Review Article

Clinicopathological features of primary angiosarcoma of the kidney: a review of 62 cases

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Abstract: Angiosarcoma (AS) is a malignant tumor occurring in less than 2% of soft tissue sarcomas. Primary involvement of the kidney is rare, its pathogenesis remains largely unknown and it has overlapping features with other tumors of the kidney. The objective of this paper is to review the case reports of primary AS of the kidney in the literature. The search terms were primary AS of the kidney, primary renal AS and primary renal hemangiosarcoma. The total cohort of the cases reviewed was 62. The mean age of presentation was 61 years old with a predilection for the male sex. Metastatic disease at the time of diagnosis accounted for 44.9% (22/49) of the cases reported and 44.4% (12/27) of patients with non-metastatic disease at diagnosis, subsequently developed metastasis. Primary AS of the kidney is a rare malignant tumor with a poor prognosis. Local recurrence and distant metastasis is common. Primary AS of the kidney shares similar clinical presentation with other renal tumors and imaging does not allow for tumor specific diagnosis. Histopathological examination and immunohistochemistry is very important for the confirmation of the diagnosis. Current treatment options include a variable combination of surgery, radiotherapy and chemotherapy.

Keywords: Angiosarcoma of the kidney; primary renal angiosarcoma (primary renal AS); primary renal hemangiosarcoma

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Introduction

Angiosarcoma (AS) is a rare and aggressive malignant tumor of vascular or lymphatic origin which accounts for <2% of soft tissue sarcomas. Approximately one third of AS occurs in the skin, one third in soft tissues and one third in other sites such as the liver, bone and breast (1-4). This paper reviews the literature for primary AS of the kidney because of its rarity and its overlapping features with other renal tumors which poses diagnostic challenges with implications for management.

Methods

PubMed, Scopus, Google Scholar and Embase (Ovid SP) databases were searched for all articles and case reports of primary AS of the kidney until April 2015. The search strategy combined medical subject heading (MeSH) descriptors and text words such as primary AS of the kidney, primary renal AS and renal hemangiosarcoma. There was no language limitation to the search and a manual search of the reference list of relevant articles was undertaken. Clinical and pathological data were extracted when available and analyzed. The clinical data included age, sex, clinical presentation, presence of metastasis, sites of metastasis, treatment modality and follow up. Pathological data included the maximum tumor dimension measured in centimeters, the laterality of the tumor and immunohistochemical (IHC) expression of the tumor cells. All cases reported prior to Prince *et al.* (5) in 1942 were excluded from this review because the definition of AS had not been clearly established at that time and this is consistent with the views of Cason *et al.* (6), Hiratsuka *et al.* (7) and Leggio *et al.* (1) in earlier reviews.

Results

Tables 1 and *2* present a summary of the clinical and pathological data of the 62 cases of primary AS of the kidney in the literature.

Discussion

Primary AS of the kidney is rare. Approximately 62 cases have been reported in the literature, mostly as case reports.

Epidemiology

Primary AS of the kidney occurs most frequently in the sixth and seventh decades (2) and this is consistent with the findings of this review with a mean age of 61 years (range, 24-95 years). It has a predilection for the male sex which accounted for 89% (54/61) of the patients in the review. There are seven reports of female patients with primary AS of the kidney in the literature (2,7,37,41,43,53,54). The left kidney was involved in 66.7% (36/54) of the patients in this review. The laterality of the tumor was not documented for eight cases (2,32,33,41,44,48,49,54) and so far, no familial predisposition have been established in spite of the occurrence of the tumor in two brothers aged 52 and 69 years respectively (22).

Etiology

Although the etiology of primary AS of the kidney is not known, the association between some exogenous risk factors and AS of other sites, especially the liver is well documented. The risk factors include thorium dioxide (thorotrast used in the past for angiography), occupational exposure to arsenic in insecticide which is used in agriculture and polyvinyl chloride in synthetic rubber industry (2,24,27,55,56). Radiotherapy and chronic lymphedema of any cause, either due to Milroy's disease or chronic infections like filariasis is also associated with the development of AS. A classical case in point is the phenomenon known as Stewart-Treves syndrome which describes AS associated with lymphedema that occurs after the treatment of breast cancer (56). However these risk factors have not been proven to have a direct causal relationship with AS of the kidney (1,21).

Clinical features

This review highlights the overlapping features between primary AS of the kidney and other renal tumors. Flank pain was the most common symptom (3,5,6,9,11,18,20-24,28,29,31,34,35,40,46,47,52). Hematuria with or without abdominal pain accounted for 45.6% (21/46) of the clinical presentation (3,5,10,11,14-16,20,22,24,34,35,41,43,45,51,52,54). Other clinical features included weight loss (6,8,12,13,22,26,34), fever (23,26,36), hemoptysis (21,23,37,39), flank or costal swelling (42), malaise and ureteric obstruction (16). One patient had spontaneous rupture with the development of retroperitoneal hematoma (29) and the tumor was an incidental finding in five patients (4,19,27,38,50).

Metastatic disease at the time of diagnosis accounted for 44.9% (22/49) of the cases reported and 44.4% (12/27) of the patients with non-metastatic disease at diagnosis subsequently developed metastasis. Approximately half of the patients with metastatic disease had two or more sites involved. The sites of tumor spread included the lung, liver, peritoneum, spleen, abdominal lymph nodes (LNs) and the soft tissues. The liver and the lungs were the most frequent site of metastasis and there were reports of metastatic disease of the bone (4,6,9,14,17,18,20,26,31,39-41,43).

Imaging

Radiological imaging alone cannot ascertain the diagnosis of AS of the kidney. It may appear as a large necrotic renal mass on computed tomography (CT) which is virtually indistinguishable from a renal cell carcinoma (2,15). Contrast-enhanced CT findings (*Figure 1*) have been variably described as heterogeneous mass with peripheral enhancement (1,7,10,27) or hypo-dense renal mass with areas of enhancement (13,34). CT imaging also helps in delineating metastatic deposits. Given the rarity of AS of the kidney and in the event of small multiple lesions to distant sites such as the lungs and liver, a large single renal mass will be suggestive of a primary AS of the kidney (2).

Preoperative diagnosis

Three patients with primary AS of the kidney have been diagnosed with CT guided fine needle aspiration cytology and the fine needle aspiration (FNA) results correlated with the histopathological and immunohistochemistry findings (15,21,36).

Pathologic findings

The histopathological feature of primary AS of the kidney is

Table 1 Clinical features of the reviewed cases of primary angiosarcoma of the kidney

Author	Age (years)	Sex	Side	Clinical presentation	Size (cm)	Mets at dx	Sites (initial and subsequent mets)
Qayyum *et al.* (8)	86	M	R	Weight loss, fatigue, dizziness	12.3	Yes	Liver, lungs
Zhang *et al.* (9)	52	M	L	Left flank pain, left leg pain	8	Yes	Liver, bone
Liu *et al.* (10)	75	M	R	Hematuria	4	No	No
Brown *et al.* (2)	68	M	R	NA	24	Yes	Liver
Brown *et al.* (2)	64	M	L	NA	30	No	No
Brown *et al.* (2)	71	M	L	NA	10	Yes	Peritoneal and periaortic LN
Brown *et al.* (2)	72	M	L	NA	NA	No	No
Brown *et al.* (2)	29	F	L	NA	3.7	NA	NA
Brown *et al.* (2)	62	M	NA	NA	NA	NA	NA
Brown *et al.* (2)	67	M	R	NA	NA	NA	NA
Brown *et al.* (2)	95	M	R	NA	15.5	Na	NA
Cason *et al.* (6)	46	M	L	Flank pain, weight loss	13	No	Bone, liver, abdominal soft tissue
Allred *et al.* (11)	67	M	R	Flank pain , hematuria	13	Yes	Lungs, liver
Peters *et al.* (12)	74	M	L	Weight loss	19	Yes	Lungs, liver, abdominal wall, head
Prince *et al.* (5)	51	M	L	Flank pain, hematuria	10	No	No
Sabharwal *et al.* (13)	67	M	L	Loin pain, weight loss, loss of appetite	13	Yes	Spleen
Chaabouni *et al.* (3)	59	M	R	Flank pain , hematuria	6.5	No	No
López Cubillana *et al.* (14)	72	M	R	Hematuria	13	No	Bone and lung
Singh *et al.* (15)	83	M	L	Hematuria	13	No	No
Askari *et al.* (16)	24	M	R	Hematuria, ureteric obstruction	9	No	No
Douard *et al.* (17)	60	M	R	NA	NA	Yes	Bone, lung
Terris *et al.* (18)	47	M	L	Flank pain	19	Yes	Diaphragm, renal artery, liver and bone
Zenico *et al.* (19)	56	M	L	Incidental finding	20	No	No
Desai *et al.* (20)	54	M	L	Flank pain, gingival bleed, hematuria	21	No	Bone
Johnson *et al.* (21)	50	M	L	Flank pain, hemoptysis	9	Yes	Liver, lung
Kern *et al.* (22)	69	M	L	Flank pain, weight loss, hematuria	26	Yes	Lung
Kern *et al.* (22)	52	M	L	Hematuria	8	Yes	Lung
Fukunaga *et al.* (4)	61	M	L	Incidental	8	No	Liver, bone and retroperitoneum
Adjiman *et al.* (23)	36	M	R	Hemoptysis, flank pain, fever	10.5	Yes	Chest wall, skin
Papadimitriou *et al.* (24)	68	M	L	Flank pain, dysuria, hematuria	10	No	No
Tsuda *et al.* (25)	77	M	L	Hematuria, renal failure	10	No	Retroperitoneum, liver
Leggio *et al.* (1)	60	M	L	Post-trauma abd pain	12	No	Spleen, peritoneum
Mordkin *et al.* (26)	75	M	L	Fever, weight loss	19	Yes	Spleen, bone, liver, soft tissue, oral cavity
Akkad *et al.* (27)	58	M	R	Incidental finding	4.5	No	No
Cerilli *et al.* (28)	67	M	R	Flank pain, hematuria	12.5	Yes	Renal vein
Aksoy *et al.* (29)	55	M	L	Abd pain, rupture with retroperitoneal hematoma	13	No	No

Table 1 (*continued*)

Table 1 (*continued*)

Author	Age	Sex	Side	Clinical presentation	Size (cm)	Mets at dx	Sites (initial and subsequent mets)
Hiratsuka *et al.* (7)	59	F	R	Hematuria	4.5	No	No
Aydogdu *et al.* (30)	77	M	L	NA	NA	NA	NA
Martínez-Piñeiro *et al.* (31)	66	M	L	Abd pain, anorexia, asthenia	11.5	No	Bone, liver, lungs
Lee *et al.* (32)	63	M	NA	NA	NA	NA	NA
Berretta *et al.* (33)	67	M	NA	NA	NA	NA	NA
Souza *et al.* (34)	75	M	L	Weight loss, flank pain, hematuria	15	No	No
Costero-Barrios *et al.* (35)	71	M	L	Hematuria, flank pain	18	No	Liver and retroperitoneum
Grapsa *et al.* (36)	65	M	R	Fever, fatigue, dyspnea	13.8	Yes	Liver, lung
Carnero López *et al.* (37)	29	F	L	Hemoptysis,	11	Yes	Lungs
Sesar *et al.* (38)	65	M	L	Incidental	4.5	NA	NA
Pauli & Strutton (39)	57	M	L	Malaise, hemoptysis,	15	Yes	Lungs , bone
Yoshida *et al.* (40)	78	M	L	Flank pain	18	Yes	Liver, bone
Juan *et al.* (41)	81	F	NA	Hematuria	5	Yes	Liver, bone
Xuan (42)	63	M	L	Pain and costal swelling	10	NA	NA
Yau *et al.* (43)	38	F	R	Hematuria, loin discomfort, bone pain	13	Yes	Bone, LN,
Garmendia *et al.* (44)	51	M	NA	NA	NA	NA	NA
Nguyen *et al.* (45)	53	M	L	Hematuria, flank pain, malaise	7	Yes	Lung
Limmer *et al.* (46)	48	M	L	Flank pain	10	No	Lung, soft tissue, muscle
Matter *et al.* (47)	62	M	L	Flank pain, abd mass	18	No	Lung
Sanyal *et al.* (48)	30	M	NA	NA	NA	No	No
Testa *et al.* (49)	NA	NA	NA	NA	NA	NA	NA
Yamamoto *et al.* (50)	68	M	R	Incidental	7	No	No
Rüb *et al.* (51)	59	M	L	Hematuria, weight loss	18	No	Lungs, liver
Celebi *et al.* (52)	57	M	R	Flank pain, hematuria	14	No	Lung, pelvis
Li *et al.* (53)	69	F	L	NA	NA	NA	NA
Witczak *et al.* (54)	44	F	NA	Hematuria	NA	NA	NA

Mets, metastasis; dx, diagnosis; M, male; F, female; L, left; R, right; NA, not available; abd, abdominal; LN, lymph node.

Table 2 Treatment and outcome of the reviewed cases of primary angiosarcoma of the kidney

Author	Treatment	Follow-up (months)	Outcome
Qayyum *et al.* (8)	Palliative (patient's wish)	NA	NA
Zhang *et al.* (9)	Nephrectomy	NA	NA
Liu *et al.* (10)	Nephrectomy, RT	6	NED
Brown *et al.* (2)	NA	6	DOD
Brown *et al.* (2)	NA	11	DOD
Brown *et al.* (2)	NA	1	DOD
Brown *et al.* (2)	NA	NA	NA
Brown *et al.* (2)	NA	1	DOD
Brown *et al.* (2)	Nephrectomy	NA	NA
Brown *et al.* (2)	Nephrectomy	NA	NA
Brown *et al.* (2)	Nephrectomy	2	DFUD
Cason *et al.* (6)	Nephrectomy, chemotherapy, RT	10	DOD
Allred *et al.* (11)	Nephrectomy, chemotherapy	3	DOD
Peters *et al.* (12)	Nephrectomy	2	DOD
Prince *et al.* (5)	Nephrectomy, RT	NA	A&W
Sabharwal *et al.* (13)	Nephrectomy, chemotherapy	1	NA
Chaabouni *et al.* (3)	Nephrectomy	1	DOD
López Cubillana *et al.* (14)	Nephrectomy, chemotherapy	5	DOD
Singh *et al.* (15)	NA	NA	NA
Askari *et al.* (16)	Nephrectomy	4	DOD
Douard *et al.* (17)	Nephrectomy	3	DOD
Terris *et al.* (18)	Nephrectomy, RT	10	DOD
Zenico *et al.* (19)	Nephrectomy	4	DOD
Desai *et al.* (20)	Nephrectomy, chemotherapy	4	DOD
Johnson *et al.* (21)	Rapid deterioration	NA	DOD
Kern *et al.* (22)	Nephrectomy	1.5	DOD
Kern *et al.* (22)	Nephrectomy	3	DOD
Fukunaga *et al.* (4)	Nephrectomy	13	DOD
Adjiman *et al.* (23)	Nephrectomy	NA	DOD
Papadimitriou *et al.* (24)	Nephrectomy	NA	A&W
Tsuda *et al.* (55)	Nephrectomy	21	DOD
Leggio *et al.* (1)	Nephrectomy	8	DOD
Mordkin *et al.* (26)	Nephrectomy, chemotherapy, S	NA	NA
Akkad *et al.* (27)	Nephrectomy	30	NED
Cerilli *et al.* (28)	Nephrectomy, RT	6	DOD
Aksoy *et al.* (29)	Nephrectomy, S	3	DOD
Hiratsuka *et al.* (7)	Nephrectomy	29	NED
Aydogdu *et al.* (30)	Nephrectomy	NA	NA
Martínez-Piñeiro *et al.* (31)	Nephrectomy	5	DOD
Lee *et al.* (32)	NA	NA	NA
Berretta *et al.* (33)	Nephrectomy, chemotherapy	NA	NA
Souza *et al.* (34)	Nephrectomy	NA	DFUD
Costero-Barrios *et al.* (35)	Nephrectomy, chemotherapy, RT	12	Recurrence
Grapsa *et al.* (36)	NA	NA	NA
Carnero López *et al.* (37)	Nephrectomy, chemotherapy	5	DOD
Sesar *et al.* (38)	Nephroureterectomy	NA	NA
Pauli & Strutton (39)	Nephrectomy, RT	2	DOD
Yoshida *et al.* (40)	Nephrectomy, immunotherapy	13	DOD
Juan *et al.* (41)	Nephrectomy, chemotherapy, RT	9	DOD
Xuan (42)	Nephrectomy	NA	NA
Yau *et al.* (43)	Nephrectomy, chemotherapy, RT	3	DOD
Garmendia *et al.* (44)	NA	NA	NA
Nguyen *et al.* (45)	Nephrectomy, chemotherapy	18	DOD
Limmer *et al.* (46)	Nephrectomy	1	DOD
Matter *et al.* (47)	Nephrectomy, chemotherapy, RT	18	DOD

Table 2 (*continued*)

Author	Treatment	Follow-up (months)	Outcome
Sanyal *et al.* (48)	Nephrectomy, RT	24	DOD
Testa *et al.* (49)	NA	NA	NA
Yamamoto *et al.* (50)	Nephrectomy, RT	19	NED
Rüb *et al.* (51)	Nephrectomy, chemotherapy	12	AWD
Celebi *et al.* (52)	Nephrectomy, chemotherapy	13	DOD
Li *et al.* (53)	NA	NA	NA
Witczak *et al.* (54)	Nephrectomy	NA	NA

NED, no evidence of disease; NA, not available; DFUD, died from unrelated disease; AWD, alive with disease; DOD, died of disease; RT, radiotherapy; S, splenectomy; A&W, alive and well.

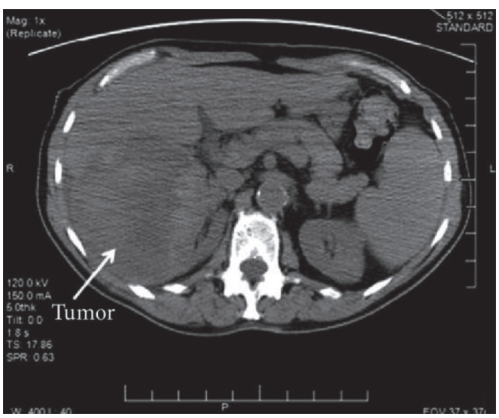

Figure 1 CT imaging of primary angiosarcoma of the right kidney reprinted from (8) with the permission of the Editor-in-Chief of *Case Reports in Pathology*. CT, computed tomography.

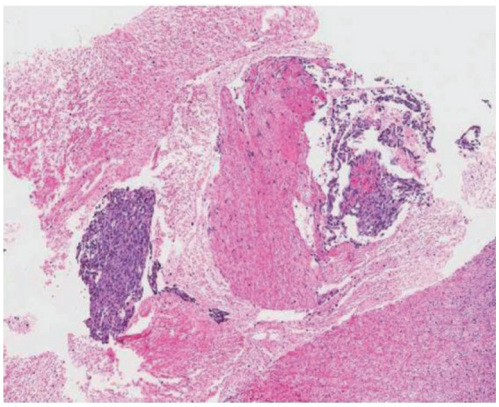

Figure 2 Microscopic features demonstrating necrosis (H&E ×100) reprinted from (8) with the permission of the Editor-in-Chief of *Case Reports in Pathology*.

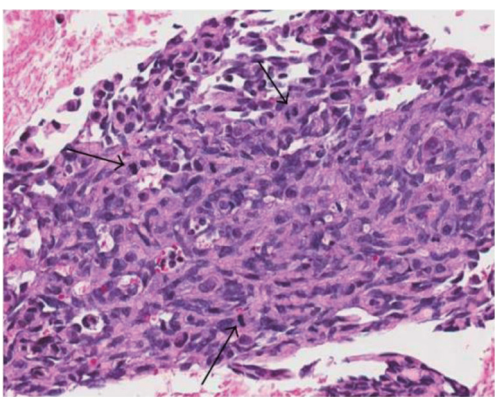

Figure 3 Microscopic section of the tumour showing vascular channels lined with endothelial cells with varying degree of pleomorphism and mitotic activity (H&E ×400) reprinted from (8) with the permission of the Editor-in-Chief of *Case Reports in Pathology*.

similar to AS of other sites. The average size of the tumor in this review is 13 cm (range, 3.7-30 cm). Primary AS of the kidney is predominantly solitary lesions. A rare instance of multifocal lesions (three) of the left kidney which measured 0.5-4.5 cm in size has been reported (38). AS of the kidney is mostly a hemorrhagic (1,3,4,9,10,13,19,25,35) ill-defined (7,10) or well circumscribed necrotic renal mass (4,8) (*Figure 2*). The renal parenchyma may be destroyed with frequent tumor extension to the perinephric fatty tissue (3,4).

Primary AS of the kidney showed multiple and irregular anastomosing vascular spaces or channels which are lined by discrete and large endothelial cells with variable degrees of cytological pleomorphism, nuclear atypia, mitotic activity (*Figure 3*) and multilayering (1,4,7,8,10,24,32,34). There was a mix of epithelioid (2,10,15) and spindle cell (4,10,15,28,40) morphological pattern.

IHC studies

Primary AS of the kidney reacts negatively for epithelial markers like epithelial membrane antigen (EMA), Cam 5.2 and AE1/AE3 (2,4,8). Although AS of the kidney is mostly negative for epithelial markers, positive expression

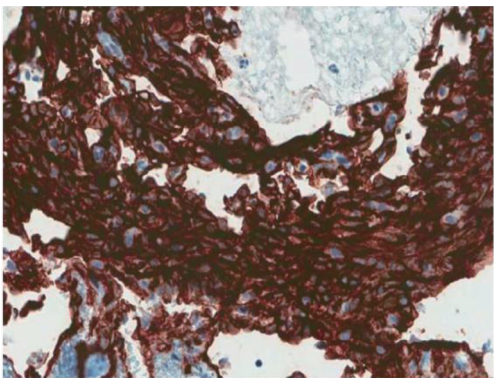

Figure 4 Immunohistochemical study of the tumour showing strong immunoreactivity for CD34 (IHC ×400) reprinted from (8) with the permission of the Editor-in-Chief of *Case Reports in Pathology*. IHC, immunohistochemical.

have been infrequently encountered in AS of other sites. A study of 80 cases of AS of the soft tissue demonstrated immunoreactivity to cytokeratins in 35% of the cases (57). This observation may reflect the rarity of primary AS of the kidney and the paucity of comprehensive IHC staining. Some positivity to epithelial markers in AS of the kidney, similar to the soft tissue counterparts may be found if larger numbers of AS of the kidney were studied. This highlights the need for a cocktail of panel of antibodies or markers in the diagnostic workup rather than a single marker. The tumor stained negative for RCC, CK8/18 (8), CD10 (4,8,27), S100, Melan-A and HMB-45 (1,2,4,9,28). Most tumor cells stained positively for endothelial markers (*Figure 4*) such as CD31, CD34 (1,2,4,8,9,15,24,27,32,34,40), FLI-1 (2,15) and factor 8-related antigen (3,4,7,14,15,27,28,34,40). Co-expression of vimentin may be present (3,10,19,40).

Aberrant expression of neuroendocrine markers in AS, which could be a potential diagnostic pitfall was recently documented (58). A case in point was the co-expression of synaptophysin in 5-10% of cells and chromogranin A in >75% of cells in a 29-year-old Afro-American lady with a hemorrhagic 3.7 cm AS of the kidney (2,58). Synaptophysin was positive in >75% of cells in the other two cases of AS reported. This finding suggested the possibility that some AS may show true neuroendocrine differentiation or it was simply a case of anomalous expression of the antigen. The aggressive clinical behavior of AS with aberrant neuroendocrine expression was similar to other AS however it remains unclear if the finding is of any clinical importance (58). The Ki-67 index of 30% (10), 40% (9) and >80% (13) is suggestive of the highly proliferative nature of the tumor.

Erythroblast transformation specific related gene (*ERG*), an ETS family transcription factor is an IHC marker with high sensitivity and specificity for vascular endothelial tumors. A study of 1,880 tumors which included vascular endothelial, mesenchymal and epithelial tumors that examined the diagnostic utility of *ERG*, suggested that *ERG* compares favorably with CD31 as a marker for AS. Ninety-six percent (96/100) AS of different clinicopathological subgroups and sites confirmed as CD31 positive, demonstrated nuclear *ERG* expression (59).

None of the cases in this review documented IHC study and expression of *PAX8* and *PAX2* markers. *PAX8* and *PAX2* belong to the family of paired box gene which encodes for nuclear transcription factors which is important in organogenesis and are excellent markers for tumors of renal, thyroid and mullerian origin (60). The expression of both markers have been documented in primary and metastatic renal epithelial tumors such as chromophobe RCC, oncocytomas, clear cell RCC, renal medullary carcinomas, papillary RCC etc. *PAX8* appears to be a more sensitive marker compared to *PAX2* (61). To the best of the knowledge of the author, the diagnostic utility of *PAX8* and *PAX2* in primary AS of the kidney awaits investigation.

Treatment

The rarity of primary AS of the kidney is largely responsible for the lack of standardized therapy. The patients were mostly treated with nephrectomy with varying combinations with chemotherapy (6,11,13,14,20,26,33,35,37,41,43,45,47,51,52), radiotherapy (5,6,10,18,28,35,39,41,43,47,48,50) and recombinant interleukin-2 therapy (40). The best treatment option for AS of the kidney remains controversial. Surgery appears to be the most effective treatment approach (31). Terris *et al.* (18) suggested that post-operative adjuvant radiotherapy may contribute to local control in a manner similar to AS of other sites, however Martínez-Piñeiro *et al.* (31) held a contrary view and observed that radiotherapy does not seem to prolong survival and chemotherapy should be added to the treatment. Mordkin *et al.* (26) suggested that chemotherapy may be used for palliative treatment, although the response is likely to be short. Zenico *et al.* (19) observed that patients who had the best response to treatment also underwent radiotherapy and chemotherapy with a median survival of 13 months (P>0.05) compared to 7 months in patients who underwent

nephrectomy only. Zenico *et al.* however emphasized that none of the patients in the cohort reviewed who was treated with chemotherapy or radiotherapy had distant metastasis at the time of diagnosis (19).

Prognosis

Primary AS of the kidney is a very aggressive tumor with a poor prognosis. The mean follow-up is 7 months (range, 1-30 months) and most patients died of the disease. Data on the treatment outcome was not available for 18 of the patients in the review and that includes the case of a male patient who developed coincidental acute myeloblastic leukemia 7 months post left radical nephrectomy (30). There is evidence to suggest that the size of the tumor seems to be the most important factor for determining the prognosis of AS of the kidney. Tumors <5 cm have a significantly better prognosis compared to larger tumor lesions. Mark *et al.* (62) in a review of 67 cases of AS reported a 5-year survival of 32% for lesions <5 cm compared to 13% for lesions >5 cm. Consistent with this finding by Mark *et al.* are the two cases of primary AS of the kidney with the longest post-operative survival in the literature. Akkad *et al.* reported a patient with AS of the kidney 4.5 cm in diameter who had no evidence of disease 30 months after surgery without adjuvant therapy (27). Hiratsuka *et al.* also reported a patient with tumor size of 4.5 cm as well and the patient was disease free after 29 months of follow-up (7).

Conclusions

Primary AS of the kidney is a rare malignant tumor with a poor prognosis. It has a propensity for both local recurrence and distant metastasis at the time of diagnosis or shortly afterwards. The pathogenesis remains unclear, it has overlapping features with other renal tumors and imaging does not allow for tumor specific diagnosis. The importance of histopathology and immunohistochemistry cannot be overemphasized in the diagnosis of the tumor. There is no optimal and standard treatment however, current treatment options include a variable combination of surgery, radiotherapy and chemotherapy.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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