagnosed before MM by 108, 35, 13 and 1 months, respectively. All the results threw the light that patients with MM had higher relative risk of

![Figure 1. The contrast-enhanced computed tomography from the case showing a heterogeneously enhancing mass with central necrosis in the down pole of right kidney, highly suggestive of renal cell carcinoma.](image-url)
developing RCC during follow-up and vice versa [12].

But, until now the root cause still remains speculative. This association cannot be explained by treatment-related development of a second malignancy. Possible explanations include genetic abnormalities, environmental exposures or immune-related mechanisms predisposing to the second malignancy. Most of all, the cytokine hypothesis was relatively more be mentioned. The presence of very high levels of interleukin (IL)-6 in one case was interesting [13]. Ozturk MA et al [5] also pointed out the importance of IL-6 in this coexistence and provide some descriptive properties of all reported synchronous RCC and MM cases. In a case report, the patient’s serum interleukin-6 level was found to be markedly elevated (2464 pg/mL, reference; <50 pg/mL) [7]. Interestingly, our patient also has a very high concentration of IL-6 (1364 pg/mL, reference; <50 pg/mL). These findings are particularly relevant in the management of patients known MM and subsequent or concomitant renal masses, especially those involving the right kidney [10], but further investigations and reports are warranted.

Herein, we report a case of patient who was diagnosed CCRCC nearly 9-months following the course of chemotherapy for MM. Review of
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the literature, this is the second case report of MM with RCC in China. The first case report was on 2002 by Zhao et al [14]. They reported a case of 67-year-old light-chain myeloma patient without chemotherapy. The left kidney mass was found 14 months of follow-up time for MM. The biopsy of the left kidney was confirmed as renal cell carcinoma. For our patient, we selected 3 million units of interferon-a subcutaneously twice a week instead of chemotherapy for the RCC. Nearly three years past, the patient was still at stable condition for these two malignancies. As far as we know, this is the first report about interferon-a on the coexistence of these two malignancies. So we propose that interferon-a may be a remedy therapy for these patients.

The important message from this report is that all the clinicians should be mindful that these two malignancies can co-exist and the risk of development of these two malignancies one with a prior history of the other is more than expected in the general population, despite for which further in-depth studies are necessary. The specialists should be alerted for this possibility when evaluating patients at diagnosis or during follow-up. All patients of MM should be carefully evaluated for complex mass lesion in the kidneys, more specifically in the right side. Similarly, any new lytic bone lesions in a patient with prior RCC should be carefully evaluated for possible MM.

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Disclosure of conflict of interest

None.

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