Scientific Research Publishing

Surgical Science, 2019, 10, 255-264
http://www.scirp.org/journal/ss
ISSN Online: 2157-9415
ISSN Print: 2157-9407

Leukemoid Reaction and Malignant Ascites in a Renal Carcinoma with Sarcomatoid Differentiation. Unusual Case Report and Literature Review

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How to cite this paper: Chávez, A.M.G., Santos, J.A.M., de Jesús Curiel Valdés, J., Chávez, M.A.G., Blanco, R.R.H. and Hernández, D.A.Á. (2019) Leukemoid Reaction and Malignant Ascites in a Renal Carcinoma with Sarcomatoid Differentiation. Unusual Case Report and Literature Review. *Surgical Science*, **10**, 255-264.
https://doi.org/10.4236/ss.2019.107027

Received: May 28, 2019
Accepted: July 27, 2019
Published: July 30, 2019

Abstract

Renal cell carcinoma represents the 16th cause of death by cancer. It is one of the most frequent kidney tumors. This tumor could behave as a good mimicker, and is frequently associated with paraneoplastic syndromes. Metastases to peritoneum, mesentery or omentum are very rare. Sarcomatoid renal cell carcinoma is a high-grade undifferentiated component that can be found in any subtypes of renal cell carcinoma, and is associated with an aggressive behavior and a poor prognosis. We present the case of a 59-year-old male, diabetic patient, with nephron preserved left nephrectomy through lumbotomy seven years ago, upper pole renal carcinoma, admitted to the emergency department with indeterminate shock. He underwent a diagnostic laparoscopy and then open surgery due to findings where a greater omentum subtotal infarction. Omentum microscopic examination resulted in vaguely differentiated neoplasia, with sarcomatoid like cells, highly positive to CD10 inmunolabeling. Even though renal cell carcinomas have unusual clinical presentations, this case is unique because of the convergence of extremely rare manifestations such as the combination of malignant ascites, peritoneal carcinomatosis, and contralateral suprarenal gland metachronous metastases at the major omentum with paraneoplastic syndrome type leukemoid reaction; which have not been reported previously in literature.

Keywords

Renal Cell Carcinoma, Sarcomatoid Differentiation, Paraneoplastic Syndrome, Leukemoid Reaction, Malignant Ascites

1. Introduction

Renal clear cell carcinoma is one of the most frequent kidney tumors, and occurs in 85% - 90% of the cases. It is originated in renal cortex, particularly in tubular epithelium. It grows slowly and usually unilaterally [1]. Smoking, obesity, hypertension, are within the most important associated risk factors, present in up to 49% of cases [2].

As this tumor could behave as a good mimicker due to paraneoplastic syndrome occurrence, it is also known as the "internist tumor" and represents a real diagnostic challenge [3].

The reports in the literature on renal carcinoma, document late recurrences, even five or ten years after the initial diagnosis. About thirty-three percent of patients have metastases at the time of diagnosis. Peritoneal dissemination is rare, and occurs only in 0.8% of the cases [4].

Sarcomatoid renal cell carcinoma is not a distinct pathologic subtype, but rather a high-grade undifferentiated component that can be found in any subtypes of renal cell carcinoma, and is associated with an aggressive behavior and a poor prognosis (median survival time of only 4 - 9 months after diagnosis). The average incidence of sarcomatoid differentiation is 8% among all renal cell carcinomas [3].

A clinical case is presented with a paraneoplastic syndrome type leukemoid reaction and malignant ascites by peritoneal spread, happening simultaneously with metachronous to major omentum metastases, as initial recurrence 7 years after a renal carcinoma.

2. Case Report

A 59-year-old diabetic patient, with nephron preserved left nephrectomy, through lumbotomy seven years ago, due to 5 cm upper pole renal carcinoma with no more details. He did not receive chemo or radiotherapy.

The patient was received in the emergency room with a three weeks' evolution colicky abdominal pain, nausea, hiporexia, left lumbar pain, decreased urine volume and chills.

In the physical examination, the patient was hypotensive and diaphoretic, with blood oxygen levels of 89%, dehydrated, generalized pallor and with pain at decompression on the left flank. He had an uncomplicated ventral hernia, in the previous site of the lumbotomy.

The laboratories test showed: 44×10^3 uL leukocytes with 77% neutrophils,

azoate elevation (Cr 3.8 mg/dL, Urea 62 mg/dL, BUN 43 mg/dL), hyperkalemia (7.3 mEq/L) and normal liver function tests.

Chest X-ray did not show pleural effusion. A contrasted abdominal tomography, performed 6 days before admission, showed: liver with no metastases, a large retroperitoneal abscess (66 × 35 mm) without associated adenopathies (**Figure 1**), peritoneal focal thickness in left flank (**Figure 2**), and a free fluid-filled cavity.

Patient was admitted in intensive care unit with abdominal sepsis, acute renal failure, uncompensated diabetes and metabolic acidosis. He came on gradual decay until mechanic ventilation and vasoactive amines support was required. Subsequent laboratories showed a progressive increase in leukocytes from 54.2 to 62.6, to 76.7 × 10^3 uL, with a C reactive protein (CRP) level of 90 mg/L and procalcitonin of 7.64 ng/mL. Several laboratory cultures, collected from different sites were performed and all of them were negative. Antibiotic treatment (ceftriaxone and metronidazole) was provided. By ultrasound-guided paracentesis 5 L of ascites was obtained, its cytological analysis showed 5.1 × 10^3 uL leucocytes, 70% PMN and 30% mononuclears.

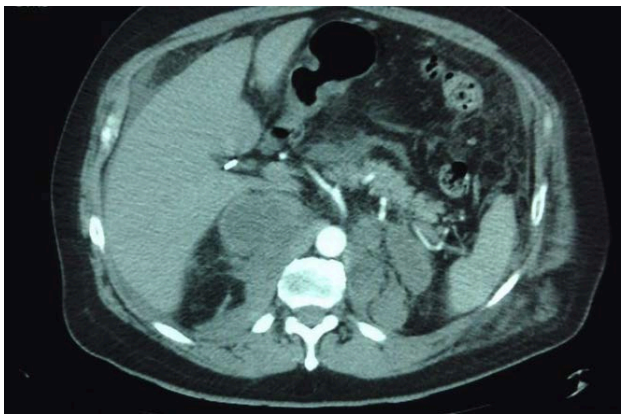

Figure 1. Metachronous metatases to contralateral suprarenal gland.

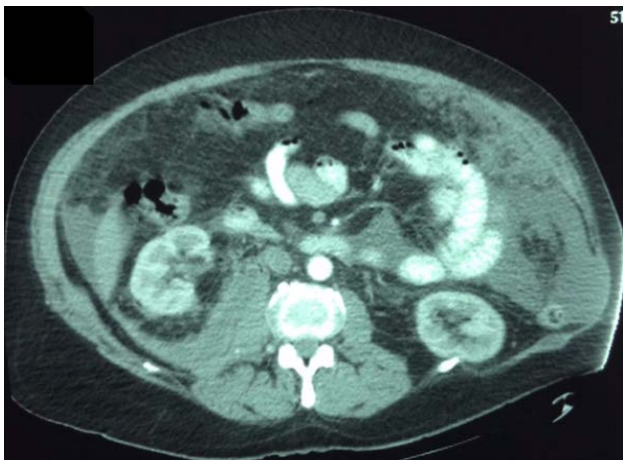

Figure 2. Omental cake by metastases to major omentum.

He underwent a diagnostic laparoscopy where additional 5 liters of ascites were obtained. The other findings were: fibrino purulent surface, generalized peritonitis, acute periappendicitis, greater omentum with nodular appearance, completely attached to the wall, fibrous and difficult to manage by laparoscopy. For this reason, it was decided to convert to open surgery where a greater omentum subtotal infarction with white, round, and no defined edges' lesion of 7 × 5 × 2 cm was found (Figure 3 and Figure 4).

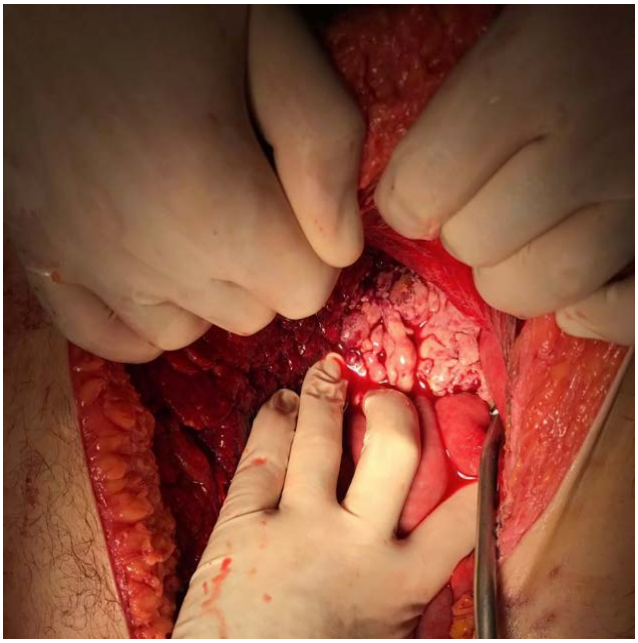

Figure 3. Greater omentumlesion. Macroscopic appearance.

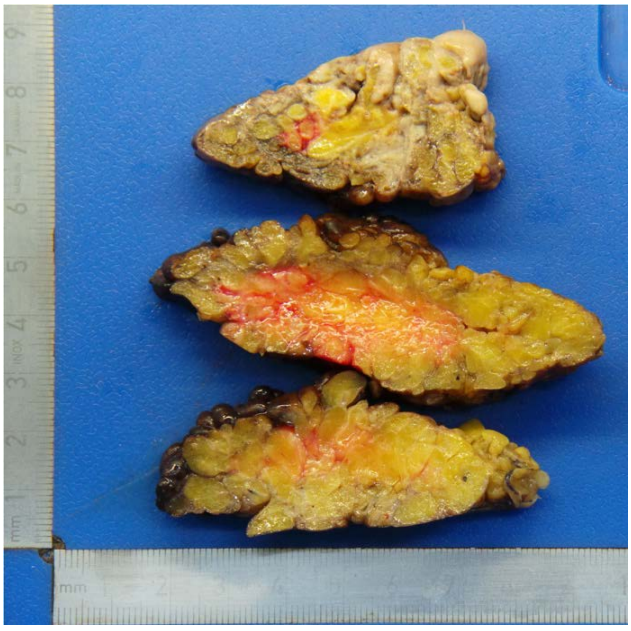

Figure 4. Bisected greater omentum, different yellow-withish areas and more solid texture.

Patient left operating room with vasopressors minimal support and with adequate uresis. Last hematic biometry showed an increase in leucocytes to 86.7 × 10^3 uL. He died 12 hours after surgery due to multiple organ failure.

Omentum microscopic examination resulted in invaguely differentiated neoplasia, arranged in nodules and diffuse inflammatory infiltrate, with sarcomatoid like cells, highly positive to CD10 inmunolabeling. Clear cells were not found but an important acute inflammation with polimorphonuclears was evident. It was diagnosed as not differentiated sarcomatoid renal cell carcinoma with omentum metastases (**Figure 5**). Appendix showed acute and chronic periappendicitis, without mucosal lesion or metastases. Ascites liquid presented not well-differentiated neoplasic cells.

3. Literature Review

Renal cell carcinoma worldwide has an incidence of 2.9% and represents the 16th cause of death by cancer, with an average age of 65 years, being more frequent in males (2:1) [5]. Histologically, several subtypes of renal carcinoma are known: clear cells (60% - 70%), papillar (5% - 15%), chromophobe (5% - 10%), oncocytic (5% - 10%) and medullar (<1%). A sarcomatoid pattern has been described in all variants [6]. There is a clinical triad when renal cancer is presented (lumbar pain, gross hematuria and palpable mass), but it just appears in 10% - 15% of patients [7].

Renal cell carcinoma is usually spread directly through lymphatic vessels or by vena cava invasion [8]. About 20% - 30% of patients got metastases when diagnosed and about 20% - 30% with confined tumors will develop further metastases [9]. The most affected organs are: lung (75%), lyphatic ganglions (60%), bones (20%), liver (18%), brain and suprarenal glands (8.5%), even when there are reports in any other part of the body [10].

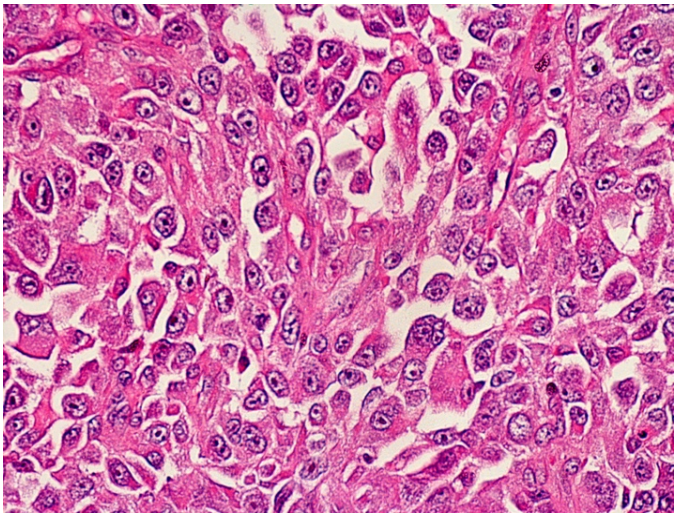

Figure 5. Epithelioid and sarcomatoid cells with visible nuclei and nucleoli, slightly hyperchromatic and with eosinophilic elongated cytoplasm.

Metastases to peritoneum, mesentery or omentum are very rare [4]. Dissemination to peritoneal cavity or its content can be via: 1) renal capsule perforation and tumor exposure to peritoneal surface or 2) through metastatic emboli that reach the root of the mesentery, thus, spreading by local circulation. The extension to the peritoneum, is associated with poor prognosis [11]. Initial expression of this type of cancer by ascites, is even more uncommon [12]. However, it is known that this kind of metastases, happens frequently in sarcomatoid tumors [9]. Development of metachronous metastases in omentum is considered extremely rare in international literature [12] [13].

Paraneoplastic syndromes are systemic manifestations of a malignant tumor with no relation with its metastatic activity. They occur in 10% - 40% of patients with renal carcinoma [14]. The most frequent are: anorexia, Stauffer syndrome, fever, hypoalbuminemia, hypercalcemia, anaemia and elevated sedimentation rate [3].

A leukemoid reaction is defined as a leukocyte measure, higher than 40×10^3 uL. When it occurs in the context of a stomach, colon, liver, gallbladder, pancreas, lung or thyroid cancerit is considered of very poor prognosis [15]. The renal carcinoma of worse prognosis is the one that has sarcomatoid differentiation [16]. Several studies demonstrated that cells in renal carcinoma are able to produce stimulating factors for e IL-6 (proinflammatory cytokine) granulocyte's colonies [17] and express its specific receptor in the surface. About 50% - 80% of the patients with renal cancer present high levels of circulating IL-6, correlated with high levels of C-reactive protein [18].

Two similar cases to the one presented here, were reported by Huang *et al.* they recommend surgical resection of metastases to manage these patients and mention the use of sumatinib (a tyrosine kinase inhibitor) as a therapeutic possibility in these cases [19].

4. Discussion

Difficulties to approach this clinical case, consisted in discerning if alterations were just because of a neoplasia or a septic problem, since clinical presentation and tomography (which suggested a retroperitoneal abscess) supported a septic origin. Even more, in this context, considering the rise of acute phase reactants was not useful to distinguish them [20].

The first ascites liquid obtained by paracentesis, did not show tumor cells but resulted in more than 250 PMN $\times$ mm^3, compatible with peritonitis which justified a diagnostic laparoscopy.

Should the patient undergo surgery? The answer is yes! Surgery allowed recognizing the oncological origin of the problem. Partially infarcted greater omentum metastases were evidenced and this finding carried out an almost total omentectomy. Metastases from renal carcinoma to the greater omentum occur in less than 1% of cases [21]. When exploring retroperitoneum, it was clear that the like abscess image, was really a tumoral activity and a metachronous metastases to the right suprarenal gland, contralateral to the original tumor in left kidney. Metachronous metastases to contralateral suprarenal gland, are also ex-

tremely rare (0.5% - 2.5%) and are well documented in literature [22] [23].

It is well known that sarcomatoid differentiation can occur in all histologic subtypes, with an incidence between 1.2 a 23.6% of renal carcinomas [24].

Cultures were always negative. Criteria to diagnose spontaneous bacterial peritonitis were not fulfilled, neither a neutrocytic ascites [25] [26]. In retrospect, this case corresponds to a malignant ascites by peritoneal carcinomatosis which could only be found in <1% of renal carcinomas [26].

After surgery, it was established that left flank tomographic image matched with a radiological sign called "omental cake" that refers a diffuse thickness of omentum what happens by infiltration of tumors like ovary, stomach and colon carcinomas [27].

Despite all tumor cells were all epithelioid and sarcomatoid, in this case it was possible to diagnose a metastatic sarcomatoid renal carcinoma with malignant ascites using immunohistochemistry (IHC). Positive vimentin was recorded, even when unspecific, it acquires value in negative CK7, CK20 and CK10 presence. CK7 and CK20 are always negative, in spite, CD10 is only negative in 25.9% of clear cell renal carcinomas and its reactivity is not reported in sarcomatoid variant.

Patient had bad prognostic due to peritoneum and retroperitoneum metastatic implication, malignant ascites and leukemoid paraneoplastic reaction. In the few cases published worldwide (**Table 1**), leukemoid reaction in renal carcinoma, has 100% mortality [15] [28]-[33].

Table 1. Renal malignant tumor cases reported in worldwide literature, associated to leukemoid reaction.

Reference	Year	Sex/Age	Leukocytes	Kind of Tumor	Outcome
Lalani *et al* (29).	1990	-	-	Renal carcinoma	Death
Milagro M *et al.* (30)	2009	-	-	Renal carcinoma with sarcomatoid differentiation	Death
Huang *et al.* (15)	2014	Woman (36)	47,200	Renal carcinoma with sarcomatoid differentiation	Death
Huang *et al.* (15)	2014	Man (56)	68,000	Renal carcinoma with sarcomatoid differentiation	Death
Yadav *et al.* (32)	2016	Man (54)	53,000	Transitional cells' renal Carcinoma	Death
Ghosh *et al* (31).	2016	Man (58)	66,000	Renal Carcinoma with sarcomatoid differenciation	Death
González *et al.*	2019	Man (59)	86,700	Renal Carcinoma with sarcomatoid differenciation	Death

5. Conclusion

Even though renal cell carcinomas commonly have unusual clinical presentations which make them difficult to diagnose, approach and treat; this clinical report is unique in all the world literature because of the convergence of extremely rare manifestations, as an initial manifestation of renal cell carcinoma recurrence with sarcomatoid differentiation. Combination of: malignant ascites, peritoneal carcinomatosis, contralateral suprarenal gland metachronous metastases at the major omentum with paraneoplastic syndrome type leukemoid reaction; have not been reported previously in literature. It is then demonstrated that Hickam statement does not always function, and that sometimes it is necessary to use the "heuristic of simplicity approach" included in Oakham principle: the simplest and most adequate explanation is also the most likely.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Jonash, E., Gao, J. and Rathmell, W. (2014) Renal Cell Carcinoma. State of the Art Review. *BMJ*, **349**, g4797. https://doi.org/10.1136/bmj.g4797

[2] Riazalhosseini, Y. and Lathrop, M. (2016) Precision Medicine from the Renal Cancer Genome. *Nature Reviews Nephrology*, **12**, 655-666. https://doi.org/10.1038/nrneph.2016.133

[3] Ljungberg, B., Bensalah, K., Canfield, S., *et al*. (2015) EAU Guidelines on Renal Cell Carcinoma: 2014 Update. *European Urology*, **67**, 913-924. https://doi.org/10.1016/j.eururo.2015.01.005

[4] Dabestani, S., Thorstenson, A., Lindblad, P., *et al*. (2016) Renal Cell Carcinoma Recurrences and Metastases in Primary Non-Metastatic Patients: A Population-Based Study. *World Journal of Urology*, **34**, 1081-1086. https://doi.org/10.1007/s00345-016-1773-y

[5] Ferlay, J., Soerjomataram, I., Ervik, M., *et al*. (2014) GLOBOCAN 2012, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 11. International Agency for Research on Cancer, Lyon.

[6] The Cancer Genome Atlas Research Network, *et al*. (2016) Comprehensive Molecular Characterization of Paillary Renal-Cell Carcioma. *NEJM*, **374**, 135-145. https://doi.org/10.1056/NEJMoa1505917

[7] Escudier, B., Porta, C., Schmidinger, M., *et al*. (2016) Renal Cell Carcinoma: ESMO Clinical Practice Guidelines for Diagnosis, Treatment and Follow-Up. *Annals of Oncology*, **27**, 58-68. https://doi.org/10.1093/annonc/mdw328

[8] Sountoulides, P., Metaxa, L. and Cindolo, L. (2011) Atypical Presentations and Rare Metastatic Sites of Renal Cell Carcinoma. A Review of Case Reports. *Journal of Medical Case Reports*, **5**, 1-9. https://doi.org/10.1186/1752-1947-5-429

[9] Acar, O., Mut, T., Saglıcan, Y., *et al*. (2016) Isolated Omental Metastasis of Renal Cell Carcinoma after Extraperitoneal Open Parcial Nephrectomy: A Case Report. *IJSCR*, **21**, 6-11. https://doi.org/10.1016/j.ijscr.2016.02.008

[10] Orestes, M., Benidir, T., Olandoski, B., *et al*. (2014) Peritoneal Metastases from

Renal Cell Carcinoma: Images in Urology. *Canadian Urological Association*, **8**, e391-e392. https://doi.org/10.5489/cuaj.2067

[11] Jennison, E., Wathuge, G.W. and Gorard, D.A. (2015) Renal Cell Carcinoma Presenting with Malignant Ascites. *JRSM Open*, **6**, 1-3. https://doi.org/10.1177/2054270415585087

[12] Yao, A., Iwamoto, H., Morizane, S., *et al*. (2012) A Case of Advance Renal Cell Carcinoma with Peritoneal Carcinomatosis Responding to Sorafenib Therapy. *International Cancer Conference Journal*, **1**, 198-200. https://doi.org/10.1007/s13691-012-0039-9

[13] Palapattu, G.S., Kristo, B. and Raifer, J. 2002) Paraneoplastic Syndromes in Urologic Malignancy: The Many Faces of Renal Cell Carcinoma. *Reviews in Urology*, **4**, 163-170.

[14] Huang, W., Wang, F., Li, Y., *et al*. (2014) Leukemoid Reaction in Sarcomatoid Renal Cell Carcinoma: A Two-Case Report. *World Journal of Surgical Oncology*, **12**, 100. https://doi.org/10.1186/1477-7819-12-100

[15] de Peralta, M., Moch, H., Amin, M., *et al*. (2001) Sarcomatoid Differentiation in Renal Cell Carcinoma: A Study of 101 Cases. *The American Journal of Surgical Pathology*, **25**, 275-284. https://doi.org/10.1097/00000478-200103000-00001

[16] Wetzler, M., Esrov, Z., Talpaz, M., *et al*. (1993) Granulocyte-Macrophage Colonystimulating Factor as a Cause of Paraneoplastic Leukaemoid Reaction in Advanced Transitional Cell Carcinoma. *Journal of Internal Medicine*, **234**, 417-420. https://doi.org/10.1111/j.1365-2796.1993.tb00765.x

[17] Blay, J.Y., Rossi, J.F., Wijdenes, J., *et al*. (1997) Role of Interleukine-6 in the Paraneoplastic Inflammatory Syndrome Associated with Renal Cell Carcinoma. *International Journal of Cancer*, **72**, 424-430. https://doi.org/10.1002/(SICI)1097-0215(19970729)72:3<424::AID-IJC9>3.0.CO;2-R

[18] Tsuchiyama, K., Ito, H., Ishida, H., *et al*. (2011) Advanced Sarcomatoid Renal Cell Carcinoma Effectively Treated with Sunitinib: Report of a Case. *Hinyokika Kiyo*, **57**, 615-618.

[19] Yaegashi, H., Izumi, K., Kitagawa, Y., *et al*. (2014) Differential Diagnosis between Bacterial Infection and Neoplastic Fever in Patients with Advanced Urological Cancer: The Role of Procalcitonin. *International Journal of Urology*, **21**, 104-106. https://doi.org/10.1111/iju.12178

[20] Staderini, F., Cianchi, F., Badii, B., *et al*. (2015) A Unique Presentation of a Renal Clear Cell Carcinoma with Atypical Metastases. *IJSCR*, **11**, 29-32. https://doi.org/10.1016/j.ijscr.2015.03.009

[21] Antonelli, A., Cozzoli, A., Simeone, C., *et al*. (2006) Surgical Treatment of Adrenal Metastasis from Renal Cell Carcinoma: A Single-Centre Experience of 45 Patients. *BJU*, **97**, 505-508. https://doi.org/10.1111/j.1464-410X.2006.05934.x

[22] Lau, W., Zincke, H., Lohse, C., *et al*. (2003) Contralateral Adrenal Metastasis of Renal Cell Carcinoma: Treatment, Outcome and a Review. *BJU*, **91**, 775-779. https://doi.org/10.1046/j.1464-410X.2003.04237.x

[23] Shuch, B., Bratslavsky, G., Martson, W., *et al*. (2012) Sarcomatoid Renal Cell Carcinoma: A Comprehensive Review of the Biology and Current Treatment Strategies. *Oncologist*, **17**, 46-54. https://doi.org/10.1634/theoncologist.2011-0227

[24] Alaniz, C. and Regal, E. 2009) Spontaneous Bacterial Peritonitis: A Review of Treatment Options. *PT*, **34**, 204-210.

[25] Lawrence, A. and Millie, M. (1999) Culture-Negative Spontaneous Bacterial Peritonitis: An Ambiguous Diagnosis without Peritoneal Biopsy. *Clinical Infectious Diseases*, **29**, 1582-1583. https://doi.org/10.1086/313560

[26] Mamlouk, M., vanSonnenberg, E., Shankar, S., *et al*. (2011) Omental Cake: Unusual Aetiologiesans CT Appearances. *Insights Imaging*, **2**, 399-408. https://doi.org/10.1007/s13244-011-0105-4

[27] Yang, S.H., Kwon, Y.H., Kang, J.G., *et al*. (1991) Leukemoid Reaction with Renal Cell Carcinoma. *Korean Journal of Urology*, **33**, 485-490.

[28] Lalani, A., Asgaonkar, D., Yadav, J., *et al*. (1990) Renal Cell Carcinoma: Presenting with Congestive Hepatosplenomegaly and Rare Haematological Complications. *The Journal of the Association of Physicians of India*, **38**, 179-180.

[29] Milagro, M., Acosta, C., Panigadi, N., *et al*. (2009) Clinical Observation. Leukemoid Reaction and Pulmonary Nodules in a Patient with Sarcomatoid Renal Cell Carcinoma. *Prensa Médica Argentina*, **96**, 385-388.

[30] Gosh, J., Surve, R., Pokharkar, A., *et al*. (2016) Sarcomatoid Carcinoma of Kidney, Presenting with Leucocutosis as Paraneoplastic Syndrome: A Case Report and Short Review. *Oncobiology and Targets*, **3**, 1-3. https://doi.org/10.18639/ONBT.2016.03.1255

[31] Yadav, R., Chaydhary, S., Yadav, P., *et al*. (2016) Paraneoplastic Fever, Leukemoid Reaction and Thrombocytosis in Transitional Cell Carcinoma of Kidney: A Rare Presentation. *Indian Journal of Case Reports*, **2**, 104-106.

[32] Chae, E.J., Kim, J.K., Kim, S.H., *et al*. (2005) Renal Cell Carcinoma: Analysis of Postopertive Recurrence Patterns. *Radiology*, **234**, 189-196. https://doi.org/10.1148/radiol.2341031733

[33] Miyao, N., Naito, S. and Ozono, S. (2011) Late Recurrence of Renal Cell Carcinoma: Retrospective and Collaborative Study of the Japanese Society of Renal Cancer. *Urology*, **77**, 379-389. https://doi.org/10.1016/j.urology.2010.07.462