Review paper

Review of renal cell carcinoma with rhabdoid features with focus on clinical and pathobiological aspects

Naoto Kuroda[1], Takashi Karashima[2], Keiji Inoue[2], Atsuko Kasajima[3], Chisato Ohe[4], Fumi Kawakami[5], Shuji Mikami[6], Keiko Matsuura[7], Masatsugu Moriyama[7], Yoji Nagashima[8], Fredrik Petersson[9], Jose I. Lopez[10], Ronald J. Cohen[11], Michal Michal[12], Ondrej Hes[12]

[1]Department of Diagnostic Pathology, Kochi Red Cross Hospital, Kochi, Japan
[2]Department of Urology, Kochi Medical School, Kochi University, Kochi, Japan
[3]Department of Pathology, Tohoku University Hospital, Sendai, Japan
[4]Department of Pathology, Kansai Medical University Hirakata Hospital, Osaka, Japan
[5]Department of Diagnostic Pathology, Kobe University Hospital, Kobe, Japan
[6]Division of Diagnostic Pathology, Keio University Hospital, Tokyo, Japan
[7]Department of Molecular Pathology, Faculty of Medicine, Oita University, Oita, Japan
[8]Division of Diagnostic Pathology, Tokyo Women's Medical University, Tokyo, Japan
[9]Department of Pathology, National University Health System, Singapore, Singapore
[10]Department of Pathology, Cruces University Hospital, BioCruces Health Research Institute, University of the Basque Country (EHU/UPV), Barakaldo, Bizkaia, Spain
[11]Uropatho Pty Ltd, Western Australia, Australia
[12]Department of Pathology, Charles University in Prague, Faculty of Medicine in Plzen, Czech Republic

Rhabdoid morphology in renal cell carcinoma (RCC) may, like sarcomatoid change, be perceived as a type of dedifferentiation, and is a poor prognostic factor. Histologically, rhabdoid neoplastic cells are round to polygonal cells with globular eosinophilic cytoplasmic inclusions and eccentric vesicular nuclei and enlarged nucleoli. All types of RCC, including clear cell, papillary, chromophobe, collecting duct carcinoma, renal medullary carcinoma, acquired cystic disease-associated RCC, ALK-positive renal cancer and unclassified RCC, may display a variably prominent rhabdoid phenotype. Immunohistochemically, the cytoplasm of rhabdoid cells shows positivity for vimentin and/or cytokeratin. Ultrastructurally, cytoplasmic whorls/aggregates of intermediate filaments correspond to light microscopically observed inclusions. Genetically, a previous report suggests that combined loss of *BAP1* and *PBRM1* may be associated with rhabdoid morphology. As with sarcomatoid change, pathologists should describe, estimate and state the proportion of tumor cells with a rhabdoid phenotype in the routine pathology report of RCC.

Key words: rhabdoid features, renal cell carcinoma, poor prognosis.

Introduction

Rhabdoid morphology in renal cell carcinoma (RCC) resembling malignant rhabdoid tumor of kidney (MRTK) was first described in 1991, but this phenomenon should be strictly distinguished from MRTK and extrarenal malignant rhabdoid tumors because the prognosis and therapeutic strategies differ significantly [1]. Recently, rhabdoid change in RCC has been proposed to constitute a type of dedifferentiation, and as with sarcomatoid change it is associated with poor prognosis [2-8]. In this article, we review RCC with rhabdoid features with special reference to clinical and pathobiological aspects.

Epidemiology

The incidence of rhabdoid change in RCC has been estimated to be between 3% and 7% [6]. The age range of patients with RCC with rhabdoid features is between the third and eighth decade with a mean age of 52 to 63 years [2-6]. The male-to-female ratio is 2 : 1 [5, 6].

Clinical features

Patients with RCC with rhabdoid features frequently present with an abdominal mass, hematuria, flank or abdominal pain and nausea [2, 4, 5, 9-12]. However, some primary as well as metastatic lesions may be incidentally discovered on radiological examinations [4, 5, 13, 14].

Imaging findings

Reported imaging features are non-specific and consist of a complex hypervascular mass on ultrasonographic examination [9]. On computed tomography (CT) examinations, a heterogeneous, irregular mass which may invade the surrounding tissue is encountered [9, 11]. Contrast enhancement on CT is frequently observed [4]. In some tumors, lymphadenopathy may be radiologically detected [9, 10, 13].

Pathological findings

Macroscopic findings

The size of the tumor ranges from 4 to 15 cm with a mean size of 9 cm [5]. The cut surface varies; it may be homogeneously white and firm [5], but areas of hemorrhage or necrosis are often seen [4, 10, 11, 13].

Microscopic findings

Rhabdoid cells are round to polygonal with globular eosinophilic cytoplasmic inclusions and eccentric pleomorphic vesicular nuclei and large nucleoli (Fig. 1A, B) [1-7]. The architectural patterns include solid, organoid or sheet-like, and neoplastic cells exhibit a variable degree of discohesion [6, 7]. Renal cell carcinoma with rhabdoid features also demonstrate sarcomatoid change in up to 22% of cases [2, 4, 6, 7]. The proportion of rhabdoid cells ranges from 5% to 90% of total tumor volume [3, 5, 6]. The underlying types of carcinoma include clear cell RCC, papillary RCC, chromophobe RCC, collecting duct carcinoma, renal medullary carcinoma, acquired cystic disease-associated RCC, ALK-positive renal cancer and unclassified RCC [1-23]. The most common histological type of RCC with rhabdoid change is clear cell RCC and up to 35% of Fuhrman grade 4 clear cell RCCs displays rhabdoid features [2-7]. Rhabdoid morphology can be seen in 9.8% of cases with clear cell RCC consisting of all grades [24]. One case of hereditary leiomyomatosis and RCC with sarcomatoid change and rhabdoid features has been described [25]. If the tumor consists of only rhabdoid neoplastic cells, pathologists should designate such a tumor as "unclassified carcinoma with a rhabdoid component" [6]. Rhabdoid features in clear cell RCC are the most frequent histology among the metastatic clear cell RCC with non-clear cell morphology [26].

Immunohistochemical findings

Rhabdoid cells are generally positive for vimentin (Fig. 2A), epithelial membrane antigen and cytokeratins [2-6, 27]. PAX8 may be expressed in these cells [10]. No myogenic markers including desmin, myoglobin, myogenin and Myo D1 are expressed by the rhabdoid cells [2, 3]. The proliferative (Ki-67)

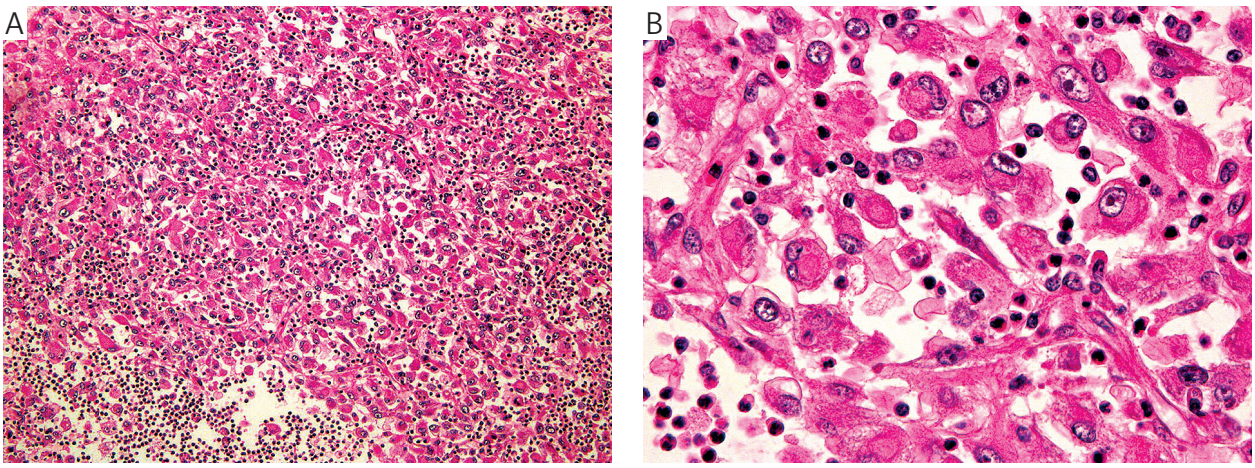

Fig. 1. Microscopic findings. A) The tumor consists of discohesive cells with eosinophilic cytoplasm and eccentric nuclei, namely rhabdoid cells. B) In high magnification of rhabdoid cells, enlarged vesicular nuclei, prominent nucleoli and abundant eosinophilic cytoplasm are observed

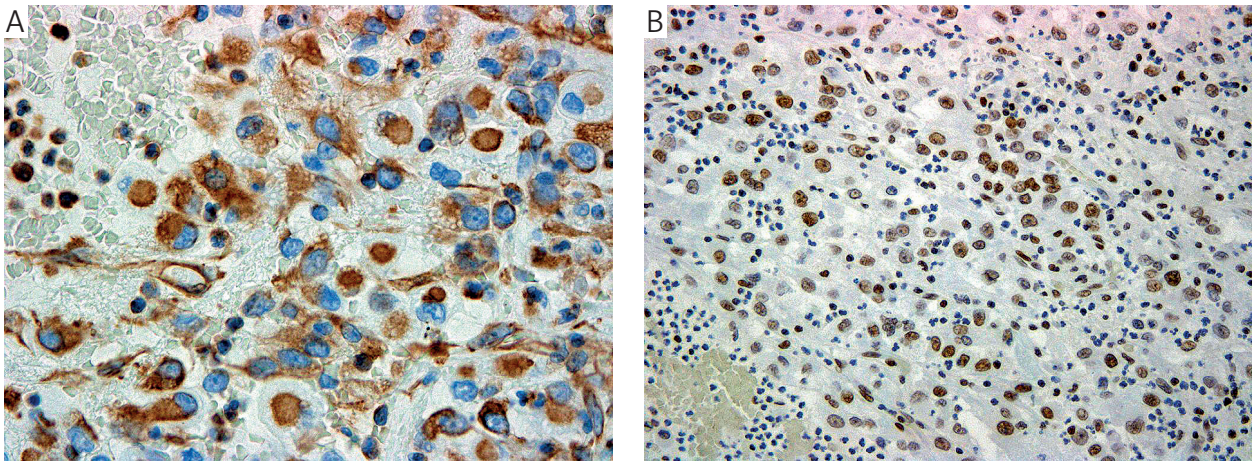

Fig. 2. Immunohistochemical findings. A) Strong vimentin positivity corresponding to eosinophilic cytoplasmic inclusions is observed. B) Nuclear positivity for INI1 is retained in rhabdoid cells

index is generally higher in rhabdoid cells, compared to non-rhabdoid tumor [3, 5, 28]. Overexpression of p53 is often observed [4]. The expression of integrase interactor 1 (INI1) is generally retained (Fig. 2B). However, loss of nuclear expression of INI1 is commonly observed in rhabdoid cells of renal medullary carcinoma [6, 17, 29]. It has been suggested that loss of Brahma (BRM) expression may be involved in the dedifferentiation of clear cell RCC exhibiting anaplastic or rhabdoid morphology [30].

Ultrastructural findings

Rhabdoid neoplastic cells ultrastructurally contain paranuclear whorls/aggregates of intermediate filaments [2, 3, 5, 6]. These whorls/aggregates of cytoskeletal intermediate filaments correspond to the cytoplasmic inclusions featuring immunohistochemical positivity for vimentin and/or cytokeratins [2, 3]. In addition, paranuclear condensation of cytoplasmic organelles with peripheral vacuolization may be observed [2].

Molecular genetic findings

Spectral karyotype analysis of primary cell culture of clear cell RCC established from skin metastasis showed hypertriploid karyotype: <3n>, –Y, +2, +der(3)t(3;5), der(5)t(5;6)x2, del(6p)x2, +6, +7x2, +iso(8)(q10)x2, +8, –9, +12, –13, –14, –15, +17, +der(19)t(19;20), +20x2, der(22)t(1;22) [31]. The G-band karyotype of ACD-associated RCC with sarcomatoid change and rhabdoid features showed the following changes: 46, X, +X, –Y[1]/43, idem, add(2)(q31), –6, –9, –14, –15, +16, –22, +mar1[6]/46, XY[2]/abnormal cell [11, 18]. These results suggest that the candidate tumor suppressor genes involving dedifferentiation in RCC such as sarcomatoid differentiation or rhabdoid change may be located on chromosomes 9, 14 and 15 [18, 31]. In RCC with rhabdoid features, the same genetic alterations including chromosome 3p loss and *VHL* gene mutation were observed in both clear cell RCC and rhabdoid components [21]. In chromophobe RCC with rhabdoid features, loss of heterozygosity of chromosomes 2, 10q, 13q and 17p in both chromophobe RCC and rhabdoid components was reported [22]. These results strongly suggest that both the RCC component and rhabdoid component are clonally related, i.e. have an identical clonal origin [21, 22]. Combined loss of *BAP1* and *PBRM1* may be associated with rhabdoid morphology, but not all tumors with rhabdoid change have shown coexistent loss of *BAP1* and *PRBM1* [32].

Differential diagnosis

Urologists, radiologists and pathologists should discriminate RCC with rhabdoid features from MRTK, renal synovial sarcoma, PNET/Ewing sarcoma, angiosarcoma, renal epithelioid angiomyolipoma, malignant lymphoma, Wilms' tumor, congenital mesoblastic nephroma (CMN), renal oncocytoma, renal hemangioblastoma, malignant mixed epithelial and stromal tumor, direct invasion of urothelial carcinoma of the renal pelvis with rhabdoid features, metastasis from malignant rhabdoid tumor of central nervous system (MRT-CNS), metastasis from pleomorphic rhabdomyosarcoma and metastasis from epithelioid sarcoma, proximal type. In these settings, the identification of a non-rhabdoid component is crucial and may require extensive sampling. MRTK can occur in adult cases [33-35]. Loss of INI1 expression supports the diagnosis of MRTK [17, 29, 35]. Renal poorly differentiated synovial sarcoma may show rhabdoid phenotype [36]. The identification of either of the fusion transcripts *SYT-SSX1* or *SYT-SSX2* is of paramount importance in establishing the definite diagnosis. PNET/Ewing sarcoma may also contain rhabdoid morphology that displays rosette formation, and strong and diffuse immunoreactivity for CD99 and FLI-1 as well as the detection of chimeric transcripts such as *EWS-FLI-1* or *EWS-*

ERG will aid in making the correct diagnosis [1, 37]. Epithelioid angiosarcoma may occur as a primary tumor in the kidney and it may demonstrate rhabdoid morphology and CD10 positivity. The identification of primitive vascular lumens and the positivity to CD31, CD34, factor VIII and FLI-1 support the diagnosis of epithelioid angiosarcoma [38]. A subset of renal epithelioid angiomyolipoma may show rhabdoid features, and in such cases the immunohistochemistry of alpha smooth muscle actin, melanosome (HMB45) and melan A is helpful [39]. In RCC with extensive rhabdoid differentiation and prominent cellular discohesion, high-grade/aggressive lymphoid neoplasms may enter the differential diagnosis. Malignant lymphomas most commonly completely lack cell cohesion and infiltrating sclerosis, and in most cases display limited amounts of cytoplasm and react positively to leukocyte common antigen [1]. Wilms' tumor may exhibit rhabdomyoblastic differentiation, but the age of patients, the presence of blastemal cells and positivity for myogenic markers are helpful diagnostic clues [1, 40]. In the distinction from CMN, the age of patients within 3 years after birth and the identification of *ETV6-NTRK3* fusion are important [1, 41]. Renal oncocytoma macroscopically shows mahogany-brown color and microscopically demonstrates a nesting pattern on the background of edematous or hyalinized stroma [1, 42, 43]. Sporadic renal hemangioblastoma consist of nests of polygonal cells and an abundant capillary network. Immunohistochemical detection of inhibin-alpha and S-100 protein may be helpful [44]. Malignant mixed epithelial and stromal tumor may exhibit rhabdoid morphology. In such a situation, the identification of an epithelial component and ovarian-like stroma is vital [45]. High-grade urothelial carcinoma may rarely impart rhabdoid phenotype [46-48]. Identification of urothelial carcinoma *in situ* and immunohistochemical positivity for cytokeratin 5/6, cytokeratin 20, p63, GATA3 and uroplakin II will assist in reaching an accurate diagnosis [49, 50]. In patients with metastasis from MRT-CNS, the clinical information (of presence of brain tumor) and the loss of INI1 immunoexpression are crucial pieces of information [29]. Pleomorphic rhabdomyosarcoma can express CD10 and CA9 [51]. In this situation, the application of myogenic markers in the immunohistochemical study is of major diagnostic significance. Epithelioid sarcoma imparts a vaguely granulomatous appearance and central necrosis. Additionally, the loss of INI1 protein occurs in epithelioid sarcoma.

Therapy

For the treatment of primary cancer, radical nephrectomy is recommended. Some cases responding to tyrosine kinase inhibitors (TKI) (sorafenib and sunitinib) have been reported [9, 52]. Stronger expression of VEGF-A in the rhabdoid component than the clear cell RCC component may suggest a better response to TKI [52]. The increased expression of the angiogenesis-related gene in RCC with sarcomatoid change and rhabdoid features may be related to the resistance of tyrosine kinase inhibitors [31].

Prognosis

Renal cell carcinoma with rhabdoid features generally behaves in an aggressive fashion, causing a rapidly fatal outcome [2-9, 16, 25, 31]. Cancer-specific mortality is 40 to 50%, and the median survival rates are within 8 to 31 months [5, 6]. Metastasis occurs in up to 70% of cases, and distant metastasis can occur in lung, bone, soft tissue, liver, skin, adrenal gland and diaphragm [4-10, 13, 14, 16-18, 25, 31]. Metastases to lymph nodes occur in approximately 20% of cases [7, 10, 16, 18, 25].

Future perspectives

It is evident that rhabdoid phenotype in RCC is associated with aggressive clinical behavior. Therefore, pathologists should describe and state the presence and extent of rhabdoid phenotype in their pathological reports. However, a minimum proportion of rhabdoid features in the total tumor volume is unnecessary for diagnostic purposes. Recently, the expression of p53, AEG-1 and MDM2 may be associated with tumor progression or prognosis [53, 54]. Therefore, it may be interesting to study the expression of p53, AEG-1 and MDM2 in RCC with rhabdoid features. Although combined loss of *BAP1* and *PBRM1* seems to be closely associated with rhabdoid phenotype, the identification of new candidate tumor suppressor genes which may be located on chromosomes 9, 14 or 16 potentially opens up future targeted therapeutic strategies [18, 31, 32]. The pathological significance of cohesive rhabdoid morphology in RCC with *ALK* gene rearrangement remains unknown [19]. Accordingly, the accumulation of cases will be necessary in order to clarify the significance of rhabdoid morphology in this category.

The authors declare no conflict of interest.

References

1. Weeks DA, Beckwith JB, Mierau GW, et al. Renal neoplasms mimicking rhabdoid tumor of the kidney. A report from the National Wilms' Tumor Study Pathology Center. Am J Surg Pathol 1991; 15: 1042-1054.
2. Gökden N, Nappi O, Swanson PE, et al. Renal cell carcinoma with rhabdoid features. Am J Surg Pathol 2000; 24: 1329-1338.

3. Kuroiwa K, Kinoshita Y, Shiratsuchi H, et al. Renal cell carcinoma with rhabdoid features: an aggressive neoplasm. Histopathology 2002; 41: 538-548.
4. Leroy X, Zini L, Buob D, et al. Renal cell carcinoma with rhabdoid features. An aggressive neoplasm with overexpression of p53. Arch Pathol Lab Med 2007; 131: 102-106.
5. Humphrey PA. Renal cell carcinoma with rhabdoid features. J Urol 2011; 186: 675-676.
6. Delahunt B, Cheville JC, Martignoni G, et al. The International Society of Urological Pathology (ISUP) grading system for renal cell carcinoma and other prognostic parameters. Am J Surg Pathol 2013; 37: 1490-1504.
7. Przybycin CG, McKenny JK, Reynolds JP, et al. Rhabdoid differentiation is associated with aggressive behavior in renal cell carcinoma. A clinicopathologic analysis of 76 cases with clinical follow-up. Am J Surg Pathol 2014; 38: 1260-1265.
8. Chapman-Fredricks JR, Herrera K, Bracho J, et al. Adult renal cell carcinoma with rhabdoid morphology represents a neoplastic dedifferentiation analogous to sarcomatoid carcinoma. Ann Diagn Pathol 2011; 15: 333-337.
9. Kapoor A, Tutino R, Kanaroglou A, et al. Treatment of adult rhabdoid renal cell carcinoma with sorafenib. Can Urol Assoc J 2008; 2: 631-634.
10. Esnakula AK, Naab TJ, Green W, et al. Extensive peritoneal carcinomatosis secondary to renal cell carcinoma with sarcomatoid and rhabdoid differentiation. BMJ Case Rep 2013; 2013: pii: bcr2013008725.
11. Al-Saidi NA, Aktar M. Sarcomatoid renal cell carcinoma with rhabdoid features. Ann Saudi Med 2013; 33: 495-499.
12. Rao Q, Xia QY, Shen Q, et al. Coexistent loss of INI1 and BRG1 expression in a rhabdoid renal cell carcinoma (RCC): implications for a possible role of SW1/SNF complex in the pathogenesis of RCC. Int J Clin Exp Pathol 2014; 7: 1782-1787.
13. Brčić I, Spajić B, Krušlin B. Chromophobe renal cell carcinoma with rhabdoid differentiation in an adult. Wien Klin Wochenschr 2012; 124: 419-421.
14. Pérez F, Jiménez-Helferman JA, Pérez-Campos A, et al. Cytological features of renal cell carcinoma with rhabdoid features. Cytopathology 2004; 15: 237-240.
15. Adsay VN, deRoux SJ, Sakr W, et al. Cancer as a marker of genetic medical disease: An unusual case of medullary carcinoma of the kidney. Am J Surg Pathol 1998; 22: 260-264.
16. Watanabe IC, Billis A, Guimarães MS, et al. Renal medullary carcinoma: report of seven cases from Brazil. Mod Pathol 2007; 20: 914-920.
17. Cheng JX, Tretiakova M, Gong C, et al. Renal medullary carcinoma: rhabdoid features and the absence of INI1 expression as markers of aggressive behavior. Mod Pathol 2008; 21: 647-652.
18. Kuroda N, Tamura M, Hamaguchi N, et al. Acquired cystic kidney-associated renal cell carcinoma with sarcomatoid change and rhabdoid features. Ann Diagn Pathol 2011; 15: 462-466.
19. Sugawara E, Togashi Y, Kuroda N, et al. Identification of anaplastic lymphoma kinase fusions in renal cancer. Cancer 2012; 118: 4427-4436.
20. Kuroda N, Kawada C, Tamura K, et al. Re-evaluation of histological type by immunohistochemical and genetic study of transcription factors (TFE3 and TFEB) of *VHL* gene mutation-negative clear cell renal cell carcinoma and other special types of renal tumor. Med Mol Morphol 2011; 44: 46-51.
21. Shannon B, Stan Wisniewski Z, Bentel J, et al. Adult rhabdoid renal cell carcinoma. Divergent differentiation of conventional (clear cell) ccarcinoma. Arch Pathol Lab Med 2002; 126: 1506-1510.
22. Shannon B, Cohen RJ. Rhabdoid differentiation of chromophobe renal cell carcinoma. Pathology 2003; 35: 228-230.
23. Kuroda N, Stake H, Miyazaki E, et al. Collecting duct carcinoma exhibiting diastase-resistant PAS-positive globular cytoplasmic inclusions and rhabdoid features arising in adult poycystic kidney disease. A case report. Int J Surg Pathol 2004; 12: 171-177.
24. López JI, Guarch R, Larrinaga G, et al. Cell heterogeneity in clear cell renal cell carcinoma. APMIS 2013; 121: 1187-1191.
25. Udager AM, Alva A, Chen YB, et al. Hereditary leiomyomatosis and renal cell carcinoma (HLRCC). A rapid autopsy report of metastatic renal cell carcinoma. Am J Surg Pathol 2014; 38: 567-577.
26. Lee C, Park JW, Suh JH, et al. Histologic variations and immunohistochemical features of metastatic clear cell renal cell carcinoma. Korean J Pathol 2013; 47: 426-432.
27. Lee L, Marsh WL, Wen P. Pathologic quiz case. An 82-year-old woman with a renal mass. Arch Pathol Lab Med 2004; 128: 109-110.
28. Klimis T, Karvounis H. Renal cell carcinoma with rhabdoid features. Divergent differentiation of conventional (clear cell) carcinoma. J BUON 2008; 13: 433-436.
29. Sigauke E, Rakheja D, Maddox DL, et al. Absence of expression of SMARCB1/INI1 in malignant rhabdoid tumors of the central nervous system, kidneys and soft tissue: an immunohistochemical study with implications for diagnosis. Mod Pathol 2006; 19: 717-725.
30. Xia Q, Rao Q, Cheng L, et al. Loss of BRM expression is a frequently observed event in poorly differentiated clear cell renal cell carcinoma. Histopathology 2014; 64: 847-862.
31. Karashima T, Fukuhara H, Tamura K, et al. Expression of angiogenesis-related gene profiles and development of resistance to tyrosine-kinase inhibitor in advanced renal cell carcinoma: Characterization of Sorafenib-resistant cells derived from a cutaneous metastasis. Int J Urol 2013; 20: 923-930.
32. Peña-Llopis S, Vega-Rubín-de-Celis S, Liao A, et al. BAP1 loss defines a new class of renal cell carcinoma. Nat Genet 2012; 44: 751-759.
33. Yasuf Y, Belmonte AH, Tchertkoff V. Fine needle aspiration cytology of a recurrent malignant tumor of the kidney with rhabdoid features in an adult. A case report. Acta Cytol 1996; 40: 1313-1316.
34. Peng HQ, Stanek AE, Teichberg S, et al. Malignant rhabdoid tumor of the kidney in an adult. Arch Pathol Lab Med 2003; 127: e371-e373.
35. Podduturi V, Campa-Thompson MM, Zhou XJ, et al. Malignant rhabdoid tumor of the kidney arising in an adult patient. Proc (Mayl Univ Med Cent) 2014; 27: 239-241.
36. Paláu LMA, Pham TT, Barnard N, et al. Primary synovial sarcoma of the kidney with rhabdoid features. Int J Surg Pathol 2007; 15: 421-428.
37. Bartholow T, Parwani A. Renal primitive neuroectodermal tumors. Arch Pathol Lab Med 2012; 136: 686-690.
38. Singh C, Xie L, Schmechel SC, et al. Epithelioid angiosarcoma of the kidney: A diagnostic dilemma in fine-needle aspiration cytology. Diagn Cytopathol 2012; 40: E131-E139.
39. Miyai K, Mullick SS, Divatia MK, et al. Renal sclerosing perivascular epithelioid cell tumor (PEComa)/angiomyolipoma with extensive rhabdoid cell features. Pathol Int 2014; 64: 247-250.
40. Shet T, Viswanathan S. The cytological diagnosis of paediatric renal tumors. J Clin Pathol 2009; 62: 961-969.
41. Anderson J, Gibson S, Sebire NJ. Expression of ETV6-NTRK in classical, cellular and mixed subtypes of congenital mesoblastic nephroma. Histopathology 2006; 48: 748-753.
42. Kuroda N, Toi M, Hiroi M, et al. Review of renal oncocytoma with focus on clinical and pathobiological aspects. Histol Histopathol 2003; 18: 935-942.
43. Kuroda N, Tanaka A. Recent classification of renal epithelial tumors. Med Mol Morphol 2014; 47: 68-75.
44. Yin W, Li J, Chan JKC. Sporadic haemangioblastoma of the kidney with rhabdoid features and focal CD10 expression: report of a case and literature review. Diagn Pathol 2012; 7: 39.

45. Sukov WR, Cheville JC, Lager DJ, et al. Malignant mixed epithelial and stromal tumor of the kidney with rhabdoid features: report of a case including immunohistochemical, molecular genetic studies and comparison to morphologically similar renal tumors. Hum Pathol 2007; 38: 1432-1437.
46. Perez-Montiel D, Wakely PE, Hes O, et al. High-grade urothelial carcinoma of the renal pelvis: clinicopathologic study of 108 cases with emphasis on unusual morphologic variants. Mod Pathol 2006; 19: 494-503.
47. Fukumura Y, Fujii H, Mitani K, et al. Urothelial carcinoma of the renal pelvis with rhabdoid features. Pathol Int 2009; 59: 322-325.
48. Terada T. Multiple cytokeratin-negative malignant tumors composed only of rhabdoid cells in the renal pelvis: a sarcomatoid urothelial carcinoma? Int J Clin Exp Pathol 2013; 6: 724-728.
49. Smith SC, Mohanty SK, Kunju LP, et al. Uroplakin II outperforms uroplakin III in diagnostically challenging setting. Histopathology 2014; 65: 132-138.
50. Amin MB, Trpkov K, Lopez-Beltran A, et al. Best practices recommendations in the application of immunohistochemistry in the bladder lesions. Report from the International Society of Urologic Pathology Consensus Conference. Am J Surg Pathol 2014; 38: e20-e34.
51. Abdou AG, Kandil M, Elshakhs S, et al. Renal cell carcinoma with rhabdoid and sarcomatoid features presented as a metastatic thigh mass with an unusual immunohistochemical profile. Rare Tumors 2014; 6: 5037.
52. Kats-Ugurlu G, Maass C, van Herpen C, et al. Better effect of Sorafenib on the rhabdoid component of a clear cell renal cell carcinoma owing to its higher level of vascular endothelial growth factor-A production. Histopathology 2011; 59: 562-576.
53. Erdem H, Oktay M, Yildirim U, et al. Expression of AEG-1 and p53 and their clinicopathological significance in malignant lesions of renal cell carcinomas. A microarray study. Pol J Pathol 2013; 64: 28-32.
54. Hejnold M, Dyduch G, Bialas M, et al. Selected morphologic features influencing the prognosis of conventional renal cell carcinomas co-expressing p53 and MDM2. Pol J Pathol 2014; 65: 29-33.

Address for correspondence

Naoto Kuroda MD
Department of Pathology
Kochi Red Cross Hospital
Shin-honmachi 2-13-51, Kochi City,
Kochi 780-8562, Japan
tel. +81-88-822-1201
fax +81-88-822-1056
e-mail: kurochankochi@yahoo.co.jp