Primary vascular tumours of the kidney

Ayo O Omiyale

ORCID number: Ayo O Omiyale 0000-0001-9955-9207.

Author contributions: Omiyale AO reviewed the literature and wrote the manuscript.

Conflict-of-interest statement: The author declares no conflict of interest for this article.

Country/Territory of origin: United Kingdom

Specialty type: Oncology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind Peer-review report's scientific quality classification
Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works

Abstract

Primary vascular tumours of the kidney are rare and may pose diagnostic difficulties because of their similar clinical, morphological, and immunohistochemical features. This article summarizes the clinical and pathological features of primary renal angiosarcoma and anastomosing haemangioma of the kidney including epidemiology, genetics, and prognosis. Renal anastomosing haemangiomas are benign neoplasms characterized by anastomosing capillary-sized vascular channels. These tumours are rare, with about 75 cases reported in the literature. Most anastomosing haemangiomas are found incidentally on ultrasound, computed tomography, or magnetic resonance imaging. Common symptoms include abdominal pain, haematuria, and abdominal mass. Renal anastomosing haemangiomas are characterized by recurrent mutations in GNAQ and GNA14 genes. The prognosis of anastomosing haemangioma is excellent.

Primary renal angiosarcomas are malignant tumours showing endothelial differentiation. To date, 76 cases have been described in the literature. Primary renal angiosarcomas are frequently symptomatic. The clinical features of renal angiosarcomas are similar to those of renal anastomosing haemangiomas, including abdominal pain, haematuria, and abdominal mass. Angiogenesis-related genes and vascular-specific receptor tyrosine kinases such as KDR, TIE1, SNRK, TEK, and FLT1 are upregulated in angiosarcomas. Primary renal angiosarcomas are highly aggressive neoplasms with a poor prognosis despite surgical treatment, chemotherapy, radiotherapy, or targeted therapy.

Key Words: Kidney; Renal tumours; Angiosarcoma; Haemangioma; Anastomosing haemangioma of the kidney; Vascular tumours

©The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Primary vascular tumours of the kidney are extremely rare. This article
ANASTOMOSING HAEMANGIOMA OF THE KIDNEY

Renal anastomosing haemangiomas are benign neoplasms characterized by anastomosing capillary-sized vascular channels. These tumours are exceptionally rare with about 75 anastomosing haemangiomas reported in the literature[5-9]. These tumours occur in a wide age range from 10 to 83 years (mean, 49 years) with a male-to-female ratio of 2:1[10].

The aetiology and risk factors for renal anastomosing haemangiomas are unknown. Some cases have been reported in the setting of end stage renal disease[11,12].

The vast majority of anastomosing haemangiomas are found incidentally on radiological evaluation for other purposes. Common symptoms include abdominal pain, haematuria, and abdominal mass[5,10].

The imaging findings are non-specific. On computed tomography, these tumours are often circumscribed, hyperdense, and heterogeneous due to fatty or non-enhancing hypodense areas and show post-contrast enhancement[13].

Renal anastomosing haemangiomas are characterized by recurrent mutations in GNAQ and GNA14 genes[14,15]. GNAQ gene encodes guanine nucleotide-binding protein G (q) subunit alpha (Ga q protein) that activates signalling pathways that regulates cell proliferation, survival, development, and function of blood vessels[14-16].

Grossly, anastomosing haemangiomas are typically small ranging from 0.1 cm to 12 cm (mean, 2.2 cm)[5,10,17]. These tumours are often well-demarcated spongy mohogany brown masses[5]. They are usually unilateral and solitary tumours; however, a few cases of bilateral[18] and multifocal[11] tumours have been described.

Histologically, anastomosing haemangiomas consist of anastomosing capillary-sized blood vessels, reminiscent of splenic sinuoids. The blood vessels are lined by bland endothelial cells. Typically, these tumours lack endothelial cell multilayering, papillary tufting, cytologic atypia, necrosis, and prominent mitotic figures. They may show extramedullary haemopoiesis, hyaline globules, and mild lymphocytic infiltrate[1,2,5,10,18].

Rarely, renal anastomosing haemangiomas may infiltrate perinephric fat, renal sinus fat[2,12], and the renal vein or its segmental branches[2,12,18,19]. The neoplastic cells are immunoreactive for CD31, CD34, ERG, FLI1, and factor VIII-related antigen (now rarely used)[5].

Renal anastomosing haemangiomas may co-exist with other renal neoplasms such as metanephric adenoma, papillary adenoma, papillary renal cell carcinoma, acquired cystic disease-associated renal cell carcinoma, and clear cell renal cell carcinoma[11,12].

Citation: Omiyale AO. Primary vascular tumours of the kidney. World J Clin Oncol 2021;12(12): 1157-1168
URL: https://www.wjgnet.com/2218-4333/full/v12/i12/1157.htm
DOI: https://dx.doi.org/10.5306/wjco.v12.i12.1157

INTRODUCTION

Although vascular tumours are relatively common in the skin and soft tissue, they are extremely rare in the kidney, ranging from benign to malignant neoplasms that may be diagnostically challenging because of the overlapping clinical, morphological and immunohistochemical features.

These tumours include renal angiosarcomas and renal haemangiomas. Various subtypes of haemangiomata have been described in the kidney including cavernous, capillary, and anastomosing haemangiomas[1-4]. However, the most common subtype is anastomosing haemangiomata[1,2,5].

This article provides an overview of the clinical and pathological features of anastomosing haemangioma of the kidney and primary angiosarcoma of the kidney, and discusses the epidemiology, genetics, and prognosis.
Most patients with renal anastomosing haemangioma, described in the literature, were treated with radical nephrectomy, reflecting a tendency to overtreat these patients, probably because of inaccurate preoperative diagnosis (Table 1).

The prognosis of anastomosing haemangioma is excellent with no evidence of recurrence, metastasis or tumour-related death at an average follow-up of 24.8 mo (range, <1-156 mo) (Table 1).

Primary Angiosarcoma of the Kidney

Renal angiosarcomas are malignant tumours showing endothelial differentiation. These tumours are very rare, with about 76 cases described in the literature as case series and reports[20-24]. There is a male-to-female ratio of 6:1, with patient age ranging from 24 years to 95 years (median, 62 years).

Although angiosarcomas arising in other anatomical sites have been associated with risk factors such as exposure to thorium dioxide, arsenic-based pesticides, polyvinyl chloride, and radiation therapy particularly for breast, endometrial and prostate cancers[25-27], no specific aetiology or risk factors have been established for primary angiosarcoma of the kidney[20,28].

The clinical features of renal angiosarcomas are identical to those of renal anastomosing haemangiomas. Common symptoms include abdominal pain, haematuria, abdominal mass, and weight loss. A rare case of spontaneous tumour rupture with retroperitoneal haematoma has been described[29].

Computed tomography imaging shows large masses with heterogeneous enhancement and hypervascularity[30].

Angiogenesis-related genes and vascular-specific receptor tyrosine kinases such as KDR, TIE1, SNRK, TEK, and FLT1, are upregulated in angiosarcomas[31]. High-level MYC gene amplifications are seen in most radiation-induced and chronic lymphoedema-associated angiosarcomas[32]. A subset of cases is characterized by PLCG1, KDR, and PTPRB mutations[33,34].

Some primary angiosarcomas, typically in young adults, have recurrent CIC gene rearrangements, with or without concurrent CIC mutations, and are characterized by upregulation of CIC-target genes including ETV1, ETV4, and ETV5[34]. Angiosarcomas with CIC gene abnormalities are associated with an inferior disease-free survival[34].

Primary renal angiosarcomas are usually large ranging from 3.6 cm to 30 cm (mean, 13 cm). Typically, they are ill-defined haemorrhagic spongy masses with necrosis[1,20].

Microscopically, these tumours range from well-formed vasoformative areas to areas with solid morphology showing sparse vasoformation. These patterns are often mixed within the same tumour. Vasoformative areas are composed of small to medium-sized anastomosing blood vessels, lined by epithelioid and/or spindled endothelial cells showing nuclear pleomorphism, endothelial papillary tufting, multilayering, intraluminal budding, and hobnailing[1,20,28]. Solid areas consist of sheets of malignant epithelioid and/or spindled cells with subtle vasoformation, cytologic atypia, and mitotic figures. Necrosis may be present. Angiosarcomas usually have a haemorrhagic background and extravasated red blood cells are seen within the tumour[1,20,28].

Epithelioid angiosarcomas are composed of sheets of large atypical polygonal or epithelioid cells with nuclear pleomorphism, high nuclear to cytoplasmic ratio, prominent central nucleoli, mitotic figures, and moderate amounts of cytoplasm. Epithelioid angiosarcomas may be mistaken for carcinoma, melanoma, or lymphoma[20,28,35-37].

The neoplastic cells are positive for CD31, ERG, FLI1, CD34, and factor VIII-related antigen[20,28,38,39]. Epithelioid angiosarcomas may be positive for epithelial markers including CK7, Cam5.2, AE1/AE3, and EMA, which may lead to a misdiagnosis of carcinoma[20].

Similar to angiosarcomas arising at other locations, renal angiosarcomas have a tendency for widespread metastasis at diagnosis or afterwards in the course of the disease. Approximately 66% of patients develop metastases, most commonly to the lung and liver. Other sites of metastasis include bone, lymph nodes, peritoneum, small bowel, soft tissue, and skin. Currently, there are no specific standardized treatment guidelines for primary renal angiosarcomas. These tumours are treated with radical nephrectomy, chemotherapy, radiotherapy, or targeted therapy (Table 2).
| Ref.                                      | Treatment       | Follow-up (mo) | Outcome |
|------------------------------------------|-----------------|----------------|---------|
| Bean et al[14]                           | Nephrectomy     | 9              | NED     |
| Bean et al[14]                           | Nephrectomy     | 84             | NED     |
| Bean et al[14]                           | Nephrectomy     | 107            | NED     |
| Memmedoğlu and Musayev[41]               | Nephrectomy     | 12             | NED     |
| Memmedoğlu and Musayev[41]               | Nephrectomy     | 12             | NED     |
| Tahir and Folwell[42]                    | Nephrectomy     | 1              | NED     |
| Pantelides et al[6]                      | Nephrectomy     | 6              | NED     |
| Downes et al[7]                          | Nephrectomy     | NA             | NA      |
| Downes et al[7]                          | Biopsy          | NA             | NA      |
| Chandran et al[8]                        | Nephrectomy     | NA             | NA      |
| Cha et al[9]                             | Nephrectomy     | 5              | NED     |
| Montgomery and Epstein[2]                | Nephrectomy     | 12             | NED     |
| Montgomery and Epstein[2]                | Nephrectomy     | 36             | NED     |
| Montgomery and Epstein[2]                | Nephrectomy     | NA             | NA      |
| Montgomery and Epstein[2]                | Excision        | 8              | NED     |
| Heidegger et al[43]                      | Nephrectomy     | 156            | NED     |
| Kryvenko et al[12]                       | Nephrectomy     | NA             | NA      |
| Kryvenko et al[12]                       | Nephrectomy     | NA             | NA      |
| Kryvenko et al[12]                       | Nephrectomy     | NA             | NA      |
| Kryvenko et al[12]                       | Nephrectomy     | NA             | NA      |
| Kryvenko et al[12]                       | Nephrectomy     | NA             | NA      |
| Kryvenko et al[12]                       | Nephrectomy     | NA             | NA      |
| Kryvenko et al[12]                       | Nephrectomy     | NA             | NA      |
| Al-Maghrabi and Al-Rashed[44]            | Partial nephrectomy | 12            | NED     |
| Caballes et al[17]                       | Nephrectomy     | 18             | NED     |
| Büttner et al[11]                        | Nephrectomy     | NA             | NA      |
| Büttner et al[11]                        | Nephrectomy     | NA             | NA      |
| Büttner et al[11]                        | Nephrectomy     | NA             | NA      |
| Büttner et al[11]                        | Nephrectomy     | NA             | NA      |
| Büttner et al[11]                        | Nephrectomy     | NA             | NA      |
| Büttner et al[11]                        | Nephrectomy     | NA             | NA      |
| Büttner et al[11]                        | Nephrectomy     | NA             | NA      |
| Lee et al[45]                            | Nephrectomy     | NA             | NA      |
| Zhao et al[46]                           | Nephrectomy     | 12             | NED     |
| Kryvenko et al[18]                       | Nephrectomy     | 7              | NED     |
Primary renal angiosarcomas are highly aggressive neoplasms with 76.3% of patients dying of tumour within 1 mo to 24 mo (mean, 7.5 mo), despite surgical and adjuvant therapy (Table 2). Poor prognostic factors for angiosarcomas occurring at other anatomic sites include age > 69 years, tumour size ≥ 5 cm, regional disease (vs localized disease), non-surgical treatment, and distant metastasis.

**CONCLUSION**

Primary vascular tumours of the kidney are rare neoplasms. Unlike primary renal
### Table 2 Treatment, follow-up, and outcome of patients with primary angiosarcoma of the kidney

| Ref.                      | Treatment                           | Follow-up (mo) | Outcome |
|---------------------------|-------------------------------------|----------------|---------|
| Costero-Barrios et al[59] | Nephrectomy, Chemo, RT              | 12             | AWD     |
| Peters et al[60]          | Nephrectomy                         | 2              | DOD     |
| Singh et al[35]           | NA                                  | NA             | NA      |
| Kern et al[61]            | Nephrectomy                         | 3              | DOD     |
| Kern et al[61]            | Nephrectomy                         | 1.5            | DOD     |
| Aydogdu et al[62]         | Nephrectomy                         | NA             | NA      |
| Akkad et al[63]           | Nephrectomy                         | 30             | NED     |
| Witzzak et al[64]         | nephrectomy                         | NA             | NA      |
| Chaabouni et al[38]       | Nephrectomy                         | 1              | DOD     |
| Johnson et al[65]         | Rapid deterioration                 | NA             | DOD     |
| Zenico et al[66]          | Nephrectomy                         | 4              | DOD     |
| Nguyen et al[67]          | Nephrectomy, Chemo                  | 18             | DOD     |
| Terris et al[68]          | Nephrectomy, RT                     | 10             | DOD     |
| Matter et al[69]          | Nephrectomy, Chemo, RT              | 18             | DOD     |
| Yoshida et al[70]         | Nephrectomy, Recombinant IL-2       | 13             | DOD     |
| Pauli and Strutton[71]    | Nephrectomy, RT                     | 2              | DOD     |
| Martinez-Piñeiro et al[72]| Nephrectomy, S                      | 4              | DOD     |
| Bernstein et al[73]       | NA                                  | NA             | NA      |
| Liu et al[36]             | Nephrectomy, RT                     | 6              | NED     |
| Yau et al[74]             | Nephrectomy, Chemo, RT              | 3              | DOD     |
| Carnero López et al[75]   | Nephrectomy, Chemo                  | 5              | DOD     |
| Kazaz et al[76]           | Nephrectomy, Chemo                  | NA             | NA      |
| Souza et al[77]           | Nephrectomy                         | 1              | DFUD    |
| Detorakis et al[78]       | Nephrectomy, Chemo                  | 11             | DOD     |
| Komoto et al[79]          | Nephrectomy                         | 9.2            | DOD     |
| Boni et al[80]            | Nephrectomy, Chemo                  | 15             | DOD     |
| Chang et al[81]           | Nephrectomy, Chemo, RT              | NA             | NA      |
| Iannacci et al[82]        | Nephrectomy                         | NA             | DOD     |
| Subramanian et al[83]     | Nephrectomy                         | NA             | NA      |
| Waqas et al[84]           | Nephrectomy, Chemo                  | NA             | NA      |
| Courley et al[85]         | Nephrectomy                         | NA             | DOD     |
| Su[86]                    | Nephrectomy, Chemo                  | NA             | DOD     |
| López Cubillana et al[87] | Nephrectomy, Chemo                  | 5              | DOD     |
| Juan et al[88]            | Nephrectomy, Chemo, RT              | 9              | DOD     |
| Prince[21]                | Nephrectomy, RT                     | NA             | A and W |
| Sesar et al[22]           | Nephroureterectomy                  | NA             | NA      |
| Testa et al[23]           | Nephrectomy                         | 27             | DFUD    |
| Xuan[24]                  | Nephrectomy                         | NA             | NA      |
| Brown et al[1]            | NA                                  | 6              | DOD     |
| Brown et al[1]            | NA                                  | 11             | DOD     |
| Brown et al[1]            | NA                                  | 1              | DOD     |
angiosarcoma, the prognosis of renal anastomosing haemangioma is excellent with no evidence of recurrence or metastasis. These tumours share similar clinical, morphological and immunohistochemical features, and must be distinguished from each other. Features that favour angiosarcomas include the presence of malignant spindled and/or epithelioid cells with a variable degree of vasoformation, cytologic atypia, prominent mitotic figures, endothelial multilayering, papillary tufting, and necrosis.
REFERENCES

1. Brown JG, Folpe AL, Rao P, Lazar AJ, Paner GP, Gupta R, Parakh R, Cheville JC, Amin MB. Primary vascular tumors and tumor-like lesions of the kidney: a clinicopathologic analysis of 25 cases. Am J Surg Pathol 2010; 34: 942-949 [PMID: 20534992 DOI: 10.1097/PAS.0b013e3181e4f32a]

2. Montgomery E, Epstein JI. Anastomosing hemangioma of the genitourinary tract: a lesion mimicking angiosarcoma. Am J Surg Pathol 2009; 33: 1364-1369 [PMID: 19606104 DOI: 10.1097/PAS.0b013e3181ad30a7]

3. Sethi S, Agarwal V, Chopra P. Cavernous hemangioma of the kidney: A report of two cases and review of the literature. Urol Ann 2012; 4: 187-190 [PMID: 23248529 DOI: 10.4103/0974-7796.102674]

4. Mehta V, Ananthanarayanan V, Antic T, Krausz T, Milner J, Venkataraman G, Pickren MM. Primary benign vascular tumors and tumorlike lesions of the kidney: a clinicopathological analysis of 15 cases. Virchows Arch 2012; 461: 669-676 [PMID: 23090628 DOI: 10.1007/s00428-012-1333-9]

5. Omiyale AO. Anastomosing hemangioma of the kidney: a literature review of a rare morphological variant of hemangioma. Ann Transl Med 2015; 3: 151 [PMID: 26244138 DOI: 10.3978/j.issn.2305-5839.2015.06.16]

6. Pantelides NM, Agrawal S, Mawson I, Hazell S, Gibbons N. An Anastomosing Haemangioma: A Rare Vascular Tumour Presenting as a Solid Renal Mass. Br J Med Surg Urol 2012; 5: 84-86 [DOI: 10.1016/j.bjmsu.2011.01.003]

7. Downes MR, Dickson BC, Cheung CC. Anastomosing haemangioma of kidney: morphologic features and diagnostic considerations of an unusual vasoformative tumour. Diagn Histopathol 2014; 20: 208-212 [DOI: 10.1016/j.dhdp.2014.03.002]

8. Chandran N, Kannan MS, Veeramani M. Renal anastomosing hemangioma: a diagnosis to ponder. Indian J Transplant 2019; 13: 59-61 [DOI: 10.4103/ijot.ijot_63_18]

9. Cha JS, Jeong YB, Kim HJ. Anastomosing hemangioma mimicking renal cell carcinoma. Korean J Urol Oncol 2016; 14: 88-92 [DOI: 10.22465/kjou.2016.14.2.88]

10. Omiyale AO, Carton J. Clinicopathological and genetic features of anastomosing haemangioma of the kidney: a narrative review. AME Med J 2021; 6: 30 [DOI: 10.21037/ajm-20-181]

11. Böttner M, Kufer V, Brunner K, Hartmann A, Amann K, Agaimy A. Benign mesenchymal tumours and tumour-like lesions in end-stage renal disease. Histopathology 2013; 62: 229-236 [PMID: 23202314 DOI: 10.1111/his.12394.x]

12. Kryvenko ON, Haley SL, Smith SC, Shen SS, Paluru S, Gupta NS, Jorda M, Epstein JI, Amin MB, Truong LD. Haemangiomas in kidneys with end-stage renal disease: a novel clinicopathological association. Histopathology 2014; 65: 309-318 [PMID: 24548339 DOI: 10.1111/his.12394]

13. O'Neill AC, Craig JW, Silverman SG, Alencar RO. Anastomosing hemangiomas: locations of occurrence, imaging features, and diagnosis with percutaneous biopsy. Abdom Radiol (NY) 2016; 41: 1325-1332 [PMID: 26960722 DOI: 10.1007/s00261-016-0690-2]

14. Bean GR, Joseph NM, Gill RM, Folpe AL, Horvai AE, Umetsu SE. Recurrent GNAQ mutations in anastomosing hemangiomas. Mod Pathol 2017; 30: 722-727 [PMID: 28084343 DOI: 10.1038/modpathol.2016.234]

15. Bean GR, Joseph NM, Folpe AL, Horvai AE, Umetse SE. Recurrent GNA14 mutations in anastomosing hemangiomas. Histopathology 2018; 73: 354-357 [PMID: 29574926 DOI: 10.1111/his.13519]

16. Urtatiz O, Van Raamsdonk CD, Gruau and Gna11 in the Endothelin Signaling Pathway and Melanoma. Front Genet 2016; 7: 59 [PMID: 27148356 DOI: 10.3389/fgen.2016.00059]

17. Caballes AB, Abelardo AD, Farolan MJ, Veloso JAD. Pediatric Anastomosing Hemangioma: Case Report and Review of Renal Vascular Tumors in Children. Pediatr Dev Pathol 2019; 22: 269-275 [PMID: 30369288 DOI: 10.1177/1093526618809230]

18. Kryvenko ON, Gupta NS, Meier FA, Lee MW, Epstein JI. Anastomosing hemangioma of the genitourinary system: Eight cases in the kidney and ovary with immunohistochemical and ultrastructural analysis. Am J Clin Pathol 2011; 136: 450-457 [PMID: 21846922 DOI: 10.1369/AJCPJPW34QCYMTM1]

19. Omiyale AO, Golash A, Mann A, Kryakiidis D, Kalyanasundaram K. Anastomosing Haemangioma of the Kidney Involving a Segmental Branch of the Renal Vein. Case Rep Surg 2015; 2015: 927286 [PMID: 26435872 DOI: 10.1155/2015/927286]

20. Omiyale AO, Carton J. Clinical and Pathologic Features of Primary Angiosarcoma of the Kidney. Curr Urol Rep 2018; 19: 4 [PMID: 29383452 DOI: 10.1007/s11934-018-0755-6]

21. Prince CL. Primary angio-endothelioma of the kidney: report of a case and brief review. J Urol 1942; 47: 787-789 [DOI: 10.1016/S0022-5347(18)31708-7]

22. Sesar P, Ulane M, Soša D, Tniski D, Tomas D. Primary renal angiosarcoma. Acta Clin Croat 2012; 51: 182

23. Testa G, Talamona G, Tufano A, Marino-Marsilia G. Primary renal angiosarcoma: a case report. Acta Urologica Italica 1998; 12: 225-227

24. Xuan Y. Primary renal angiosarcoma: one case report and literature review. Chin J Clin Oncol 2008; 5: 229-230 [DOI: 10.1007/s11805-008-0229-6]

25. Penel N, Grosjean J, Robin YM, Vansemeyerter L, Clisant S, Adenis A. Frequency of certain established risk factors in soft tissue sarcomas in adults: a prospective descriptive study of 658 cases.
Zhao M. Radiologic findings of renal hemangioma: report of three cases. *Korean J Radiol* 2013; 14: 255-262 [PMID: 23826335 DOI: 10.12659/ajcr.902939]

Leggio L, Addolorato G, Abenavoli L, Ferrulli A, D'Angelo C, Mirijello A, Vonghia L, Schinazzi G, Arena V, Perrone L, Citterio F, Bonomo L, Rapaccini GL, Capelli A, Barone C, Gasbarrini G. Primary renal angiosarcoma: a rare malignancy. A case report and review of the literature. *Urol Oncol* 2006; 24: 307-312 [PMID: 16818182 DOI: 10.1016/j.urolonc.2005.10.002]

Antonescu CR, Yoshida A, Guo T, Chang NE, Zhang L, Agaram NP, Qin LX, Brennan MF, Singer S, Maki RG. KDR activating mutations in human angiosarcomas are sensitive to specific kinase inhibitors. *Cancer Res* 2009; 69: 7175-7179 [PMID: 19723655 DOI: 10.1158/0008-5472.CAN-09-2068]

Guo T, Zhang L, Chang NE, Singer S, Maki RG, Antonescu CR. Consistent MYC and FLT4 gene amplification in radiation-induced angiosarcoma but not in other radiation-associated atypical vascular lesions. *Genes Chromosomes Cancer* 2011; 50: 25-33 [PMID: 20949568 DOI: 10.1002/gcc.200827]

Singh C, Xie L, Schmechel SC, Manivel JC, Pambuccian SE. Epithelioid angiosarcoma of the kidney: a diagnostic dilemma in fine-needle aspiration cytology. *Diagn Cytopathol* 2012; 40 Suppl 2: E131-E139 [PMID: 21698784 DOI: 10.1002/dc.21762]

Liu H, Huang X, Chen H, Wang X, Chen L. Epithelioid angiosarcoma of the kidney: A case report and literature review. *Oncol Lett* 2014; 8: 1155-1158 [PMID: 25120677 DOI: 10.3892/ol.2014.2292]

Li N, Li W, Li Z. Primary renal epithelioid angiosarcoma with transitional cell carcinoma in renal pelvis. *Zhonghua Wu Nei Za Zhi* 1997; 35: 294-295 [PMID: 10374567]

Chaabouni A, Rebai N, Chahebouh K, Fourati M, Bouaouida M, Slimen MH, Bahloul A, Mihi NR. Primary renal angiosarcoma: Case report and literature review. *Can Urol Assoc J* 2013; 7: E430-E432 [PMID: 23826057 DOI: 10.5489/cuaj.1396]

Iacovelli R, Orlando V, Palazzo A, Cortesi E. Clinical and pathological features of primary renal angiosarcoma. *Can Urol Assoc J* 2014; 8: E223-E226 [PMID: 24839487 DOI: 10.5489/cuaj.1585]

Zhang C, Xu G, Liu Z, Xu Y, Lin F, Baklauev VP, Chekhonin VP, Peltzer K, Mao M, Wang X, Wang G, Zhang C. Epidemiology, tumor characteristics and survival in patients with angiosarcoma in the United States: a population-based study of 4537 cases. *Jpn J Clin Oncol* 2019; 49: 1092-1099 [PMID: 31612920 DOI: 10.1093/jjco/hyz113]

Memmedolu A, Musayev J. Spontaneous rupture of the kidney in the patients with synchronous renal hemangioma and nephrogenic hypertension. *Turk J Urol* 2015; 41: 231-234 [PMID: 26623154 DOI: 10.5152/tud.2015.48264]

Tahir M, Folwell A. Anastomosing haemangioma of kidney: a rare subtype of vascular tumour of the kidney mimicking angiosarcoma. *ANZ J Surg* 2016; 86: 838-839 [PMID: 25041271 DOI: 10.1111/ans.12779]

Heidigger I, Pichler R, Schäfer G, Zelger B, Aigner F, Bektic J, Horninger W. Long-term follow up of renal anastomosing hemangioma mimicking renal angiosarcoma. *Int J Urol* 2014; 21: 836-838 [PMID: 24650180 DOI: 10.1111/iju.12433]

Al-Maghrabi HA, Al Rashid AS. Challenging Pitfalls and Mimickers in Diagnosing Anastomosing Capillary Hemangiomata of the Kidney: Case Report and Literature Review. *Am J Case Rep* 2017; 18: 255-262 [PMID: 28286335 DOI: 10.12659/ajcr.902939]

Lee HS, Koh BH, Kim JW, Kim YS, Rhim HC, Cho OK, Hahn CK, Woo YN, Park MH. Radiologic findings of renal hemangioma: report of three cases. *Korean J Radiol* 2006; 7: 60-63 [PMID: 17152931 DOI: 10.3348/kjr.2000.1.1.60]

Zhao M, Li C, Zheng J, Sun K. Anastomosing hemangioma of the kidney: a case report of a rare subtype of hemangioma mimicking angiosarcoma and review of the literature. *Int J Clin Exp Pathol* 2013; 6: 757-765 [PMID: 23573324]
Primary vascular tumours of the kidney

Omiyale AO. Primary vascular tumours of the kidney

47 Tao LL, Dai Y, Yin W, Chen J. A case report of a renal anastomosing hemangiomia and a literature review: an unusual variant histologically mimicking angiosarcoma. *Diagn Pathol* 2014; 9: 159 [PMID: 25102914 DOI: 10.1186/s13000-014-0159-3]

48 Abboudi H, Tschobobko B, Carr C, DasGupta R. Bilateral Renal Anastomosing Hemangiomas: A Tale of Two Kidneys. *J Endourol Case Rep* 2017; 3: 176-178 [PMID: 29279869 DOI: 10.1089/cenr.2017.0015]

49 Silva MA, Fonseca EKUN, Yamauchi FI, Baroni RH. Anastomosing hemangioma simulating renal cell carcinoma. *Int Braz J Urol* 2017; 43: 987-989 [PMID: 28727378 DOI: 10.1590/S1677-5538.IBJU.2016.0653]

50 Berker NK, Bayram A, Tas S, Bakir B, Caliskan Y, Ozcan F, Kilicaslan I, Ozluk Y. Comparison of Renal Anastomosing Hemangiomas in End-Stage and Non-End-Stage Kidneys: A Meta-Analysis With a Report of 2 Cases. *Int J Surg Pathol* 2017; 25: 488-496 [PMID: 28436289 DOI: 10.1177/1066896917706025]

51 Perdik M, Datseri G, Liapis G, Chondros N, Anastasiou I, Tzardi M, Delladetsima JK, Drakos E. Anastomosing hemangioma: report of two renal cases and analysis of the literature. *Diag Pathol* 2017; 12: 14 [PMID: 28118845 DOI: 10.1186/s13000-017-0597-4]

52 Wetherell DR, Skene A, Manya K, Manecksha RP, Chan Y, Bolton DM. Anastomosing haemangioma of the kidney: a rare morphological variant of haemangioma characteristic of genitourinary tract location. *Pathology* 2013; 45: 193-196 [PMID: 23250038 DOI: 10.1097/PAT.0b013e32835c782b]

53 Manohar V, Krishnanurthy S, Ranganathan J, Pai VD. A case of giant anastomosing hemangioma of the kidney with extramedullary hematopoiesis: A great mimicker. *Indian J Pathol Microbiol* 2020; 63: 292-294 [PMID: 32317537 DOI: 10.4103/ijpm.IJPM.434.18]

54 Johnstone KJ, Stratton GM, Perry-Keene JL, Hazratwala K, Delahunt B. Multifocal anastomosing haemangioma of the kidney with intravascular growth and sinus fat invasion: a rare benign mimic of angiosarcoma. *Pathology* 2020; 52: 394-396 [PMID: 32111399 DOI: 10.1016/j.pathol.2020.01.0681]

55 Tran TA, Perricone P. Anastomosing hemangioma with fatty changes of the genitourinary tract: a lesion mimicking angiomylipoma. *Cen European J Urol* 2012; 65: 40-42 [PMID: 24578924 DOI: 10.5173/cjenu.2012.01.ar15]

56 Zhang W, Wang Q, Liu YL, Yu WJ, Liu Y, Zhao H, Zhuang J, Jiang YX, Li YJ. Anastomosing hemangioma arising from the kidney: a case of slow progression in four years and review of literature. *Int J Clin Exp Pathol* 2015; 8: 2208-2213 [PMID: 25973131]

57 Cheon PM, Rebello R, Naqvi A, Popovic S, Bonert M, Kapoor A. Anastomosing hemangioma of the kidney: radiologic and pathologic distinctions of a kidney cancer mimic. *Curr Oncol* 2018; 25: e220-e223 [PMID: 29962849 DOI: 10.3747/co.25.3927]

58 Chou S, Subramanian V, Lau HM, Achan A. Renal Anastomosing Hemangiomas With a Diverse Morphologic Spectrum: Report of Two Cases and Review of Literature. *Int J Surg Pathol* 2014; 22: 369-373 [PMID: 23816283 DOI: 10.1016/j.ijsp.2013.06.050]

59 Costero-Barrios CB, Oros-Ovalle C. Primary renal angiosarcoma. *Gac Med Mex* 2004; 140: 463-466 [PMID: 15456157]

60 Peters HJ, Nuri M, Münzenmaier R. Hemangiendothelioma of the kidney: a case report and review of the literature. *J Urol* 1974; 112: 723-726 [PMID: 4548091 DOI: 10.1016/s0022-5347(17)57586-5]

61 Kern SB, Gott L, Faulkner J 2nd. Occurrence of primary renal angiosarcoma in brothers. *Arch Pathol Lab Med* 1995; 119: 75-78 [PMID: 7802558]

62 Aydogdu I, Turhan O, Sari R, Ates M, Türk M. Coincidental acute myeloblastic leukemia in a patient with renal angiosarcoma. *Haematologica (Budap)* 1999; 74: 313-317 [PMID: 10438072]

63 Akkad T, Tsanakov A, Pelzer A, Peschel R, Bartsch G, Steiner H. Early diagnosis and straight forward surgery of an asymptomatic primary angiosarcoma of the kidney led to long-term survival. *Int J Urol* 2006; 13: 1112-1114 [PMID: 16903939 DOI: 10.1111/j.1442-2042.2006.01490.x]

64 Witecz W, Szubiatrski F, Szmytinski C, Rajca Z, Staszczyzk S. Renal hemangiomia. *Pol Tyg Lek* 1993; 48: 483-484 [PMID: 8170817]

65 Johnson VV, Gaertner EM, Crotthers BA. Fine-needle aspiration of renal angiosarcoma. *Arch Pathol Lab Med* 2002; 126: 478-480 [PMID: 11906578 DOI: 10.5858/2002-126-0478-FNAOAR]

66 Zenico T, Sacconanni M, Salomone U, Bertovich E. Primary renal angiosarcoma: case report and review of world literature. *Tumori* 2011; 97: e6-e9 [PMID: 21899448 DOI: 10.1700/950.10412]

67 Nguyen T, Auquier MA, Renard C, Cordonnier C, Saint F, Remond A. Hemoptysis and spontaneous rupture of a primary renal angiosarcoma: a case report. *J Radiol* 2010; 91: 1313-1317 [PMID: 21242919 DOI: 10.1016/j.jrad.2010.06.021]

68 TErris D, Plaine L, Steinfeld A. Renal angiosarcoma. *Am J Kidney Dis* 1986; 8: 131-133 [PMID: 3740662 DOI: 10.1016/s0272-6386(86)80126-3]

69 Matter IE, Flury R, Hailermariam S, Hauri D, Sulser T. Angiosarcoma of the kidney. Case report and review of the literature. *Urologe A* 1999; 38: 65-68 [PMID: 10081105 DOI: 10.1007/s001200050248]

70 Yoshida K, Ito F, Nakayawa H, Maeda Y, Tomoe H, Aiba M. A case of primary renal angioma. *Rare Tumors* 2009; 1: e28 [PMID: 21139907 DOI: 10.4081/rt.2009.e28]

71 Pauli JJ, Stratton G. Primary renal angiosarcoma. *Pathology* 2005; 37: 187-189 [PMID: 16028856 DOI: 10.1080/0303789750058979]

72 Martínez-Piñeiro I, López-Ferrer P, Picazo ML, Martínez-Piñeiro JA. Primary renal angiosarcoma.
Case report and review of the literature. *Scand J Urol Nephrol* 1995; 29: 103-108 [PMID: 7618041 DOI: 10.3109/00365595901980547]

73 **Bernstein ML**, Leclerc JM, Bunin G, Brisson L, Robison L, Shuster J, Byrne T, Gregory D, Hill G, Dougherty G. A population-based study of neuroblastoma incidence, survival, and mortality in North America. *J Clin Oncol* 1992; 10: 323-329 [PMID: 1732433 DOI: 10.1200/JCO.1992.10.2.323]

74 **Yau T**, Leong CH, Chan WK, Chan JK, Liang RH, Epstein RJ. A case of mixed adult Wilms' tumour and angiosarcoma responsive to carboplatin, etoposide and vincristine (CEO). *Cancer Chemother Pharmacol* 2008; 61: 717-720 [PMID: 17571263 DOI: 10.1007/s00280-007-0529-1]

75 **Carnero López B**, Fernández Pérez I, Carrasco Alvarez IA, Lázaro Quintela ME, López Jato C, Jorge Fernández M, Gentil González M, Vázquez Tuñas L, Castellanos Diez J. Renal primary angiosarcoma. *Clin Transl Oncol* 2007; 9: 806-810 [PMID: 18158986 DOI: 10.1007/s12094-007-0144-y]

76 **Kazaz IO**, Ersoz S, Colak F, Teoman AS, Kazaz SN, Karaguzel E, Kutha O. Primary renal angiosarcoma: a case report and a short review of literature. *Indian J Pathol Microbiol* 2020; 63: S44-S46 [PMID: 32108626 DOI: 10.4103/IJPM.IJPM_66_19]

77 **Souza OE**, Etchebehere RM, Lima MA, Monti PR. Primary renal angiosarcoma. *Int Braz J Urol* 2006; 32: 448-450 [PMID: 16953913 DOI: 10.1590/s1677-55382006000400011]

78 **Deterakis EE**, Chryssou E, Raisakis M, Androulidakis E, Heretis I, Haniotis V, Karantanas A. Primary renal angiosarcoma: radiologic-pathologic correlation and literature review. Tumor* 2013; 99: e11-e16 [PMID: 24158076 DOI: 10.1700/1334.14817]

79 **Komoto H**, Kitajima K, Kawanaka Y, Yoshimura N, Kunimoto R, Yokoyama H, Shinkai Y, Kaizuka Y, Yamamoto S, Kihara T, Kimura N, Hirota S, Yamakado K. CT Findings of Primary Renal Angiosarcoma. *Case Rep Oncol* 2021; 14: 212-216 [PMID: 33776706 DOI: 10.1159/000512015]

80 **Boni A**, Cochetti G, Sidoni A, Bella M, Mancini M, Maccarrone L, Picci P. Primary Angiosarcoma of the Kidney: Case Report and Comprehensive Literature Review. *Open Med* (Wars) 2019; 4: 443-455 [PMID: 31410364 DOI: 10.1515/mod-2019-0048]

81 **Chang CW**, Chien CC, Juan YS, Chueh KS. Primary renal angiosarcoma mimicking urothelial carcinoma - A case report and literature reviews. *Urol Case Rep* 2021; 34: 101407 [PMID: 33145170 DOI: 10.1016/j.eucr.2020.101407]

82 **Iannacci G**, Crispino M, Cifarelli P, Montella M, Panarese I, Ronchi A, Russo R, Tremiterra G, Luise R, Sapere P. Epithelioid angiosarcoma arising in schwannoma of the kidney: report of the first case and review of the literature. *World J Surg Oncol* 2016; 14: 29 [PMID: 26842370 DOI: 10.1186/s12957-016-0789-5]

83 **Subramanian H**, Parepadil P, Srinivas BH, Gochhait D, Ks S. Primary Renal Angiosarcoma With Lymph Node Metastasis- A Rare Intriguing Malignancy With a Grim Outcome. *Urology* 2015; 133: 14-16 [PMID: 33621584 DOI: 10.1016/j.urology.2015.02.016]

84 **Waqs M**, Rahim W, Shohab D, Khawaja MA, Ali Z, Mamnoon N. Primary Renal Epithelioid Angiosarcoma. *J Coll Physicians Surg Pak* 2018; 28: S66-S68 [PMID: 29482713 DOI: 10.29271/jcpsp.2018.03.566]

85 **Gourley E**, Digman G, Nicolas M, Kaushik D. Primary renal angiosarcoma. *BJM Case Rep* 2018; 2018 [PMID: 30061122 DOI: 10.1136/bcr-2017-222672]

86 **Su VC**. Angiosarcoma of kidney with calcification: A rare case report. *Kuohsing J Med Sci* 2017; 33: 367-368 [PMID: 28738979 DOI: 10.1016/j.kjms.2017.03.009]

87 **López Cubillana P**, Martínez Barba E, Server Pastor G, Prieto González A, Ferri Níguez B, Cao Carrasco L, Martínez Barba E, Cathey WJ, McDivitt RW. Primary renal angiosarcoma: a case report. *Pathol Res Pract* 2009, 205: 347-351 [PMID: 19147300 DOI: 10.1016/j.prp.2008.11.005]

88 **Juan CJ**, Yu CY, Hsu HH, Chian CP, Huang GS, Fan HC, Lin CC, Ching Jiunn Wu JW, Hsiao HS, Chen CY, evolution of a renal angiosarcoma. *Hepatol Case Rep* 2021; 7: 152-158 [PMID: 34483968 DOI: 10.1016/j.heca.2021.02.016]

89 **Hiratsuka Y**, Nishimura H, Kajiwara I, Matsuoka H, Kawamura K. Renal angiosarcoma: a case report. *Int J Urol* 1997; 4: 90-93 [PMID: 9179675 DOI: 10.1111/j.1442-2042.1997.tb00148.x]

90 **Adjiman S**, Zerbib M, Flam T, Brochard M, Deslignières S, Boissonnas A, Debré B, Steg A. Genitourinary tumors and HIV1 infection. *Eur Urol* 1990; 18: 61-63 [PMID: 2401309 DOI: 10.1016/0302-2838(90)90109-9]

91 **Limmer S**, Wagner T, Leippbrand E, Arnholdt H. Primary renal hemangiosarcoma. Case report and review of the literature. *Pathologe* 2001; 22: 343-348 [PMID: 11572116 DOI: 10.1007/s0029200104817]

92 **Darlington D**, Anitha FS. Primary Renal Angiosarcoma Mimicking Renal Cell Carcinoma: A Case Report. *Cureus* 2019; 11: e3841 [PMID: 30891382 DOI: 10.7759/cureus.3841]

93 **Alfred CD**, Cathey WJ, McDvitt RW. Primary renal angiosarcoma: a case report. *Hum Pathol* 1981; 12: 665-668 [PMID: 7196879 DOI: 10.1016/s0046-8177(81)80054-8]

94 **Fukunaga M**. Angiosarcoma of the kidney with minute clear cell carcinomas: a case report. *Pathol Res Pract* 2009, 205: 347-351 [PMID: 19147300 DOI: 10.1016/j.prp.2008.11.005]

95 **Desai MB**, Chell Q, Naickh JB, Weiner R. Primary renal angiosarcoma mimicking a renal cell carcinoma. *Urol Radiol* 1989; 11: 30-32 [PMID: 2734970 DOI: 10.1016/BF02926469]

96 **Saharwala S**, John NT, Kumar RM, Kekre NS. Primary renal angiosarcoma. *Indian J Urol* 2013;
Omiyale AO. Primary vascular tumours of the kidney

29: 145-147 [PMID: 23956520 DOI: 10.4103/0970-1591.114040]

Heo SH, Shin SS, Kang TW, Kim GE. Primary renal angiosarcoma with extensive hemorrhage: CT and MRI findings. *Int Braz J Urol* 2019; 45: 402-405 [PMID: 30735338 DOI: 10.1590/S1677-5538.IBJU.2018.0375]

Mordkin RM, Dahut WL, Lynch JH. Renal angiosarcoma: a rare primary genitourinary malignancy. *South Med J* 1997; 90: 1159-1160 [PMID: 9386065 DOI: 10.1097/00007611-199711000-00023]

Berretta M, Rupolo M, Buonadonna A, Canzonieri V, Brollo A, Morra A, Berretta S, Bearz A, Tirelli U, Frustaci S. Metastatic angiosarcoma of the kidney: a case report with treatment approach and review of the literature. *J Chemother* 2006; 18: 221-224 [PMID: 16736893 DOI: 10.1179/joc.2006.18.2.221]

Lodhi HT, Inayat F, Munir A, Ilyas G. Primary renal angiosarcoma: a diagnostic and therapeutic challenge. *BMJ Case Rep* 2018; 2018 [PMID: 30244222 DOI: 10.1136/bcr-2018-225484]

Cason JD, Waisman J, Plaine L. Angiosarcoma of the kidney. *Urology* 1987; 30: 281-283 [PMID: 3629777 DOI: 10.1016/0090-4295(87)90258-5]

Askari A, Novick A, Braun W, Steinmuller D. Late ureteral obstruction and hematuria from de novo angiosarcoma in a renal transplant patient. *J Urol* 1980; 124: 717-719 [PMID: 7005464 DOI: 10.1016/s0022-5347(17)55362-6]

Guan H, Zhang L, Zhang Q, Qi W, Xie S, Hou J, Wang H. Primary angiosarcoma arising in an angionymiolipoma of the kidney: case report and literature review. *Diagn Pathol* 2018; 13: 53 [PMID: 30111336 DOI: 10.1186/s13300-018-0730-z]

Papadimitriou VD, Stamatiou KN, Takos DM, Adamopoulos VM, Heretis IE, Sofras FA. Angiosarcoma of the kidney: a case report and review of literature. *Urol J* 2009; 6: 223-225 [PMID: 19711281]

Celebi F, Pilanci KN, Saglam S, Balci NC. Primary renal angiosarcoma with progressive clinical course despite surgical and adjuvant treatment: A case report. *OncoLett* 2015; 9: 1937-1939 [PMID: 25789072 DOI: 10.3892/ol.2015.2902]

Rüb J, Bauer S, Pastor J, Noldus J, Palisaar RJ. Primary renal angiosarcoma. Uncommon manifestation of a rare malignancy. *Urologe A* 2015; 54: 849-853 [PMID: 25805159 DOI: 10.1007/s00120-015-3809-0]

Zhang HM, Yan Y, Luo M, Xu YF, Peng B, Zheng JH. Primary angiosarcoma of the kidney: case analysis and literature review. *Int J Clin Exp Pathol* 2014; 7: 3555-3562 [PMID: 25210734]

Tsuda N, Chowdhury PR, Hayashi T, Anami M, Iseki M, Koga S, Matsuya F, Kanetake H, Saito Y, Horita Y. Primary renal angiosarcoma: a case report and review of the literature. *Pathol Int* 1997; 47: 778-783 [PMID: 9413038 DOI: 10.1111/j.1440-1827.1997.tb04457.x]

Grapsa D, Sakellariou S, Politis E. Fine-needle aspiration cytology of primary renal angiosarcoma with histopathologic and immunocytochemical correlation: a case report. *Diagn Cytopathol* 2014; 42: 872-876 [PMID: 24166896 DOI: 10.1002/dc.23051]

Qayyum S, Parikh JG, Zafar N. Primary renal angiosarcoma with extensive necrosis: a difficult diagnosis. *Case Rep Pathol* 2014; 2014: 416170 [PMID: 25133004 DOI: 10.1155/2014/416170]

Garmendia JC, López García JA, Acinas García O, Garrido Rivas C, Sanroma Ortueta C, Arocena Lanz F. Angiosarcoma of the kidney. *Actas Urol Exp* 1989; 13: 223-224 [PMID: 2763892]

Sanyal B, Mehrotra ML, Gupta S, Pant GC. Radiotherapy in renal angiomyxosarcoma. *BMJ Case Rep* 2017; 72: 85-86 [PMID: 574526]

Cerilli LA, Hufmann HT, Anand A. Primary renal angiosarcoma: a case report with immunohistochemical, ultrastructural, and cytogenetic features and review of the literature. *Arch Pathol Lab Med* 1998; 122: 929-935 [PMID: 9786357]

Douard A, Pasticier G, Dernièere C, Wallerand H, Ferrière JM, Bernhard JC. Primary angiosarcoma of the kidney: case report and literature review. *Prog Urol* 2012; 22: 438-441 [PMID: 22657265 DOI: 10.1016/j.purol.2011.11.006]

Yamamoto Y, Iizuki H, Harada A, Taura R, Kishimoto T, Tanimoto S, Fukumori T, Takahashi M, Nishihata MA, Kanayama HO, Sano N, Uema K. A case of renal capsular hemangiosarcoma. *Hinyokika Kiyo* 2006; 52: 215-217 [PMID: 16617877]
