Primary Extramedullary Plasmacytoma of the Kidney: A Case Report and Literature Review

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Abstract: Extramedullary plasmacytomas (EMPs) usually occur in the upper respiratory tract, the occurrence in the kidney is extremely rare. The present study reported a case of primary renal plasmacytoma in a 46-year-old male patient with frequent and urgent urination, nocturia increased due to renal failure. Computed tomography (CT) imaging showed a 60×58mm enhanced mass at the lower pole of the right kidney. Following the radical nephrectomy, histopathological and immunohistochemistry analysis of the resected specimen supported the diagnosis of plasmacytoma. Bone marrow biopsy and total body skeletal survey was performed to demonstrate that there were no evidence of multiple myeloma (MM) and bone lesions. Consequently, a diagnosis of a primary renal EMP was proposed. Subsequently, the patient was treated with 4 course of chemotherapy VAD (vincristine, epirubicin and dexamethasone) + cyclophosphamide + thalidomide, and he was disease-free during 4 years’ follow-up time. The current study also presents a review of the literatures. Treatment of primary renal EMP is surgery, radiotherapy, chemotherapy or a combination of those, even hematopoietic stem cell transplantation may be also an option. Long-term follow-up is a necessity for systemic control due to the possibility to transform into MM.

Keywords: Plasmacytoma; Myeloma; Kidney; Therapy.

Introduction

Extramedullary plasmacytoma (EMP) is a rare malignant neoplasm that develops due to uncontrolled plasma cell proliferation and monoclonal plasmacytic infiltration [¹]. EMP typically affects patients at their middle ages, and is more common for male. Risk factors of plasmacytomas still remain unconfirmed. However, prior radiation exposure has been suggested [²]. Isolated primary EMP occurs more commonly in the nasopharynx, larynx and upper respiratory tract, whereas EMP due to hematogenous spread of multiple myeloma (MM) mainly occurs in gastrointestinal tract, pleura, testis, skin, peritoneum, liver, endocrine glands and lymph nodes [³]. EMPs retroperitoneal infiltration, especially primary renal plasmacytoma is very rare. Herein we report a rare case of primary renal EMP with direct parenchymal invasion of the kidney causing renal failure.

Case Presentation

A 46-year-old man was admitted to our hospital in December 9, 2011. He already had 1-year history of increasing facial, blepharal and pretilial edema, frequent and urgent urination, and increasing nocturia, but he did not have odynuria, dysuria, hematuria, loin pain, hydrothorax, ascites, anorexia, weight loss, or stone disease. His past medical history was unremarkable. Physical examination revealed no swollen lymph nodes. His both renal regions were sensitive to percussion, and his neurologic deficit was non-evident.

Laboratory tests at admission were as follows: blood cell counts were normal; serum creatinine was raised significantly; C-reactive protein and erythrocyte sedimentation rate were also elevated; test for Bence-Jones protein was negative; serum and urine electrophoresis for paraproteins were normal. Enhanced computed tomography (CT) imaging showed a 60×58mm enhanced mass at the lower pole of the right kidney, without any swollen lymph nodes (Fig. 1). Then the radical nephrectomy was performed, which showed that the renal interstitial cells were infiltrated by plasma cells diffusely with the expression of immunoglobulin (Ig) kappa highly but Ig lambda partly (Fig. 2), the

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in abdominal B-scan ultrasonography, blood and urine immuno-fixation electrophoresis, Bence-Jones proteins test, etc. By 2016-02-28, he had and still kept disease-free for over 4 years.

Primary renal EMP is rare, here we summarized its clinical characteristics and treatment according to our experiences and relevant literatures by 2016, as follows:

Clinical presentation
Primary renal EMPs often have no typical clinical manifestation. They may be found by physical examination, even presented by the symptom of obstruction, pain or bleeding, which depended on the mass’s volume and the site of involvement. Only some rare case have the symptoms of extramedullary hematopoiensis. Our patient presented increasing facial, blepharal, pretibial edema due to renal injury and was found a mass in the right kidney. Direct renal failure may be a common lesion due to plasma cell dyscrasias. The detailed mechanisms of kidney injury in plasma cell malignancies include cast nephropathy, amyloid light-chain amyloidosis, monoclonal Ig deposition disease, glomerulonephritis, hyperviscosity syndrome, hypercalcemia, tumor lysis syndrome, tubulointerstitial nephritis, and direct parenchymal invasion by plasma cells.

Imaging examination
CT and magnetic resonance imaging (MRI) are complementary techniques in evaluating the size and location of the renal EMP and the involvement of the adjacent structures. The CT features were described as heterogeneously enhancing mass, tumor or nodule, which can be well enhanced with peripheral or with gradual filling towards the center of the lesion, some even show the secondary changes occasionally with hemorrhage necrosis and punctate calcification. On MR images, most renal EMP were displayed as tumor with intermediate or slightly higher signal intensity on the T1-weighted, moderate-to-high signal intensity on the T2-weighted images and heterogeneous enhancement on the contrast-enhanced MRI. Although MRI was superior to CT in identifying the malignant characters of the soft tissue mass, it could not distinguish plasmacytoma from other probable causes, such as squamous cell and adenocystic carcinoma. 18F-fluorodeoxyglucose (18F-FDG) is a successful avid agent for diagnosis and monitoring of disease status in plasmacytoma, so the ability to perform the whole-body examinations that enable sensitive detection of intramedullary and extramedullary lesions in one session is a major advantage of fluorodeoxyglucose positron emission tomography computer tomography (FDG PET/CT) over MRI. Furthermore, 18F-FDG PET/CT has been found to be
useful in staging, identifying optimal sites for biopsy, restaging, and monitoring response to treatment for MM and related plasma cell dyscrasias [9]. Nevertheless, 18F-FDG uptake is also common in benign entities such as physiological uptake and the use of 18F-FDG PET/CT in EMPs is limited in the literature owing to the small number of cases. Overall, the imaging appearance of renal EMPs are very limited distinctly.

Pathological and immunohistochemical findings
The primary EMP of the kidney showed the plasma cells was often extended and infiltrated to the renal capsule even perirenal adipose tissue. In histology, the plasma cell is nodular lesions isolated with no obvious boundaries to surrounding tissue, and in microscope, it is distributed diffusely with mature, immature or anaplastic plasma cells. Immunophenotyping with CD38 (+), CD138 (+), IgA, IgD, IgG, IgM, IgE, kappa light chain, and lambda light chain antibody are helpful to differentiate EMPs from other tumors, and AE1/AE3(-) can distinguish between with epithelial tumors [10].

Diagnosis
To the best of our knowledge, the primary renal EMP is lack in the evidence of typical clinical symptoms and specific laboratory tests, so the diagnosis may be difficult. In clinic, once the neoplasm is found in the kidney and be confirmed to be infiltrated by plasma cell, the diagnostic criteria of primary EMPs were as follows: 1) neoplasm confined to the primary site, with or without lymphonodus’ lesion; 2) serum and urine protein electrophoresis, immunoelectrophoresis, urine Bence Jones proteins were probably negative, but there were no other lesions, also no evidence of systemic signs and symptoms associated with MM or other soft tissues plasmacytoma through general systematic physical examination including the bone marrow biopsy and radiological examination. So the diagnosis of primary renal EMP can be made only after detailed clinical, hematological, biochemical, radiological, molecular-pathologic and immunohistochemical investigations excluding the possibility of localized presentation of MM such as in our case [11].

Treatment
Talking about the treatment of the EMP, controversy exists in the optimal treatment of EMP, but the current reported experiences of treating primary EMPs indicate that surgery, radiotherapy, chemotherapy or a combination of those are the optional choice. As primary renal EMP always showed an isolated mass, so initial management was surgical with radical nephrectomy of the lesion kidney, but partial nephrectomy was also reported. Furthermore, plasmacytomas are generally very radiosensitive, so radiation therapy is also a therapeutic modality for EMP. Certain studies reported that local radiotherapy might achieve excellent local control [12], but no does-response relationship was observed now. The optimal radiation should be considered if feasible. However, there is no recommendation for adjuvant radiotherapy to patients who have undergone complete surgical excision with negative margins [13].

Chemotherapy is advisable for patients who have a generalized EMP, refractory or relapsed disease. But efficacy of chemotherapy is poorly studied and based mostly on case reports or small retrospective studies of patients. Regimens used for MM can be considered. Furthermore, thalidomide combined with dexamethasone or alkylating agents were used to be effective and increase the response rate [14]. Thalidomide had been reported to have not only an antiangiogenic effect, but also to act a role directly on myeloma cells [15], so from this perspective, thalidomide could be expected to have some effect on extramedullary masses. In 2013, Sekiguchi Y, et al [16] had summarized 27 cases of EMP who were treated with thalidomide from 2005 to 2011, they reported that thalidomide was effective but it’s duration of effect was relatively short and immature myeloma might be resistant to thalidomide. González-Porras et al [17] reported that thalidomide in combination with cyclophosphamide and dexamethasone was effective in soft-tissue plasmacytomas. In the present study, patients who received regimens containing novel drugs, such as bortezomib, tended to have better responses [18]. Other chemotherapy regimens need to be further developed.

As is known to us, autologous and allogeneic hematopoietic stem cell transplantation (HSCT) have been widely used to the patients with MM, however, the use of HSCT in the management of EMP were restricted to few reports. The role of HSCT in the management of EMPs was not defined. But it was reported that autologous HSCT could be able to achieve responses in extramedullary sites even in patients who had no response to chemotherapy despite a serologic response [14]. And high-risk plasmacytoma patients with deletion of chromosome, plasma blastic morphology, high LDH with extramedullary disease such as plasmacytoma in central nervous system should have allogeneic HSCT as consolidation early in the course of the disease to achieve maximal survival benefits [14]. But there is a paucity of prospective data from HSCT randomized trials, especially in primary renal EMPs. Unquestionably, more experience is needed to study the effect of HSCT in EMPs in general.

Prognosis
Compared to solitary bone plasmacytoma, EMP demonstrates a relatively low risk of progression to MM. The survival at 10 years of EMP is 70% [13], and the rate of progression to MM is lower than in solitary bone plasmacytoma, ranging from 11~30% at ten years [19]. The primary renal EMP’s prognosis is different in the literatures. Radiotherapy and serum β2 microglobulin<3.5 mg/L were found to be favorable prognostic factors for EMP patients [20]. A higher failure rate in “high grade” tumours using the MM grading criteria and reminded that tumours >5 cm were at higher risk of failure [13].

Literature review
An internet PubMed search was performed for the literature review with the key words “extramedullary plasmacytoma, kidney, retroperitoneal, renal”. A total of 18 patients of primary renal EMP were reported in the English literature from 1990 to 2016 (Table 1) [2,4,6,11,21-34]. In our review, primary renal EMP occurred mainly in adult with ages from 28 years to 83 years, the male/female ratio of which was 13: 5. Common clinical features of the reviewed patients include pains in back, lumbar or abdomen, sometimes with hematuria, edema, abdominal distention, etc. However, 6 of them did not have these common symptoms and were diagnosed by ultrasonography or CT scanning. Swollen masses were found by CT scanning or ultrasonography in kidneys of all the patients, but at different locations: in the left kidney of...
Table 1. The detailed clinical features of the 18 primary renal EMPs reported in English literatures from 1990 to 2016.

<table>
<thead>
<tr>
<th>Authors [Ref]</th>
<th>Age (years)/gender</th>
<th>Presentation</th>
<th>Location</th>
<th>SPE IgG κ↑</th>
<th>Bence-Jones protein</th>
<th>Treatment Surgery</th>
<th>Chemotherapy</th>
<th>Radiotherapy</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Igel TC, et al [21]</td>
<td>64/M</td>
<td>asymptomatic</td>
<td>L</td>
<td>IgM κ↑</td>
<td>-</td>
<td>RN</td>
<td>NO</td>
<td>YES</td>
<td>alive after 16 years</td>
</tr>
<tr>
<td>Kanoh T, et al [22]</td>
<td>76/F</td>
<td>hematuria, abdominal distention, back pain</td>
<td>L</td>
<td>NA</td>
<td>-</td>
<td>RN</td>
<td>NO</td>
<td>NO</td>
<td>died after 2 months</td>
</tr>
<tr>
<td>Kobayashi H, et al [23]</td>
<td>83/M</td>
<td>abdominal pain and palpable mass</td>
<td>L</td>
<td>N</td>
<td>-</td>
<td>RN</td>
<td>NO</td>
<td>NO</td>
<td>died 10 days postoperatively</td>
</tr>
<tr>
<td>Shustik C, et al [24]</td>
<td>31/M</td>
<td>asymptomatic</td>
<td>NA</td>
<td>IgG κ↑</td>
<td>NA</td>
<td>RN</td>
<td>NO</td>
<td>NO</td>
<td>alive after 33 months</td>
</tr>
<tr>
<td>Chen TC, et al [25]</td>
<td>28/M</td>
<td>abdominal pain, jaundice, tea-colored urine and clay stool</td>
<td>R</td>
<td>IgG κ↑</td>
<td>+</td>
<td>NO</td>
<td>YES</td>
<td>YES</td>
<td>alive after 1 year</td>
</tr>
<tr>
<td>Park SY, et al [26]</td>
<td>39/M</td>
<td>asymptomatic</td>
<td>L</td>
<td>N</td>
<td>NA</td>
<td>RN</td>
<td>YES</td>
<td>YES</td>
<td>died after 34 months</td>
</tr>
<tr>
<td>Yazici S, et al [27]</td>
<td>67/F</td>
<td>asymptomatic</td>
<td>L</td>
<td>κ↑</td>
<td>NA</td>
<td>RN</td>
<td>NO</td>
<td>NO</td>
<td>alive after 6 months</td>
</tr>
<tr>
<td>Yang GF, et al [28]</td>
<td>76/F</td>
<td>back pain</td>
<td>L</td>
<td>N</td>
<td>NA</td>
<td>RN</td>
<td>NO</td>
<td>NO</td>
<td>NA</td>
</tr>
<tr>
<td>Klein T, et al [29]</td>
<td>82/F</td>
<td>Hematuria, hydronephrosis</td>
<td>R</td>
<td>NA</td>
<td>NA</td>
<td>RN</td>
<td>NO</td>
<td>NO</td>
<td>NA</td>
</tr>
<tr>
<td>Ozkok A, et al [31]</td>
<td>68/M</td>
<td>edema, dyspnea, and low urinary output</td>
<td>L</td>
<td>N</td>
<td>-</td>
<td>NO</td>
<td>YES</td>
<td>YES</td>
<td>died after 14 years</td>
</tr>
<tr>
<td>Zhang SQ, et al [32]</td>
<td>46/F</td>
<td>asymptomatic</td>
<td>L</td>
<td>NA</td>
<td>+</td>
<td>PN</td>
<td>NO</td>
<td>NO</td>
<td>alive after 9 months</td>
</tr>
<tr>
<td>Berquist SW, et al [33]</td>
<td>51/M</td>
<td>hematuria</td>
<td>L</td>
<td>IgG↑</td>
<td>NA</td>
<td>PN</td>
<td>NO</td>
<td>NO</td>
<td>alive after 28 months</td>
</tr>
<tr>
<td>Hu G, et al [34]</td>
<td>70/M</td>
<td>asymptomatic</td>
<td>R</td>
<td>NA</td>
<td>NA</td>
<td>PN</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

EMP, extramedullary plasmacytoma; F, female; M, male; L, left kidney; R, right kidney; NA, not available; N, normal; SPE, serum protein electrophoresis; Ig, immunoglobulin; ↑, increased; +, positive; -, negative; PCN, plasma cell neoplasm; RN, radical nephrectomy; PN, partial nephrectomy.
12 patients, in the right kidney of 5 patients, and in the allograft of 1 kidney transplant patient. For the therapy, 12 patients underwent radical nephrectomy of the lesion kidney, 3 patients received partial nephrectomy. However, only 3 patients received adjuvant chemotherapy, and only 5 patients were treated with adjuvant radiation therapy. Chemotherapy regimens were vincristine, doxorubicin, dexamethasone, and thalidomide, etc. Prognosis varied in different literatures, with survival time range from 10 days to 16 years (Detailed informations were seen in Table 1).

Discussion

Plasmacytoma is a clonal plasma cell malignancy, its cells usually reside in the medullary cavity of bone marrow, but when spreading to the cortical bones, or spreading hematogenously to other organs, they may cause extramedullary diseases. In practical terms, isolated primary plasmacytoma is compounded with solitary bone plasmacytoma and extrametamyelogenous plasmacytoma. Solitary bone plasmacytoma just means plasma cell myeloma come from the bone cortex without evidence of any other lesion, while extrametamyelogenous plasmacytoma so called EMP was defined by the updated WHO classification (2008) as localized plasma cell neoplasm that arose in soft tissues other than bone. In the Surveillance, Epidemiology and End Results (SEER) Program (1992-2004) of United States, the data displayed that the incidence of plasmacytoma are indistinguishable from those of renal cell carcinoma but tissue biopsy showing monoclonal plasma cell histology, with 18F-FDG PET/CT. Radiological findings in renal plasmacytoma just means plasma cell myeloma without any evidence of MM and plasmacytoma of other sites is the only way to diagnosis. A comprehensive search in PubMed database for patients with renal EMPs identified only dozens of reports. However, more cases might have occurred because some cases were underdiagnosed or underreported. A treatment regimen of local surgery, local radiotherapy, chemotherapy or a combination of them may be initiated. Most of these cases had received surgery such as radical nephrectomy, a few combined with radiotherapy or chemotherapy. In addition that, some of them were deficiency in the outcome and prognosis, but the longest follow-up time was 16 years. As per the case-based experience in the literature, factors that influenced the good prognosis in our case are early presentation, a single site of involvement, localization, absence of M protein, and prompt medical attention and treatment. Although the general prognosis and outcome for EMP is good, long-term follow-up in terms of disease recurrence and progression is mandatory.

Conflict of interest

The author have no conflict of interest to declare.

References


