Synchronous Kaposi sarcoma and renal cell carcinoma in an elderly male patient (a very uncommon reported entity): A case report

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Abstract. Based on the literature, there are only three reports available to date on synchronous Kaposi sarcoma (KS) and renal cell carcinoma (RCC), at least to the best of our knowledge. The present study reports a rare case of synchronous classic KS and clear cell RCC. A 69-year-old male presented with painful, purplish nodular lesions on the dorsal aspect of his hands and feet. He had no chronic medical illnesses or prior surgical interventions. An excisional biopsy of one of the lesions revealed a nodular dermal lesion with numerous vascular channels and interlacing spindle cells. A 2.5 cm-enhancing mass was found in a contrast-enhanced computed tomography scan of the abdomen, suggesting RCC or metastasis. A partial nephrectomy was performed, and the histopathological findings were consistent with clear cell RCC. The patient responded well to paclitaxel and topical imiquimod (5%), and the skin lesions disappeared. Both KS and RCC are vascular tumors, and their pathogenesis is commonly affected by an angiogenic factor known as vascular endothelial growth factor (VEGF). A complete response of KS was observed after sorafenib, an inhibitor of VEGF receptors, was administered for the treatment of metastatic renal cancer. This reinforces the fact that there is a common therapeutic and pathogenetic pathway between these two neoplasms. Synchronous KS and clear cell RCC are rare findings. Their simultaneous appearance may be triggered by the common enhancing angiogenic factor, VEGF.

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Introduction

Kaposi sarcoma (KS) is an atypical multicentric tumor that mainly originates in the skin of the lower extremities. It can occur in four clinical forms, including classic KS, endemic KS, human-acquired immunodeficiency syndrome-related epidemic KS (AIDS-related KS) and transplantation-associated KS (1). This tumor commonly consists of proliferating spindle cells and capillary vessels, presenting as multiple vascular tumors, and may develop as cutaneous lesions, invasive lymph nodes, or visceral tumors (2). The human immunodeficiency virus (HIV), human herpesvirus-8 (HHV-8) and immunosuppressive treatment all play a role in the development of KS (1,3,4). The more susceptible sex is usually males in their 70 and 80s (5). The simultaneous occurrence of several different tumors, such as a primary tumor with a metastatic tumor or a metastatic tumor with an inflammatory lesion has been previously reported as the association of KS with several malignant diseases like lymphomas, leukemias and multiple myeloma. However, its co-existence with a solid tumor, such as renal cell carcinoma (RCC), is extremely rare (6,7). Based on the literature and to the best of our knowledge, there are only three reports available to date that mention this finding (7-9). RCC represents a heterogenous group of cancers originating from renal tubular epithelial cells. Its incidence increases according to age and the male sex (10). The present study reports a rare case of synchronous classic KS and clear cell RCC in a 69-year-old male patient with no chronic disease or history of surgical intervention.

Case report

Patient information. A 69-year-old man was referred by a dermatologist to the Hiwa Oncology Hospital (Sulaimani, Iraq) after presenting with painful, purplish nodular lesions on the dorsal aspect of his hands and feet for a duration of 2 months (Fig. 1).

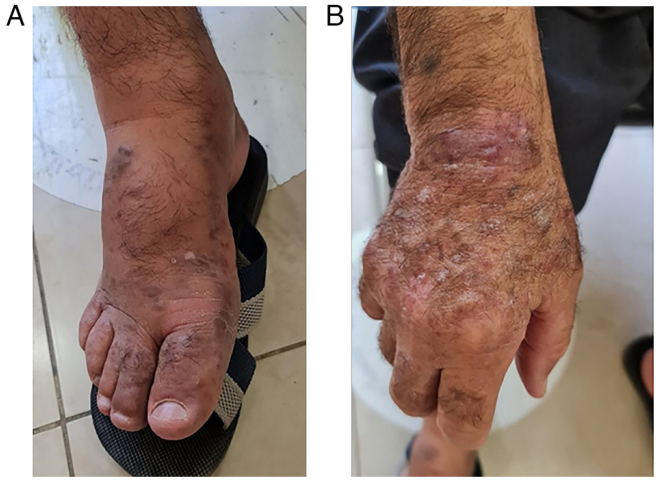

Figure 1. Multiple purplish-bluish lesions over the dorsal aspect of the (A) right foot and (B) right hand.

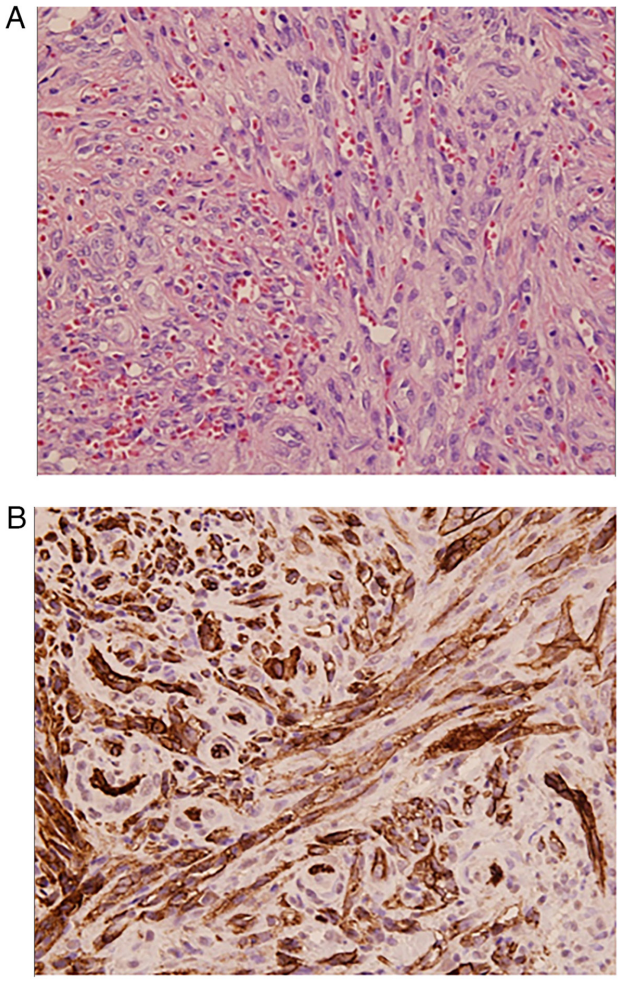

Figure 2. (A) The image shows fascicles of spindled cells with red blood cells within the narrow slit-like spaces. (B) A strong diffuse cytoplasmic reaction to CD31 staining is evident.

Clinical findings. He had no chronic medical illnesses or prior surgical interventions. He had used various prescribed topical agents, such as trichloroacetic acid (TCA) solution and topical steroids without any response.

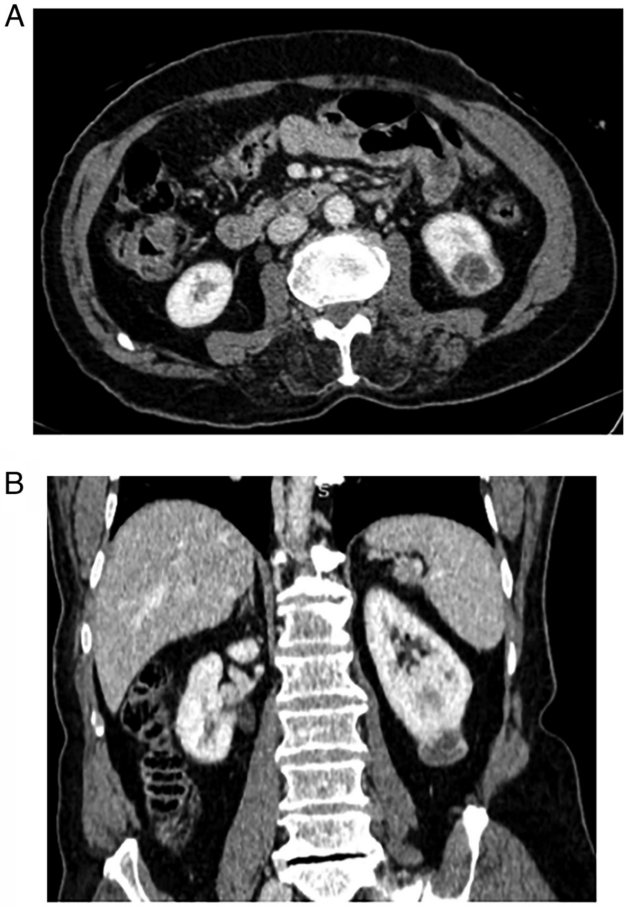

Figure 3. (A) Axial and (B) coronal sections of contrast-enhanced computed tomography of the abdomen and pelvis show a left lower pole-enhancing cystic mass.

Diagnostic assessment. An excisional biopsy of one of the lesions revealed a nodular dermal lesion with numerous vascular channels and interlacing spindle cells. Immunohistochemical examinations (previously conducted by another center) revealed a positive reaction to CD31 (Fig. 2). He was referred to an oncology center. After a metastatic workup, a 2.5 cm enhancing mass was found in a contrast-enhanced CT of the abdomen, suggesting RCC or metastasis (Fig. 3).

Therapeutic intervention. A partial nephrectomy was performed, and the histopathological examinations (previously conducted by another center) were in line with clear cell RCC with a pathological stage of pT1a (Fig. 4). The patient then received six cycles of paclitaxel (100 mg/m^2) intravenously every 14 days, along with topical imiquimod (5%) three times weekly. He responded to the treatment, and the skin lesions disappeared (Fig. 5).

Follow-up. The post-operative period was uneventful. After 1 year, his follow-up imaging revealed no recurrent renal mass.

Discussion

The dermatologist, Moritz Kaposi, was the first to report several cases of KS in elderly males and described it as a multifocal pigmented sarcoma of the skin (11). KS is a rare

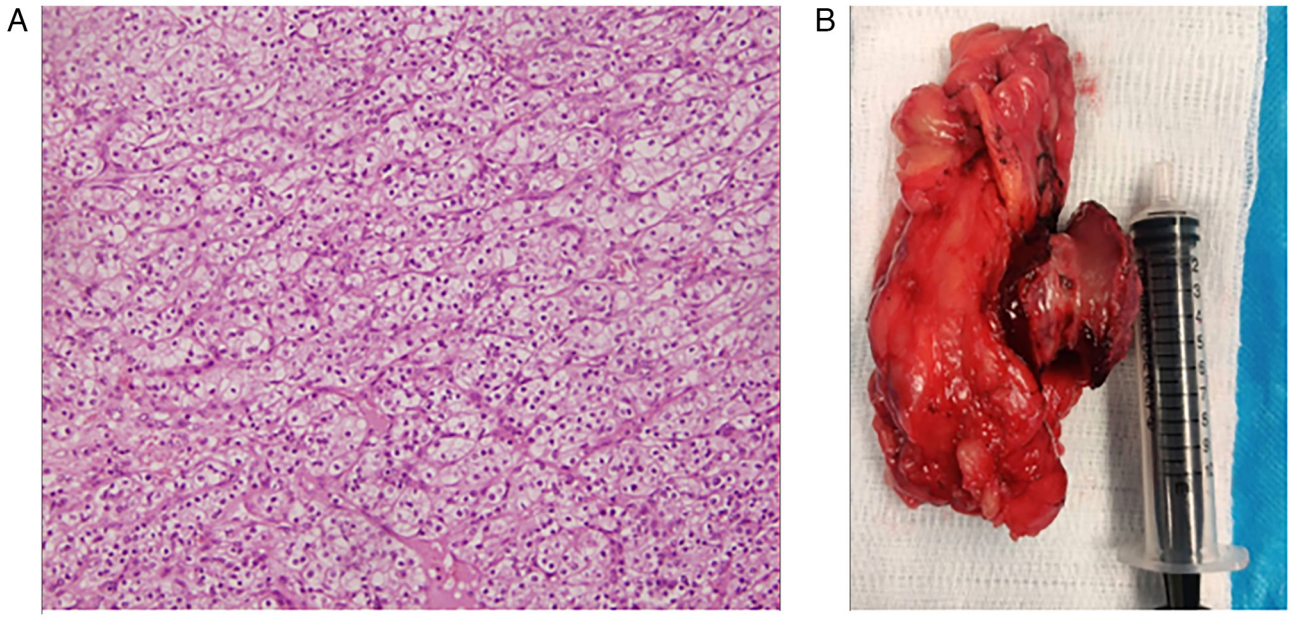

Figure 4. (A) Tubulocystic pattern with clear cytoplasmic staining in the microscopic examination, (B) Image of the gross appearance of the mass with surrounding fat and a nested pattern.

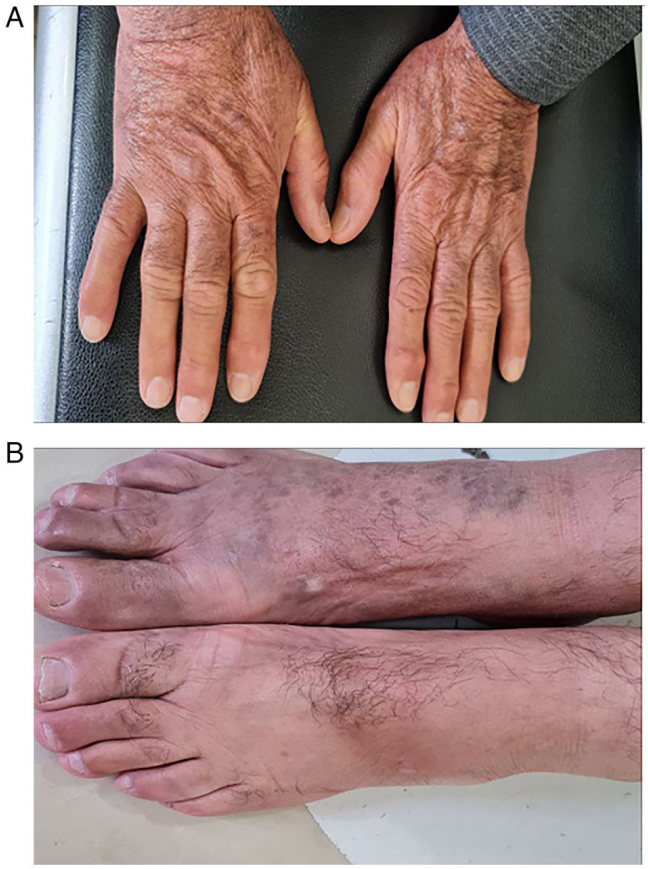

Figure 5. Follow-up image of the patient after 1 year, illustrating the disappearance of the lesions on both the dorsal aspects of the (A) hands and (B) feet.

neoplasm that develops from endothelial cells and is classified into four epidemiological forms: Classic KS, endemic KS, AIDS-related KS and transplantation-associated KS (1). Classic KS most commonly occurs in elderly male patients of Arabic, Southern European, and Jewish ancestry. Individuals who were born in countries where classic KS is prevalent are therefore at a higher risk of developing KS (4). In some African countries, KS has been known for decades prior to the emergence of HIV (12). This form is known as endemic, and it is much more aggressive than the classic form. AIDS-related KS commonly occurs in HIV-affected homosexual males (12).

It has been revealed that a significant association exists between immunosuppression and KS (1). Another study reported that the incidence of KS was 200-fold higher in recipients of organ transplants in comparison to the general population (11). The exact etiology of KS has yet to be understood; however, infection with HHV-8 is strongly related to the neoplasm, and it has been reported in >95% of KS cases of all epidemiological forms (13). It can affect the coding of the factors and cytokines that regulate cellular proliferation, immune responses and apoptosis, inducing the transformation of endothelial cells (1). It is worth mentioning that in the present case report, the patient was free from any chronic or acquired disease, and his past surgical and medical treatment was also negative. For this reason, the three forms of endemic KS, AIDS-related KS and transplantation-associated KS were excluded. The patient described herein was an elderly male and compatible with the criteria of classic KS, in which the majority of the classic KS cases are elderly males.

Classic KS usually appears as painless, bluish-red demarcated lesions on the distal parts of the lower extremities, and histologically the lesions are often similar to granulated tissue. In the majority of cases, the lesions grow gradually and merge to form large plaques. On some occasions, solitary lesions can form nodular and brownish-red tumors (14). The KS in the present study manifested as painful, purplish nodular lesions on the dorsal aspects of the hands and feet.

In the literature, the association of KS with various diseases and cancers has been discussed (4,7,15). Multicentric Castleman

disease (MCD) refers to a lymphoproliferative disorder that is associated with secondary B-cell lymphoma development. It has recently been revealed that a subclass of this disorder is linked to KS-associated herpesvirus (KSHV), in which KSHV infection can be found in almost all HIV-associated cases of MCD and 50% of HIV-negative patients (4). Several scholars have mentioned the concurrence of KS and psoriasis, which presents a diagnostic challenge due to the resemblance between the lesions of both conditions (15,16). Furthermore, another epidemiological study revealed a high risk of KS in patients with psoriasis (17). Magri *et al* (13) also reported a rare case of KS following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in an 83-year-old female patient. They considered that various cofactors may have been involved in the development of KS, including steroid administration, older age, and infection with SARS-CoV-2 (13). Synchronous tumors in the same individual are regarded as a subject of interest with the hope of shedding light on the factors that are involved in promoting the neoplastic process or identifying criteria that place an individual at risk of developing various malignancies. The biological mechanisms behind the association of KS with different malignancies have not yet been well-established, although some individuals may be susceptible to some common initiators of malignant alterations (18). An association of KS with multiple types of cancer, such as leukemia, multiple myeloma, thymoma, non-Hodgkin's lymphoma, Hodgkin's lymphoma and malignant melanoma has been reported (14). Iscovic *et al* (19) conducted a study on 1,000 Jewish patients with classic KS and found that 61 cases were affected by a second neoplasm, and increasing risks of non-Hodgkin's lymphoma and cutaneous malignant melanoma were detected. The simultaneous appearance of KS and RCC is a very infrequent condition (7). To the best of our knowledge, only three such cases have been published to date. The first one was reported by Giatrakou *et al* (7), in which the case was affected by classic KS and two coexistent kidney tumors: Clear cell RCC and chromophobe RCC. The case was recovered from the KS after the removal of the kidney tumors (7). The second case was synchronous KS and RCC in a non-infected HIV homosexual male who was managed by tumor resection (8). In addition, another case of synchronous AIDS-related KS with renal cell adenocarcinoma in a 42-year-old homosexual male was reported (9). The present case is the first report of synchronous classic KS and clear cell RCC, followed by the case of Giatrakou *et al* (7).

Both KS and RCC are vascular tumors, and their pathogenesis is commonly affected by an angiogenic factor known as vascular endothelial growth factor (VEGF). A complete response of KS was observed after sorafenib, an inhibitor of VEGF receptors, was administered for the treatment of metastatic renal cancer (7,20). This reinforces that there is a common therapeutic and pathogenetic pathway between these two neoplasms, and VEGF plays a significant role in their oncogenesis (7). KS can be easily suspected depending on the clinical manifestations; however, a clinical diagnosis alone is not sufficient. A histopathological diagnosis remains the standard method for the confirmation of KS, although this needs to be performed by an experienced pathologist (21). The treatment strategy for KS commonly depends on several factors, including skin lesion number, disease extension, symptoms, comorbidities, and the rate of tumor growth. Thus, the management of KS can be ranged from local therapy for cutaneous disease to systemic therapy in cases with visceral and symptomatic lesions. For the treatment of localized skin lesions, a number of options like ionizing radiation, cryotherapy, photodynamic therapy and surgical excision have been frequently used. However, in aggressive cases involving the skin, lymph nodes, and visceral organs, chemotherapy is a necessary option (22). Cytotoxic chemotherapy has been reported as the treatment of choice for KS. DNA-damaging agents, such as doxorubicin and paclitaxel are in the first line of treatment (21). In the case described herein, after conducting a partial nephrectomy, the case was administered six cycles of paclitaxel every 2 weeks with topical imiquimod (5%) three times weekly, and the patient completely responded to the treatment.

In conclusion, synchronous KS with clear-cell RCC is a rare finding. Clear-cell RCC can be found incidentally during the workup of the KS. Their simultaneous appearance may be triggered by the common enhancing angiogenic factor, VEGF.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

RB was a major contributor to the conception of the study, and the surgeon who managed the case. HOA and FHK were involved in the design of the study, literature search and review of studies for the inclusion of related studies, and in the drafting of the manuscript. BS was the oncologist who performed the oncological analysis. BAA, IA, RSA and RKA were involved in the literature review, in the design of the study, the critical revision of the manuscript, and the processing of the figures. RB and BS confirm the authenticity of all the raw data. RJR and SHT were the radiologists who performed the assessment of the subjects' Kaposi sarcoma and renal cell carcinoma. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Written informed consent was obtained from the patient.

Patient consent for publication

Written informed consent was taken from the patient for the publication of any related information and images or illustrations.

Competing interests

The authors declare that they have no competing interests.

References

1. Agbaht K, Pepedil F, Kirkpantur A, Yilmaz R, Arici M and Turgan C: A case of Kaposi's sarcoma following treatment of membranoproliferative glomerulonephritis and a review of the literature. Ren Fail 29: 107-110, 2007.
2. Mitsuyasu RT, Colman MF and Sun NC: Simultaneous occurrence of Hodgkin's disease and Kaposi's sarcoma in a patient with the acquired immune deficiency syndrome. Am J Med 80: 954-958, 1986.
3. Cheung MC, Pantanowitz L and Dezube BJ: AIDS-related malignancies: Emerging challenges in the era of highly active antiretroviral therapy. Oncologist 10: 412-426, 2005.
4. Boshoff C and Weiss RA: Epidemiology and pathogenesis of Kaposi's sarcoma-associated herpesvirus. Philos Trans R Soc Lond B Biol Sci 356: 517-534, 2001.
5. Moore A, Peretz I, Yosef L, Goldstein DA, Goldvaser H, Horn S, Edel Y and Zer A: Potential association between Kaposi sarcoma and gout: An exploratory observational study. Sarcoma 2020: 8844970, 2020.
6. Paksoy N: Simultaneous occurrence of Kaposi sarcoma and tuberculosis; Kaposi sarcoma and lymphoma in the same lymph node: A report on two HIV-positive patients from Zimbabwe. Rev Soc Bras Med Trop 52: e20180188, 2019.
7. Giatrakou S, Leodara V, Siatelis A, Papadavid E, Theodoropoulos K, Safioleas K, Stamatakos M and Stavrianeas NG: P91 clearance of non AIDS-Kaposi sarcoma after removal of coexistent clear cell renal cell and chromophobe renal cell carcinomas. Melanoma Res 20: e81-e82, 2010.
8. Meuthen I, Vossbeck H, Marx FJ, Hummerich W and Saborowski F: Kaposi's sarcoma and renal cell carcinoma in a male homosexual without detectable HIV infection-case report and review of the literature. Onkologie 18: 151-154, 1995.
9. Azón-Masoliver A, Moreno A, Gatell JM and Mascaró JM: Renal cell adenocarcinoma associated with AIDS-related Kaposi's sarcoma. AIDS 4: 818-819, 1990.
10. Hsieh JJ, Purdue MP, Signoretti S, Swanton C, Albiges L, Schmidinger M, Heng DY, Larkin J and Ficarra V: Renal cell carcinoma. Nat Rev Dis Primers 3: 17009, 2017.
11. Cesarman E, Damania B, Krown SE, Martin J, Bower M and Whitby D: Kaposi sarcoma. Nat Rev Dis Primers 5: 9, 2019.
12. Beral V, Peterman TA, Berkelman RL and Jaffe HW: Kaposi's sarcoma among persons with AIDS: A sexually transmitted infection? Lancet 335: 123-128, 1990.
13. Magri F, Giordano S, Latini A and Muscianese M: New-onset cutaneous Kaposi's sarcoma following SARS-CoV-2 infection. J Cosmet Dermatol 20: 3747-3750, 2021.
14. Iscovich J, Boffetta P, Franceschi S, Azizi E and Sarid R: Classic Kaposi sarcoma: Epidemiology and risk factors. Cancer 88: 500-517, 2000.
15. Brambilla L, Genovese G, Tourlaki A and Della Bella S: Coexistence of Kaposi's sarcoma and psoriasis: Is there a hidden relationship? Eur J Dermatol 28: 320-325, 2018.
16. Yoo J, Jo M, Kim MS, Choi KH, Park HJ and Jue MS: Hidden pictures of Kaposi's sarcoma in psoriatic lesions: A diagnostic challenge. Ann Dermatol 28: 749-752, 2016.
17. Hemminki K, Liu X, Ji J, Sundquist J and Sundquist K: Kaposi sarcoma and Merkel cell carcinoma after autoimmune disease. Int J Cancer 131: E326-E328, 2012.
18. Safai B, Miké V, Giraldo G, Beth E and Good RA: Association of Kaposi's sarcoma with second primary malignancies: Possible etiopathogenic implications. Cancer 45: 1472-1479, 1980.
19. Iscovich J, Boffetta P and Brennan P: Classic Kaposi's sarcoma as a first primary neoplasm. Int J Cancer 80: 173-177, 1999.
20. Ardavanis A, Doufexis D, Kountourakis P and Rigatos G: A Kaposi's sarcoma complete clinical response after sorafenib administration. Ann Oncol 19: 1658-1659, 2008.
21. Schneider JW and Dittmer DP: Diagnosis and treatment of Kaposi sarcoma. Am J Clin Dermatol 18: 529-539, 2017.
22. Passarelli A, Galdo G, Pellegrino T, Roviello G, Aieta M, Aviello G and Conca R: Therapeutic management of a symptomatic Kaposi's sarcoma patient with renal failure undergoing haemodialysis: A case report. Dermatol Reports 14: 9113, 2021.