1-1-2019

Sarcoid-Like Reaction Associated with Renal Cell Carcinoma - A Case Report.

Asma Iftikhar

Muhammad A I Cheema

Preethi Ramachandran

Sonu Sahni
Touro College of Osteopathic Medicine (New York), sonu.sahni@touro.edu

Recommended Citation

Iftikhar, A., Cheema, M. A. I., Ramachandran, P., & Sahni, S. (2019). Sarcoid-like reaction associated with renal cell carcinoma – A case report. *Respiratory Medicine Case Reports, 27*, [Article 100847].

Respiratory Medicine Case Reports 27 (2019) 100847

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

Case report

Sarcoid-like reaction associated with renal cell carcinoma – A case report

Asma Iftikhar[a], Muhammad A.I. Cheema[a], Preethi Ramachandran[b], Sonu Sahni[c,d,*]

[a] New York - Presbyterian Queens, Division of Pulmonary, Critical Care and Sleep Medicine, Flushing, NY, 11355, USA
[b] Brookdale University Hospital Medical Center, Division of Hematology and Oncology, Brooklyn, NY, 11212, USA
[c] Brookdale University Hospital Medical Center, Department of Internal Medicine, Brooklyn, NY, 11212, USA
[d] Touro College of Osteopathic Medicine, Department of Primary Care, New York, NY, 10027, USA

ARTICLE INFO

Keywords:
Renal cell carcinoma
Sarcoid like reaction
Paraneoplastic syndrome
Metastatic disease

ABSTRACT

Renal cell carcinoma (RCC) is a highly vascular tumor, which may spread to the lungs and other organs. It often presents with localized or systemic manifestation, including paraneoplastic syndromes. Sarcoidosis is a systemic granulomatous inflammatory disease characterized by non-caseating granulomas that typically afflicts the respiratory system. In the absence of any evidence of systemic sarcoidosis they are referred to as sarcoid-like reactions. Non-caseating epithelioid granulomas, also regarded to sarcoid-like granulomas have been described in association with certain malignancies such as carcinomas of the breast, colon, seminoma, and Hodgkin's lymphoma. However, sarcoid like reaction associated with renal cell carcinoma is uncommon. Herein we present a rare case of a patient with renal cell carcinoma with mediastinal lymphadenopathy initially thought to metastatic disease, though revealed a sarcoid-like reaction with review of literature.

1. Introduction

Renal cell carcinoma (RCC) is a highly vascular tumor, which may spread to the lungs and other organs via the hematogenous or lymphatic route. Patients with RCC can present with local or systemic manifestations which may be due to metastases or paraneoplastic syndromes. The pulmonary manifestations of RCC are many and varied as patients may present with hemoptysis, pleural effusion, pulmonary embolism or arteriovenous fistulas [1]. Though rare, RCC may also spread through the lymphatic system and involve the mediastinal lymph nodes. This may lead to mediastinal and hilar lymphadenopathy and rarely may it present as a sarcoid-like reaction. Herein we present a rare case of a patient with diagnosed RCC presenting with mediastinal lymphadenopathy initially thought to metastatic disease, which later was determined to be sarcoid-like reaction.

2. Case report

A 45-year-old obese Asian female with only significant past medical history of RCC diagnosed one year prior for which she underwent left partial nephrectomy presented to our outpatient with a chief complaint of progressively worsening dyspnea on exertion, palpitations and wheezing over the previous 3 months. She denied any history of smoking or alcohol use. She also denied history of chest pain, dizziness, weight loss or fever. Her weight was noted to be 88.9 kg with a BMI of 37.69 kg/m^2. Vital signs were within normal limits with a blood pressure of 130/90 mmHg, pulse of 74 beats/min and O_2 saturation of 96% on room air. On physical examination, she was noted to be obese with no evidence of respiratory distress. Lungs were clear to auscultation bilaterally. Abdominal and neurological examination were unremarkable. Laboratory values are summarized in Table 1.

Patient underwent CT scan of the chest with contrast for persistent dyspnea which revealed bilateral enlarged hilar lymph nodes measuring 1.4 × 1.7 cm and 2.1 × 3.1 cm which have been shown in Fig. 1.

A subsequent positron emission tomography (PET) scan revealed that there were several mildly enlarged, mildly hypermetabolic mediastinal and bilateral hilar lymph nodes. A right paratracheal lymph node had a measurement of 4.0 SUV. The patient then underwent a bronchoscopy with biopsy which showed endobronchial lesion in the anterior segment of their right superior lobe, subcarinal and right hilar lymphadenopathy. The biopsy showed evidence of non-necrotizing granulomatous inflammation. Fungal and AFB stains were negative. Histological slides have been displayed in Fig. 2. The patient has remained well and has been following as an outpatient. Periodic spirometry and flow volumes loops are being conducted without ant observed changes in pulmonary function.

* Corresponding author. Brookdale University Hospital Medical Center, Department of Internal Medicine, Brooklyn, NY, 11212, USA.
E-mail address: sahni.sonu@gmail.com (S. Sahni).

https://doi.org/10.1016/j.rmcr.2019.100847
Received 24 February 2019; Received in revised form 14 April 2019; Accepted 14 April 2019

Table 1
Laboratory values.

Laboratory Test	Results
Hemoglobin	13.3 g/dl
Hematocrit	47.7%,
White blood cells	7.7 K/ul
Platelets	288 K/ul
Sodium	140 mmol/L
Potassium	3.7 mmol/L
Chloride	105 mmol/L
Blood urea nitrogen	13 mg/dl
Creatinine	0.7 mg/dl
Glucose	89 mg/dl
Thyroid stimulating hormone	0.61 μl U/ml

3. Discussion

Granulomatous inflammation is a type of chronic inflammatory process that is characterized by accumulation of epithelioid and multinucleated giant cells [2]. In the absence of systemic sarcoidosis granulomas are traditionally formed in response to perceived foreign substances that the immune system is unable to eliminate or they immune mediated. Foreign body granulomas form around commonly iatrogenic material such as talc, sutures or other fibers that are large enough to preclude phagocytosis by a single macrophage. Immune mediated granulomas may be caused by numerous agents including bacterial and fungal organisms however it is possible that granulomas may be formed idiopathically.

3.1. Sarcoid-like reaction

Sarcoid-like reactions refer to the development of non-caseating epithelioid cell granulomas in patients who do not fulfill the criteria for systemic sarcoidosis. It has been reported that approximately 4–14% of cancer patients exhibit sarcoid-like reactions [3]. The sarcoid-like reaction was first described by Wolbach in 1911 [4] and has been reported in multiple different malignancies such as breast, rectal, cystic duct carcinoma [5] and in renal cell carcinoma [6,7]. Cancer associated sarcoid reactions have been observed in both patients with hematologic malignancies or solid tumors [8]. The etiologies of sarcoid-like reactions are not clear. A proposed theory focuses on soluble antigenic factors, shed by tumor cells or released in tumor necrosis in which these soluble factors are carried by lymphatic vessels to the draining lymph nodes, where they may induce a T cell mediated host response similar to a hypersensitivity reaction leading to the formation of epithelioid cell granulomas [9,10].

3.2. Features of sarcoid-like reactions

Histologically, the granulomas of sarcoid-like reaction are indistinguishable from those of systemic sarcoidosis. They usually consist of central focus of epithelioid cells admixed and surrounded by rim of lymphocytes [11]. Giant cells of both the Langerhans and foreign body type are common. Some investigators have reported epithelioid cell granulomas in lymph nodes accompanied by the sinus histiocytes [12]. Sarcoid like reactions are relatively infrequent directly at the tumor site and frequently occur in organs which can be reached by dendritic cells but without direct tumor involvement [9]. The pathogenesis is poorly understood, but the granulomatous inflammation has been related by an anti-neoplastic immune response [3].

Sarcoid reactions are characterized by the by T-zone in lymph nodes and composed of different inflammatory cells within the epithelioid cell granuloma and contain dendritic cells and T lymphocytes. Distribution and demarcation of the granuloma can be correlated with the ratio of CD4/CD8 cells. Thus, T cell mediated immune response and antigen dependent pathways are common for the formation of granulomas. This pathogenesis is the same are same for sarcoidosis and sarcoid-like reactions. In sarcoid-like reactions, CD8 cells are present more frequently when compared to the CD4 cells [13].

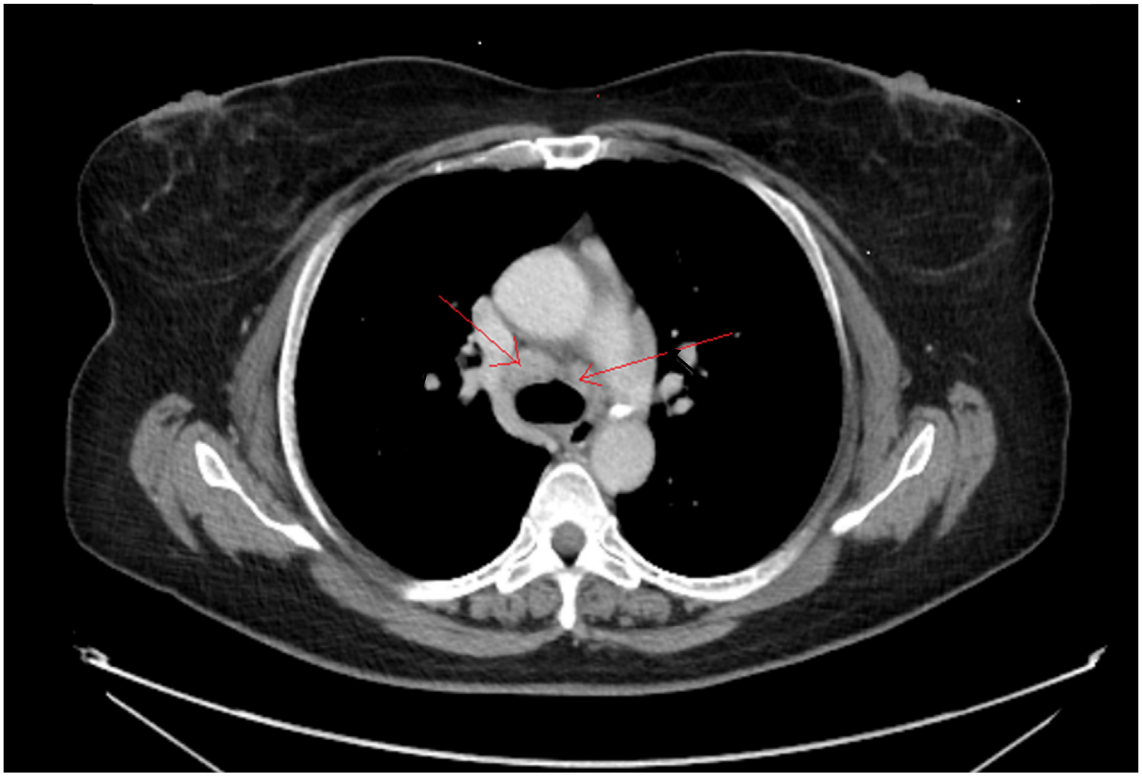

Fig. 1. Computer tomography of the chest with contrast which showed enlarged mediastinal lymph nodes.

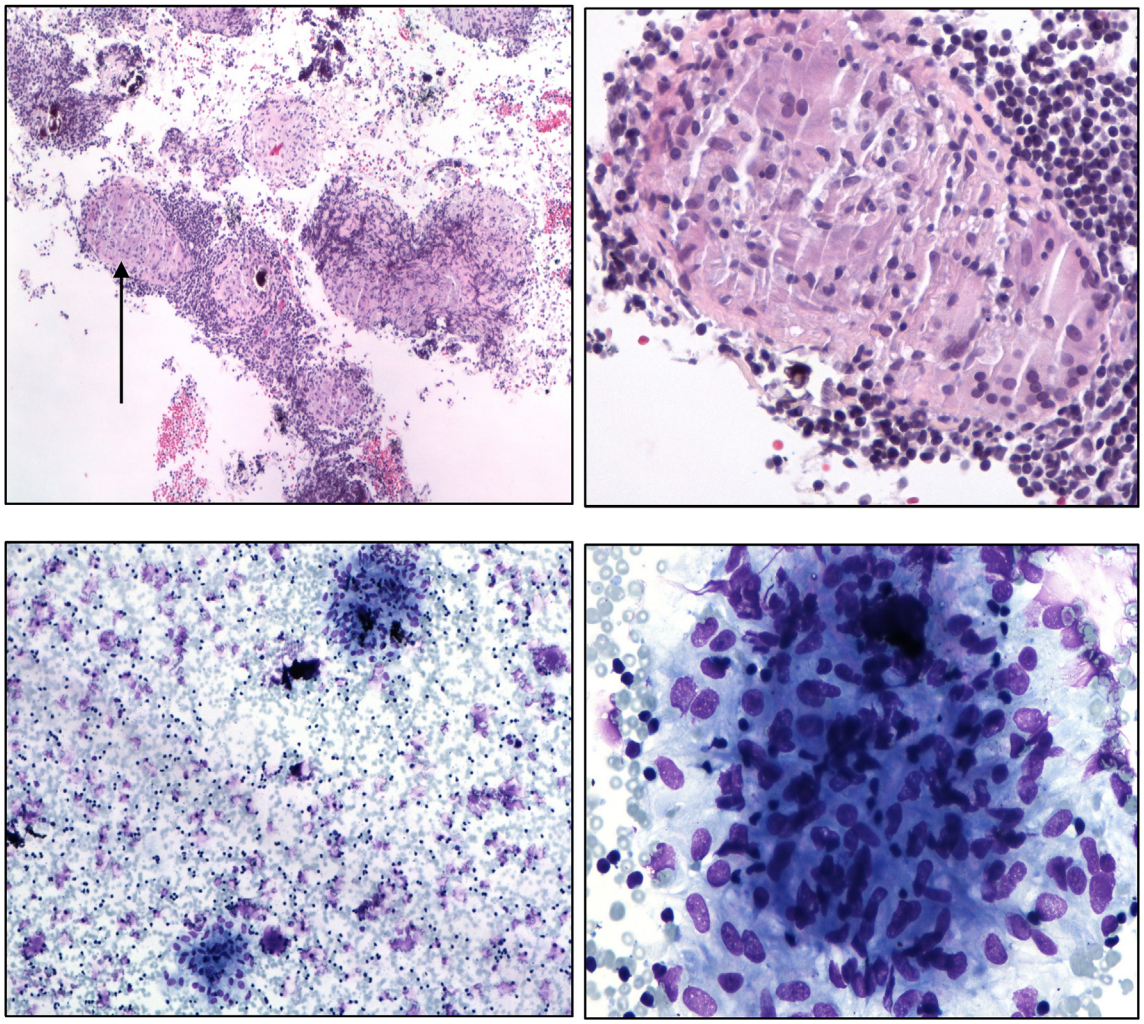

Fig. 2. In clockwise fashion: Top left: Hematoxylin and eosin stain of biopsied lymph node showing granuloma 10x; top right: Hematoxylin and eosin stain of biopsied lymph node showing granuloma 40x; bottom right Diff-Quik of biopsied lymph node showing granuloma 40x; bottom left: Diff-Quik staining of biopsied lymph node showing granuloma 10x.

Table 2
Cases of renal cell carcinoma with granulomatous sarcoid-like reaction.

Clinical features	Renal tumor histology	Reference
60 y.o. M - left renal mass, lung nodules of clear cell adenocarcinoma with extensive SLR	Not microscopically examined	Moder et al. (1990) [18]
55 y.o. F - Renal mass in kidney infiltrated by sarcoidosis, liver solid masses and abdominal lymph nodes consistent with sarcoidosis,	Clear cell RCC with sarcoidosis	Bottone et al. (1993) [19]
56 y.o. M - Renal mass	RCC with SLR	Cambell et al. (1993) [20]
44 y.o. M - Renal failure with renal Mass	Papillary –type RCC with SLR	Marinides et al. (1994) [2]
39 y.o. M - Renal mass	Clear cell RCC with sarcoidosis	Lucci et al. (2002) [6]
62 y.o. F - Renal Mass	Clear cell RCC with SLR	Kovacs et al. (2004) [7]
72 y.o. M - Renal Mass	Sarcomatoid RCC with SLR	Piscioli et al. (2008) [21]
44-65 y.o./3M - Renal mass	Clear cell RCC without SLR	Narasimhaiah et al. (2011) [22]
62 y.o. M - Renal mass	Peritumor sarcoid-like reaction	Simon et al. (2012) [23]
62 y.o M- Renal mass	RCC with SLR within tumor	Burhan et al. (2013) [24]
41 y.o. M - Renal cell mass	Bone marrow sarcoid-like reaction	Timothy et al. (2014) [25]

F – Female; M – Male; RCC – Renal cell carcinoma; SLR – Sarcoid like reaction.

3.3. Sarcoid-like reaction in renal cell carcinoma

Incidence of lymph node metastasis of renal cell carcinoma is inconsistence ranging from 5% to 50% [14]. Only 5% to 8.8% of RCC cases have been reported to metastasize after limited hilar or regional lymph node dissection [15,16] and up to 38% with formal extended retroperitoneal lymphadenectomy [17]. The discovery of sarcoid-like reaction in the setting of renal cell carcinoma is rare with very few cases being reported in the literature. A few of such cases have been outlined in Table 2.

Sarcoid-like reaction was noted to primarily limited to the kidney except for one case reported by Bottone et al. in which the sarcoid-like granuloma was present in liver and abdominal lymph nodes [19].

Though the role of lymph node dissection is still controversial in the setting of RCC it is important to understand the drainage of lymph in and around the renal system. As lymphatic drainage of kidney is differs

from right to left, right renal tumors mostly drain in the interaortocaval nodes and left sided tumors drain to post aortic and paraaortic nodes. Formation of a granulomatous reaction is not dependent upon the lymph node drainage but in fact, sarcoid-like reactions may be a marker of an immunologically mediated antitumor response of macrophages activated by T-lymphocytes [9].

Active granulomatous inflammatory conditions such as tuberculosis, sarcoidosis, Cryptococcus may cause accumulation of fluorodeoxyglucose (FDG) on PET scanning and may cause false positives in the setting of malignancy. FDG measurement on PET scanning provides quantitative data in the form of standardized uptake value (SUV). A value 2.5 SUV or greater has been used as cut off value indicative of malignancy though various inflammatory cells such as neutrophils and activated macrophages may also show increased uptake.

Clinicians should also take into consideration the possibility of true sarcoidosis in the setting of malignancy. Review of the literature has identified a moderate association between sarcoidosis and malignancies. In the setting of kidney cancer there appears to be a relative risk of 1.55 for developing sarcoidosis [26]. For a clinician it is important to differentiate between diagnosis of systemic sarcoidosis associated with malignancy and sarcoid like reaction. In the diagnostic workup certain characteristics favor one diagnosis over another. Granulomas isolated to the vicinity of tumor or to the draining lymph node of tumor are seen more commonly in sarcoid like reactions. In addition, presence of B-cells and sinus histiocytes in the granuloma air on the side of sarcoid like reaction over systemic sarcoid disease [27]. The entity of sarcoidosis in malignancy must be differentiated from sarcoid-like reaction as management and patient outcomes differ.

Our patient presented with a renal tumor, in which there was an abnormal uptake on PET scanning mimicking metastasis of RCC. After further diagnostics, the abnormal PET scan was found to be secondary to a sarcoid-like reaction.

4. Conclusions

The discovery of sarcoid-like reaction in the setting of renal cell carcinoma is rare with very few cases has being reported in the literature. In our case sarcoid-like reaction was found in the lung and was found to be secondary to RCC, after other causes of granulomatous disease such as tuberculosis and sarcoidosis were excluded. It is important to know that these reactions may mimic metastatic disease.

Conflicts of interest

None.

Financial disclosure

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmcr.2019.100847.

References

[1] A. Agrawal, S. Sahni, A. Iftikhar, A. Talwar, Pulmonary Manifestations of Renal Cell Carcinoma, Respiratory Medicine, (2015).
[2] G.N. Marinides, I. Hajdu, R.O. Gans, A unique association of renal carcinoma with sarcoid reaction in the kidney, Nephron 67 (4) (1994) 477–480.
[3] J.B. Craun, K.P. Banks, M.N. Clemenshaw, R.W. Moren, Sarcoid like reaction of neoplasia causing hypermetabolic thoracic adenopathy in setting of extrathoracic malignancy: report of two cases and a review of the differential diagnostic considerations, J. Nucl. Med. Technol. 40 (4) (2012) 231–235.
[4] S.B. Wolbach, A new type of Cell Inclusion, not Parasitic, associated with disseminated granulomatous lesions, J. Med. Res. 24 (2) (1911) 243–258 7.
[5] D. Mereles, N. Ehlken, S. Kreuscher, S. Ghofrani, M.M. Hoeper, M. Halank, F.J. Meyer, G. Karger, J. Buss, J. Juenger, N. Holzapfel, C. Opitz, J. Winkler, F.F. Herth, H. Wilkens, H.A. Katus, H. Olschewski, E. Grunig, Exercise and respiratory training improve exercise capacity and quality of life in patients with severe chronic pulmonary hypertension, Circulation 114 (14) (2006) 1482–1489.
[6] S. Lucci, R. Rivolta, M. Fazi, L. Iorio, G.F. Raschella, G. Merlino, R. Giordano, A. Redler, Sarcoidosis and clear cell carcinoma of the kidney: the sixth case? Il G. Chir. 23 (3) (2002) 75–78.
[7] J. Kovacs, A. Varga, M. Bessenyei, S. Gomba, Renal cell cancer associated with sarcoid-like reaction, Pathol. Oncol. Res. 10 (3) (2004) 169–171.
[8] R.M. Pujol, X. Matias-Guiu, M. Planaguma, J.M. de Moragas, Chronic lymphocytic leukemia and cutaneous granulomas at sites of herpes zoster scars, Int. J. Dermatol. 29 (9) (1990) 652–654.
[9] H. Brincker, Sarcoid reactions in malignant tumours, Cancer Treat Rev. 13 (3) (1986) 147–156.
[10] R. Bassler, F. Birke, Histopathology of tumour associated sarcoid-like stromal reaction in breast cancer. An analysis of 5 cases with immunohistochemical investigations, Virchows Arch. A Pathol. Anat. Histopathol. 412 (3) (1988) 231–239.
[11] G. Gorton, F. Linell, Malignant tumours and sarcoid reactions in regional lymph nodes, Acta Radiol. 47 (5) (1957) 381–392.
[12] B. Hogstedt, Sarcoid-like lesions (epithelioid cell granulomatosis) of regional lymph nodes in association with carcinoma of the cervix, Acta Radiol. Ther. Phys. Biol. 7 (1) (1968) 12–16.
[13] A. Kurata, Y. Terado, A. Schulz, Y. Fujioka, F.E. Franke, Inflammatory cells in the formation of tumor-related sarcoid reactions, Hum. Pathol. 36 (5) (2005) 546–554.
[14] D.G. Skinner, R.B. Colvin, C.D. Vermillion, R.C. Pfister, W.F. Leadbetter, Diagnosis and management of renal cell carcinoma. A clinical and pathologic study of 309 cases, Cancer 28 (5) (1971) 1165–1177.
[15] A. Minervini, L. Lilas, G. Morelli, C. Traversi, S. Battaglia, R. Cristofani, R. Minervini, Regional lymph node dissection in the treatment of renal cell carcinoma: is it useful in patients with no suspected adenopathy before or during surgery? BJU Int. 88 (3) (2001) 169–172.
[16] J.P. Siminovitch, J.E. Montie, R.A. Straffon, Lymphadenectomy in renal adenocarcinoma, J. Urol. 127 (6) (1982) 1090–1091.
[17] A. Sigel, S. Chlepas, K.M. Schrott, P. Hermanek, [Surgery of the kidney tumor], Chirurg 52 (9) (1981) 545–553.
[18] K.G. Moder, S.C. Litin, T.A. Gaffey, Renal cell carcinoma associated with sarcoidlike tissue reaction, Mayo Clin. Proc. 65 (11) (1990) 1498–1501.
[19] A.C. Bottone, M. Labarbera, A. Asadourian, A. Barman, C. Richie, Renal sarcoidosis coexisting with hypernephroma, Urology 41 (2) (1993) 157–159.
[20] F. Campbell, A.G. Douglas-Jones, Sarcoid-like granulomas in primary renal cell carcinoma, Sarcoidosis 10 (2) (1993) 128–131.
[21] I. Piscioli, S. Donato, L. Morelli, F. Del Nonno, S. Licci, Renal cell carcinoma with sarcomatoid features and peritumoral sarcoid-like granulomatous reaction: report of a case and review of the literature, Int. J. Surg. Pathol. 16 (3) (2008) 345–348.
[22] D.A. Narasimhaiah, M.T. Manipadam, K. Aswathaman, S. Krishnamoorthy, Renal cell carcinoma associated with granulomatous reaction, Saudi journal of kidney diseases and transplantation : an official publication of the Saudi Center for Organ Transplantation, Saudi Arab. 22 (6) (2011) 1211–1214.
[23] S. Ouellet, R. Albadine, R. Sabbagh, Renal cell carcinoma associated with peritumoral sarcoid-like reaction without intratumoral granuloma, Diagn. Pathol. 7 (2012) 28.
[24] W. Burhan, Z. Al Rowaie, E. Rajih, M. Akhtar, Sarcoid-like granulomatous reaction in renal cell carcinoma: report of a case with review of the published reports, Ann. Saudi Med. 33 (6) (2013) 614–618.
[25] T.F. Madden, S.J. Baccei, Diffuse bone marrow sarcoid-like reaction associated with renal cell carcinoma, Skeletal Radiol. 43 (12) (2014) 1761–1766.
[26] A. Chopra, A. Nautiyal, A. Kalkanis, M.A. Judson, Drug-induced sarcoidosis-like reactions, Chest 154 (3) (2018) 664–677.
[27] A. Chopra, M.A. Judson, How are cancer and connective tissue diseases related to sarcoidosis? Curr. Opin. Pulm. Med. 21 (5) (2015) 517–524.