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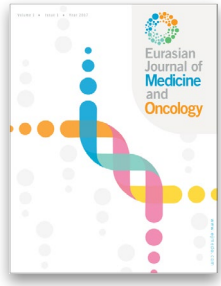

Case Report

Sarcomatoid Transformation of Cromophobe Renal Cell Carcinoma: An Unusual Pathology. Our Experience, Definition of Therapeutic Guidelines and Review of Literature

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Abstract

Chromophobe renal cell carcinoma (ChRCC) accounts for 4-6% of RCC1. Most of ChRCC have good prognosis, but sarcomatoid transformation implies poor prognosis factor2. Although sarcomatoid RCC was initially described as an own histological entity3, despite the fact that its transformation mechanism is not known, it is nowadays recognized that this histology represents a transformation or dedifferentiation of a high-grade malignant neoplasia originating from any other histological subtype of RCC2. ChRCC with sarcomatoid differentiation is very rare, with a few reported cases and there is no consensus about the treatment of patients affected by this variant of RCC in the guidelines. Therefore, we consider appropriate to present these two cases and review the literature, focusing on the incidence and the current therapeutic options.

Keywords: Renal cell carcinoma, Chromophobe renal cell carcinoma, Sarcomatoid transformation

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Chromophobe renal cell carcinoma (ChRCC) accounts for 4-6% of RCC.[1] Most of ChRCC have good prognosis, but sarcomatoid transformation implies poor prognosis factor.[2] Although sarcomatoid RCC was initially described as an own histological entity,[3] despite the fact that its transformation mechanism is not known, it is nowadays recognized that this histology represents a transformation or dedifferentiation of a high-grade malignant neoplasia originating from any other histological subtype of RCC.[2] ChRCC with sarcomatoid differentiation is very rare, with a few reported cases and there is no consensus about the treatment of patients affected by this variant of RCC in the guidelines. Therefore, we consider appropriate to present these two cases and review the literature, focusing on the incidence and the current therapeutic options.

Case Report

Case 1 — A Caucasian 58-year-old male, smoker, with any other relevant clinical background. He attended the emer-

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gency room because of a right hypochondrium pain with a palpable mass for two weeks together with 15 Kgs weight loss in the last two months. Ultrasound imaging showed a 15 cm solid mass that seemed to come from right kidney affecting the underlying liver parenchyma. The abdominal computed tomography (CT) identified a solid tumour in the upper and middle third of the right kidney, with central areas of necrosis. Perirenal and anterior pararenal fat involvement was evident. The tumour caused displacement and mass effect on the right hepatic lobe, without being able to rule out tumour infiltration of the right hepatic lobe (Figs. 1 and 2). Due to the important vascularization of the renal mass, two renal arteries were first embolized and after six days an open radical right nephrectomy was performed, which required cholecystectomy plus hepatic segmentectomy due to tumour infiltration. Postoperative evolution was favourable, without complications, and he was discharged twelve days after surgery.

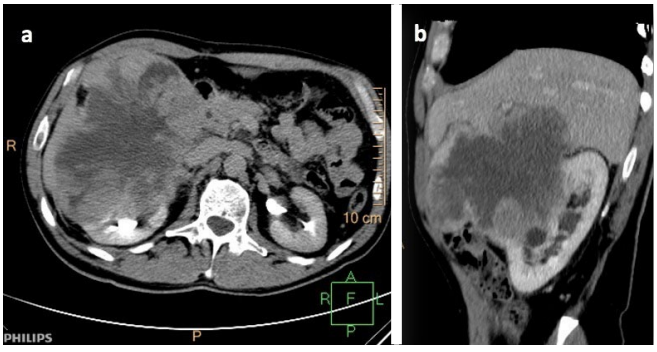

Figure 1. CT scan with contrast of Case 1. Large right renal solid tumour with significant central necrosis infiltrating the hepatic parenchyma and extending to the anterior abdominal wall. Sagittal reconstruction in portal phase **(a)** and axial view in excretory phase **(b)**.

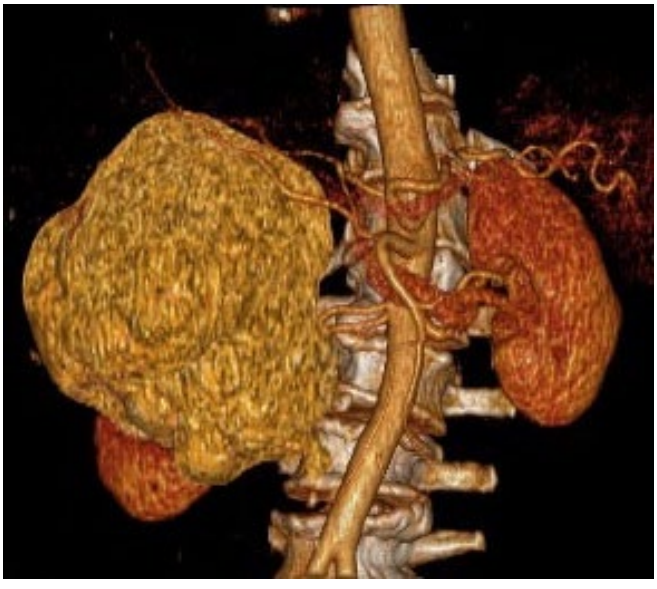

Figure 2. Arterial phase contrast-enhanced CT and 3D volume rendering reconstruction. Large right renal solid mass. Two right renal arteries are identified. Case 1.

Histopathological analysis showed a ChRCC with extensive sarcomatoid dedifferentiation. The pathologic stage was pT4NxM1. The tumour had a maximum diameter of 18 cm, with sarcomatoid features present in 95% of the tumour and tumour necrosis present in >50%. Tumour infiltration of the perirenal fat and adrenal gland was observed. The surgical margins of the surgical specimen were affected and there was lymphovascular invasion.

Regarding the immunohistochemical profile, sarcomatoid dedifferentiation areas have expression of actin, CD10, Cytokeratin AE1/-AE3 (CK AE1/A3) and Cytokeratin 7 (CK7). They do not have expression of calponin, caldesmon, desmin, RCC, HMB45, Melan A and PAX 8. The chromophobe cell carcinoma areas express CK7 and Ver-EP4; however, they present negativity to CD117, RCC and CD10. Colloidal iron staining had a diffuse cytoplasmic expression (Fig. 3).

After surgery, systemic treatment was started with Nivolumab plus Ipilimumab. Two months after surgery, the patient was admitted at hospital due to deterioration of the general condition, by biliary sepsis. An abdominal ultrasound showed an adenopathic conglomerate at retroperitoneal level of approximately 20 cm, as well as dilatation of the intrahepatic biliary tract. The patient presented progressive clinical worsening and died three months after radical nephrectomy.

Case 2 — A 53-year-old man with no clinical history of interest except gastroesophageal reflux disease. He presents lumbar pain of 6 months of evolution accompanied by weight loss of 10 kg in the last two months. For this reason, MRI of the lumbar spine was performed, showing retroperitoneal lymphadenopathies of up to 7 cm compressing the inferior vena cava. A thoracic-abdominal-pelvic CT showed the presence of a 10-cm renal mass in the middle third of the right kidney infiltrating the perirenal fat, with compression of the inferior vena cava and thrombosis of this and multiple retroperitoneal adenopathies (Fig. 4). Right radical nephrectomy and hilar and cava lymphadenectomy were performed by open surgery. Postoperative evolution was satisfactory, and he was discharged on the 10th postoperative day.

Histopathological analysis showed a 12-cm renal neoplasm with a 40% component of ChRCC and poorly differentiated carcinoma (60%) with areas of sarcomatous morphology, extensive squamous differentiation with presence of keratinization and horny pearls, focal tubular differentiation and extensive areas of necrosis (Fig. 5). There was infil-

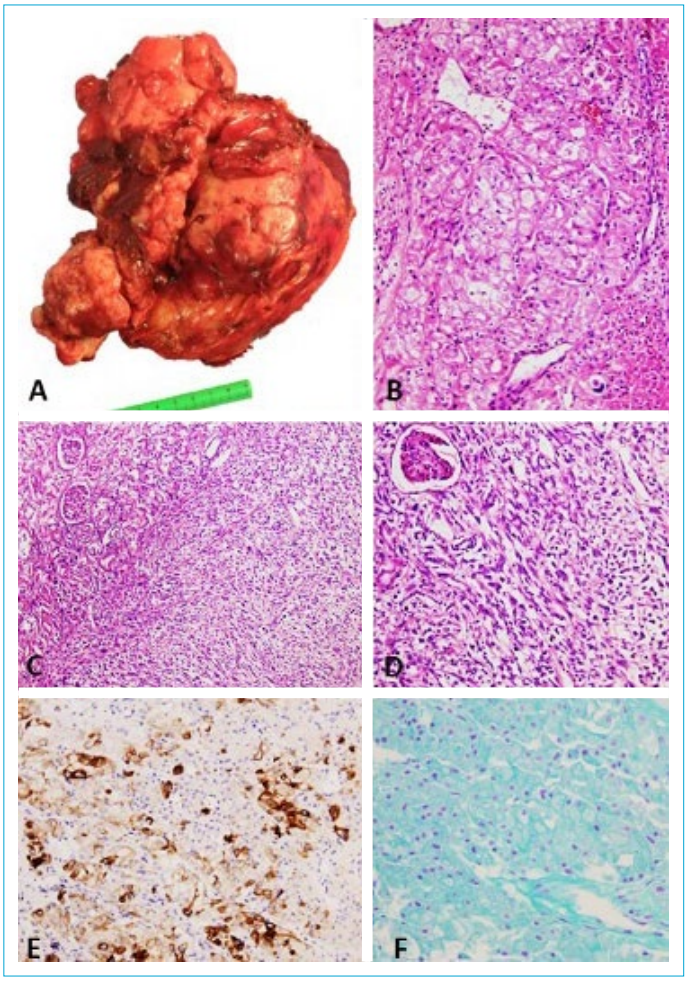

Figure 3. Radical nephrectomy surgical specimen completely occupied by the large renal mass **(a)**. Chromophobe carcinoma component with cords of well-demarcated clear cytoplasmatic cells and well-defined membranes **(b)**. Sarcomatoid spindle-cell component infiltrating the renal parenchyma **(c)**. Sarcomatoid spindle-cell component with marked nuclear atypia **(d)**. Focal expression of Cytokeratin-7 in chromophobe carcinoma cells. Intense and diffuse positivity with coloidal iron staining **(f)**. Case 1.

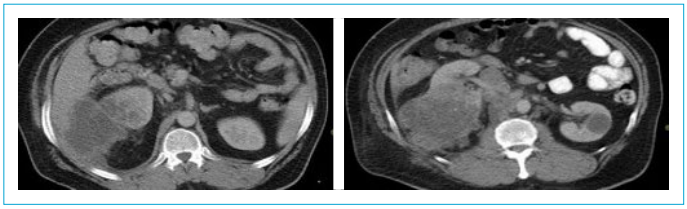

Figure 4. Contrast-enhaced CT images in portal phase. Large solid right renal mass with central necrosis infiltrating the hepatic parenchyma and posterior abdominal Wall. Retroperitoneal hiliar and interaortocava adenopathy. Case 2.

tration of the renal sinus fat and perirenal fat. There were metastases of poorly differentiated carcinoma in retroperitoneal lymph nodes. The surgical margins of the surgical specimen were affected. Clinical stage pT3aG3pN2M0.

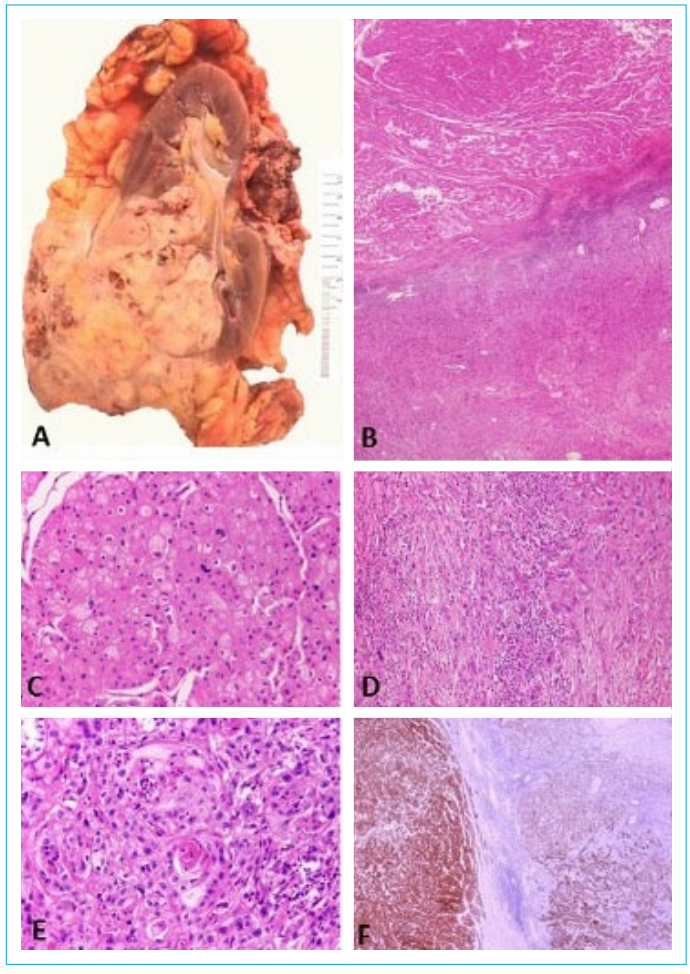

Figure 5. Surgical specimen of radical nephrectomy with evidence of large renal mass in the middle and lower third with extensive infiltration of perirenal adipose tissue **(a)**. Chromophobe carcinoma component in the upper half and sarcomatoid component in the lower half of the image **(b)**. Chromophobe component with isolated cells of clear cytoplasm and predominance of cells with eosinophilic cytoplasm. Note the characteristic nuclei (in raisins) **(c)**. Sarcomatoid spindle-cell component with marked nuclear atypia **(d)**. Area of squamous differentiation with keratinization in corneal Pearl **(e)**. Intense posivity for cytokeratin 7 in the chrommophobe carcinoma component (left) with lower expression in the sarcomatoid component (right) **(f)**. Case 2.

Three months after surgery, he presented extensive recurrence of the tumour in the retroperitoneum and died 7 months after surgery.

Discussion

ChRCC is the third most common histological subtype of RCC (3-7%).[4,5] It was first described as a distinct subtype of RCC by Thoenes et al. in 1985[6] and World Health Organization (WHO) Classification gave it its own entity in 1998.[7] It arises from the intercalated cells of the cortical segment of the collecting system. Therefore, these tumours have dif-

ferent morphologic, histopathologic and structural characteristics. The most frequent cause associated with ChRCC is smoking. Mean age of incidence is the sixth decade with almost equivalent sex predilection. As for the clinical condition, the classic triad of renal cancer (pain, palpable mass and haematuria) is seen in less than 40%.[5] Our patients had abdominal pain in the case 1 and lumbar pain in the case 2, and both patients had a palpable voluminous abdominal mass on examination, although they did not report haematuria.

Sarcomatoid RCC was first described by Farrow et al. in 1968[3] and sarcomatoid dedifferentiation can be seen in any RCC subtype, being more common in males. It has been described that ChRCC is the third most common subtype associated with it.[5,6,8] No minimum percentage of sarcomatoid dedifferentiation is required to stablish the diagnosis of sarcomatoid RCC.[9]

On histopathological analysis, ChRCCs contain large polygonal cells with distinct cell borders and reticulated cytoplasm, which may stain diffusely with Hale's colloidal iron.[6] The sarcomatoid pattern has similar features to sarcomas, with spindle cells, high cellularity and cellular atypia. However, there are important differences since primary renal sarcomas are extremely rare in adults (<1%) and, in addition, do not contain classic areas of RCC.[10] For the diagnosis of ChRCC with sarcomatoid transformation it is necessary to see both histopathological types,[11] as in our clinical cases, where the surgical specimen, in addition to both morphologies, showed cytoplasmic staining with colloidal iron, as well as expression of CD10 and CK AE1/AE3 and CK7 in the areas of dedifferentiation. Squamous differentiation in ChRCC, as in case 2, is exceptional.

Both the WHO 2016 Classification and the International Society of Urological Pathology (ISUP) have recommended not grading ChRCC until there is a specific system for it, because nuclear irregularities, nuclear pleomorphism and the presence of nucleoli are findings intrinsically present in this type of tumours, so they do not fit the nuclear grading criteria of either the old Furhman or the new nucleolar grading of the ISUP9. However, several authors have advocated the value of a histologic grading system.[12-17] In 2010, Paner et al.[12] proposed a three-tiered system, based on clustering and nuclear anaplasia, where grade 3 tumours have marked anaplasia or sarcomatoid changes. Recently, Ohashi et al.[16] analysed this system and concluded that there was low statistical significance between the three grades, as well as minimal differences between grades 1 and 2. These authors propose a grading system in two categories, high and low grade, using sarcomatoid dedifferentiation and necrosis as parameters. Likewise, Avulova et al.[17] reflect that Paner et al grading does not provide additional prognostic value when considering the TNM stage and the presence of sarcomatoid dedifferentiation and, therefore, propose a grading system with 4 levels, incorporating coagulative tumour necrosis to the system proposed by Paner et al. Grade 1 tumours with or without necrosis would continue to be grade 1 (very low risk), grade 2 tumours without necrosis would continue to be grade 2 (low risk), grade 3 tumours would be the grade 2 of Paner et al, but with tumour necrosis (intermediate risk) and grade 4 would include all sarcomatoid ChRCC and those with marked anaplasia (high risk). This system establishes a new histopathologic grading standard for ChRCC and could serve as the basis for a new WHO grading system.[18] Based on this system, our clinical cases would be classified as grade 4 because of the sarcomatoid differentiation they present.

ChRCC is generally a tumour of low malignant potential that rarely recurs, metastasizes or causes mortality,[19] whereas patients with sarcomatoid RCC seem to have the worst prognosis of all renal cell tumours and most patients present with an advanced stage at diagnosis and rarely survive >1 year.[20-24] This is confirmed by our clinical cases, since one of our patients presented at diagnosis with pain in the right renal fossa, palpable mass and probable hepatic infiltration in the staging CT, and the other presented with lumbar pain and palpable abdominal mass with weight loss of 10 kg in the last two months.

The most important prognostic factors include the percentage of the sarcomatoid component (<50% vs >50%), vascular invasion and advanced TNM stage, the latter being an independent predictor of survival.[21] It is worth noting the extensive sarcomatoid transformation that was observed in the surgical specimen of our clinical cases, being 95% in case 1, as far as we know, the highest percentage described in the literature. Besides, they presented lymphovascular invasion in the specimen as well as tumour necrosis, factors that justify the poor prognosis of both patients.

Table 1 shows the results published by Bian et al. in 20192 and their references[2,11,24,25-29] on the described cases of ChRCC with sarcomatoid transformation, to which we have added both cases we present. They are four females and six males, most of them with large renal masses and advanced stage. Only four of them have a survival of more than 12 months after diagnosis.

Regarding the treatment of sarcomatoid RCC, while in localized disease tumour resection remains the standard of care,[30] in metastatic disease the role of cytoreductive nephrectomy prior to systemic treatment is controversial[31] because of the potential delay in the initiation of systemic

Table 1. Relationship of ChRCC with sarcomatoid transformation. Clinical features and evolution.

Author	Age/Sex	Dimensión (cms)	TNM	Metástasis	Survival	Sarcomatoid component (%)
Hes et al.[25]	74/M	12	T2bNxMx	No	Death in 3,5 months	Not available
Itoh et al.[26]	74/M	19	T4NxM1	Yes	Death in a month	Not available
Viswanathan et al.[27]	45/F	20	T2NxM1	Yes	Death in a month	Not available
Quiroga-Garza et al.[23]	63/F	6	T1bN1M1	Yes	Alive in 10 months	70%
Gong et al.[11]	72/M	7	T1bNxM1	Yes	Not available	Not available
Tanaka et al.[28]	77/M	2,5	T1aN0M0	No	Alive in 12 months	Not available
Daga et al.[29]	40/F	16	T2bN0M1	Yes	Alive in 12 months	40-50%
Bian et al.[2]	63/F	14	T2bN0M0	No	Alive in 12 months	20%
Case 1	58/M	18	pT4NxM1	Yes	Death in 3 months	95%
Case 2	53/M	12	pT3aN2M0	No	Death in 7 months	60%

therapies due to the time required for postoperative recovery.[32] Alevikazos et al.[33] defend that there is an increase in survival if cytoreductive nephrectomy is performed, even in patients with stage IV at diagnosis, provided that they are carefully selected and with an acceptable operative risk. In addition, patients who undergo surgery may have palliative benefits, such as a decrease in local symptoms of the renal mass and haematuria.[34]

Provided the use of percutaneous renal biopsy could diagnose this subtype earlier in order to initiate systemic therapy first, determining the presence of sarcomatoid dedifferentiation can be difficult, because they are commonly large heterogeneous masses, being this component only focally present, which could lead to underdiagnosis.

That is why to date, detailed histopathological analysis after surgery is the most reliable diagnostic method for this rare entity of sarcomatoid transformation of ChRCC.[31]

In metastatic RCC, prognostic scales have been developed to stratify patients into risk groups. According to the MSKCC/Motzer scale, five criteria are associated with poorer survival: high corrected calcium, low Karnofsky Index, low haemoglobin, high LDH and more than 1 year from diagnosis to initiation of systemic therapy. Sarcomatoid differentiation is not mentioned in this classification; in contrast, the IMDC (International Metastatic RCC Database Consortium), which also includes parameters such as elevated neutrophils and platelets, does take into account the histopathological variants of RCC.[35] The arrival of immunotherapy has taught us that the efficacy of treatment varies depending on risk according to these prognostic scales, with Ipilimumab plus Nivolumab being effective in patients with intermediate/poor prognosis, but not in patients with favourable risk.[36]

Despite the fact that our patients had advanced disease at the time of diagnosis, with hepatic involvement in one of them, and since they were patients with Performance Status 0, it was decided to perform first a radical surgery. In case 1, an open radical right nephrectomy was performed and subsequently and early, given the rapid postoperative recovery, systemic treatment with Nivolumab plus Ipilimumab. Although this patient started systemic treatment one month after surgery, he had a poor evolution, requiring hospital admission for treatment of biliary sepsis in relation to tumour progression, which led to his death three months after diagnosis. In case 2, an open radical nephrectomy plus hilar and vena cava lymphadenectomy was performed without administering adjuvant immunotherapy treatment, because this surgery was performed 10 years ago. He had a rapid tumour progression, observed three months after diagnosis, and died 7 months after diagnosis.

Sarcomatoid differentiation in ChRCC is an indicator of low response to systemic therapies.[7,35,37] Renal tumours with sarcomatoid differentiation show a different molecular basis with high expression of programmed cell death protein (PD-1) and its ligand 1 (PD-L1) in tumour cells and high levels of tumour-infiltrating lymphocytes,[31,38] which explains their greater response to immune checkpoint inhibitors.

A post hoc analysis of the CheckMate 214 trial,[34] which compared Ipilimumab plus Nivolumab with Sunitinib in patients with intermediate/poor prognosis RCC, identified patients with sarcomatoid histology and their outcomes. This study concluded that patients with sarcomatoid RCC with ≥1% PDL1 expression treated with Ipilimumab plus Nivolumab had longer overall survival than those treated with Sunitinib.[39] Based on these results, the Society for Cancer Immunotherapy recommends the combination of Nivolumab plus Ipilimumab as first line for sarcomatoid RCC[40] and its use has led to increased life expectancy in patients with metastatic RCC.[41] There are at least two clinical trials underway to study the relationship between sarcomatoid RCC and PD1 and PDL expression,[31] so more knowledge about this lethal disease is expected in the coming years.

Conclusions

Sarcomatoid transformation can be seen in any histologic subtype of RCC and ChRCC with sarcomatoid transformation is rare and carries a poor prognosis. Cytoreductive surgery plus immunotherapy is a therapeutic option, although further studies are needed to determine its true efficacy.

Disclosures

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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References

1. Al Ghamdi MH, Al Shabyli NA, Alayed A. Chromophobe renal cell carcinoma presenting as a cystic renal mass: Case report and review of the literature. Am J Case Rep 2019;20:631–4.
2. Bian L, Duan J, Wang X, Yang Y, Zhang X, Xiao S. Sarcomatoid chromophobe renal cell carcinoma: a case report and review of the literature. Am J Case Rep 2019;20:1225–30.
3. Farrow G, Harrison E, Utz D. Sarcomas and sarcomatoid and mixed malignant tumours of the kidney in adults- Part III. Cancer 1968;22:556–63.
4. Moch H, Cubilla A, Humphrey PA, Reuter VE, Ulbright TM. The 2016 WHO classification of tumours of the urinary system and male genital organs-Part A: renal, penile and testicular tumours. Eur Urol 2016;70:93–105.
5. Bharti S, Ram Choudhary G, Jyotsna Bharti N, Kumar Garg P, BS A, Abhay Elhence P. Sarcomatoid chromophobe renal cell carcinoma with Heterologous component. Iran J Pathol 2020;15:57–61.
6. Thoenes W, Störkel S, Rumpelt HJ. Human cromophobe cell renal carcinoma. Virchows Arch B Cell Pathol Incl Mon Pathol 1985;48:207–17.
7. Moch H, Ohashi R. Chromophobe renal cell carcinoma: current and controversial issues. Pathology 2021;53:101–8.
8. Cheville JC, Lohse CM, Zincke, Weaver AL, Leibovich BC, Frank I, et al. Sarcomatoid renal cell carcinoma: an examination of underlying histologic subtype and an analysis of associations with patient outcome. Am J Surg Pathol 2004;28:435–41.
9. Delahunt B, Cheville JC, Martignoni G, Humphrey PA, Magi-Galluzzi C, McKenney, et al. The International Society of Urology Pathology (ISUP) grading system for renal cell carcinoma and other prognostic parameters. Am J Surg Pathol 2013;37:1490–504.
10. Shuch B, Bartslavsky G, Linehan WM. Sarcomatoid renal cell carcinoma: a comprehensive review of the biology and current treatment strategies. The Oncologist 2012;17:46–54.
11. Gong Y, Sun X, Haines GK 3rd, Pins MR. Renal cell carcinoma, chromophobe type, with collecting duct carcinoma and sarcomatoid components. Arch Pathol Lab Med 2013;127:38–40.
12. Paner GP, Amin MB, Alvarado-Cabrero I, Young AN, Stricker HJ, Moch H, et al. A novel tumour grading scheme for chromophobe renal cell carcinoma: prognostic utility and comparison with Fuhrman nuclear grade. Am Surg Pathol 2010;34:1233–40.
13. Cheville JC, Lohse CM, Sukov WR, Thompson RH, Leibovich BC. Chromophobe renal cell carcinoma: the impact of tumour grade on outcome. Am J Surg Pathol 2012;36:851–6.
14. Steffens S, Janssen M, Roos FC, Becker F, Steinestel J, Abbas M, at al. The Fuhrman grading system has no prognostic value in patients with non sarcomatoid chromophobe renal cell carcinoma. Hum Pathol 2014;45:2411–6.
15. Delahunt B, Eble JN, Egevad L, Samaratunga H. Grading of renal cell carcinoma. Histopathology 2019;74:4–17.
16. Ohashi R, Martignoni G, Hartmann A, Hartmann A, Caliò A, Segala D, et al. Multi-institutional revaluation of prognostic factors in chromophobe renal cell carcinoma: proposal of a novel two-tiered grading scheme. Virchows Arch 2020;476:409–18.
17. Avulova S, Cheville JC, Lohse CM, Gupta S, Potretzke TA, Tsivian M, et al. Grading Chromophobe Renal Cell carcinoma: evidence for a four-tiered classification incorporating coagulative tumor necrosis. Eur Urol 2021;79:225–31.
18. Lopez-Beltrán A, Montironi R, Cimadamone A, Cheng L. Grading of chromophobe renal cell carcinoma: do we need it? Eur Urol 2021;79:232–3.
19. Lauer SR, Zhou M, Master VA, Osunkoya AO. Chromophobe renal cell carcinoma with sarcomatoid differentiation: a clinicopathologic study of 14 cases. Anal Quant Cytopathol Histpathol 2013;35:77–84.
20. Delahunt, B. Sarcomatoid renal carcinoma: the final common differentiation pathway of renal epitelial malignancies. Pathology 31 Pathology 1999;31:185–90.
21. De Peralta-Venturina M, Moch H, Amin M, Tamboli P, Hailemariam S, Mihatsch M, et al. Sarcomatoid differentiation in renal cell carcinoma: a study of 101 cases. Am J Surg Pathol 2001;25:275–84.
22. Mian BM, Bhadkamkar N, Slaton JW, Pisters PW, Daliani D, Swanson DA, et al. Prognostic factors and survival of patients with sarcomatoid renal cell carcinoma. J Urol 2002;167:65–70.
23. Quiroga-Garza G, Khurana H, Shen S, Ayala AG, Ro JY. Sarcomatoid chromophobe renal cell carcinoma with heterologous sarcomatoid elements. A case report and review of the literature, Arch Pathol Lab Med 2009;133:1857–60.
24. Murguía-Pérez M, Hernandez-Gonzalez M, Alcántara-Vázquez A. Carcinoma renal sarcomatoide. Revisión de 7 casos con análisis de inmunohistoquímica. Rev Esp Patol 2010;43:73–8.
25. Hes O, Michal M, Kinkor Z, Tomes P, Zůchová M, Nápravník I. Sarcomatous chromophobe cell renal carcinoma: 2 case re-

ports. Cesk Pathol 1999;35:15–9.
26. Itoh T, Chikai K, Ota S, Nakagawa T, Takiyama A, Mouri G, et al. Chromophobe renal cell carcinoma with osteosarcoma-like differentiation. Am J Surg Pathol 2002;26:1358–62.
27. Viswanathan S, Desai SB, Prabhu SR, Amin MB. Squamous differentiation in a sarcomatoid chromophobe renal cell carcinoma: An unusual case report with review of the literature. Arch Pathol Lab Med 2008;132:1672–74.
28. Tanaka Y, Koie T, Hatakeyama S, Hashimoto Y, Ohyama C. Chromophobe renal cell carcinoma with concomitant sarcomatoid transformation and osseous metaplasia: A case report. BMC Urol 2013;13:15–9.
29. Daga D, Dana R, Kothari N. Chromophobe renal cell carcinoma with sarcomatoid changes: Case report and review of literature. Cent European J Urol 2014;67:31–4.
30. Merril MM, Wood CG, Tannir NM, Slack RS, Babaian KN, Jonasch E, et al. Clinically nonmetastatic renal cell carcinoma with sarcomatoid differentiation: Natural history and outcomes after surgical resection with curative intent. Urol Oncol 2015;33:166.e21–9.
31. Blum KA, Gupta S, Tickoo SK, Chan TA, Russo P, Motzer RJ, et al. Sarcomatoid renal cell carcinoma: biology, natural history and management. Nat Rev Urol 2020;17:659–78.
32. Kutikov A, Uzzo RG, Caraway A, Reese CT, Egleston BL, Chen DY, et al. Use of systemic therapy and factors affecting survival for patients undergoing cytoreductive nephrectomy. BJU Int 2010;106:218–23.
33. Alevikazos M, Gaitanidis A, Nasioudis D, Msaouel P, Appleman LJ. Sarcomatoid renal cell carcinoma: population-based study of 879 patients. Clin Genitourin Cáncer 2019;17:447–53.
34. Motzer RJ, Tannir NM, McDermott DF, Arén Frontera O, Melichar B, Choueiri TK, et al. Nivolumab plus Ipilimumab versus Sunitinib in advanced renal-cell carcinoma. N Engl J Med 2018;378:1277–90.
35. Korenbaum C, Pierard L, Thiéry A, Story F, Lindner V, Lang H, et al. Treatments, outcomes, and validity of prognostic scores in patients with sarcomatoid renal cell carcinoma: a 20-year single-institution experience. Clin Genitourin Cancer 2018;16:577–86.
36. Motzer RJ, Rini BI, McDermott DF, Arén Frontera O, Hammers HJ, Carducci MA, et al. Nivolumab plus ipilimumab versus sunitinib in first-line treatment for advanced renal cell carcinoma: extended follow-up of efficacy and safety results from a randomised, controlled, phase 3 trial. Lancet Oncol 2019;20:1370–85.
37. Ged Y, Chen Y, Knezevic A, Casuscelli J, Redzematovic A, DiNatale RG, et al. Metastatic chromophobe renal cell carcinoma: presence or absence of sarcomatoid differentiation determines clinical course and treatment outcomes. Clin Genitourin Cancer 2019;17:678–88.
38. Debien V, Thouvenin J, Lidner V, Barthélémy P, Lang H, Flippot R, et al. Sarcomatoid dedifferentiation in renal cell carcinoma: from novel molecular insights to new clinical opportunities. Cancers (Basel) 2019;12:99.
39. Tannir NM, Signoretti S, Choueiri TK, McDermott DF, Motzer RJ, Flaifel A, et al. Efficacy and safety of nivolumab plus ipilimumab versus sunitinib in first-line treatment of patients with advanced sarcomatoid renal cell carcinoma. Clin Cancer Res 2021;27:78–86.
40. Rini BI, Battle D, Figlin RA, Hammers H, Hutson T, Jonasch E, et al. The society for immunotherapy of cancer consensus statement on immunotherapy for the treatment of advanced renal cell carcinoma (RCC). JITC 2019;20:354.
41. Buonerba C, Dolce P, Iaccarino S, Scafuri L, Verde A, Costabile F, et al. Outcomes associated with first-line anti-PD-1/PD-L1 agents vs. Sunitinib in patients with sarcomatoid renal cell carcinoma: a systematic review and meta-analysis. Cancers (Basel) 2020;12:408.