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Case Report

Coexistence of multiple myeloma and Kaposi Sarcoma in a patient with rheumatoid arthritis

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Abstract Kaposi sarcoma (KS) is a neoplasm of factor VIII-producing endothelial cell origin with inflammatory basis. KS has gained much attention following its prevalence among patients with acquired immune deficiency syndrome (AIDS).[1] KS is classified into four epidemiologic forms including classic, African, AIDS associated and iatrogenic. Iatrogenic KS is a subtype of KS, commonly developed among medically immunosuppressed patients. One of the autoimmune diseases which might be associated with KS due to immunosuppression is Rheumatoid arthritis (RA). RA is a systemic autoimmune disorder which affects synovial membrane of multiple joints and requires long term medical treatments with immunosuppressive drugs.[2] On the other hand, associations of specific malignancies are also reported in those RA patients, under treatments with methotrexate or immunomodulatory drugs. Here we present a patient diagnosed and treated with RA who later developed multiple myeloma (MM) and KS.

Key words
Acantholytic, ATPC2, 'dilapidated brick wall appearance'.

Introduction

Here we present a 78-year-old female patient, diagnosed with RA from 10 years ago. Her medical records indicated that she had been diagnosed with RA by an expert rheumatologist and had been under drug treatments. Her treatments since RA diagnosis included prednisolone 5 mg daily, Calcium-D tablets daily, and alendronate tablets weekly. Methotrexate 15 mg weekly, was added since 7 years. One year ago, she experienced episodes of thoracolumbar pain, fatigue, decreased appetite and weight lost. MRI imaging of her spinal column demonstrated compressed fracture in 1st lumbar vertebrae **(Figures 1-2)**.

There were two major differential diagnoses: multiple myeloma and metastasis. The patient's skull X ray showed innumerable small lytic lesions giving classical "salt and pepper" appearance **(Figure 3)**.

Her initial laboratory findings indicated hemoglobin levels of 9.5 g/ dl, ESR level of 125 mm and LDH levels of 268 mg/dl **(Table 1)**.

Moreover, she went under bone marrow aspiration (BMA) with suspicion of MM. Her BMA indicated 90% plasma cell dyscrasia and diagnosis of MM was ascertained. She went under treatment with anti-myeloma drugs i.e. Bortezomib and dexamethasone. For maintenance therapies, she received Thalidomide 100 mg daily to inhibit the decrease of white blood cells. After 3 months she was referred to dermatology clinic due to

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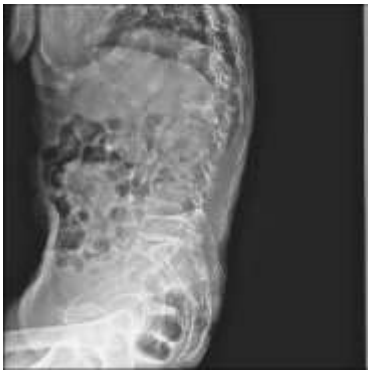

Figure 1 Lateral lumbosacral x ray showing diffuse osteoporosis associated with compressed wedge fracture of L1.

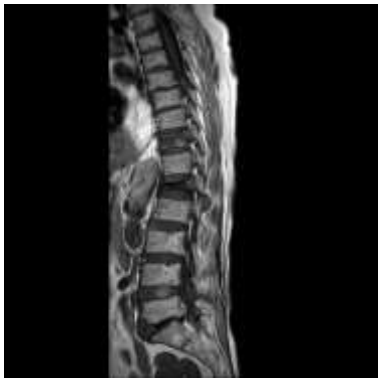

Figure 2 MRI of thoracolumbar shows area of bone marrow replacement (normal fatty is bright on T1W&T2W sequences- abnormal marrow is dark) associated with compressed wedge fracture of L1.

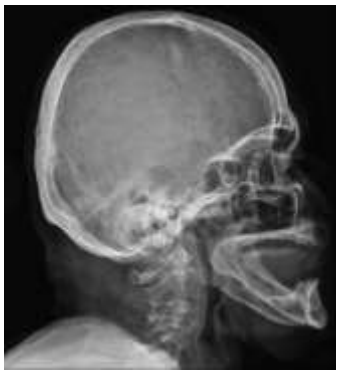

Figure 3 The skull x ray demonstrate innumerable small lytic lesions giving classical "salt and pepper" appearance.

Table 1 Laboratory findings before treatment

Biochemical Test	*Values*
ESR (mm)	125
WBC (/mm3)	4900
Neutrophils (%)	64.4
Lymphocytes (%)	25.7
Monocyte (%)	8.3
Platelet (/mm3)	291000
RBC (Mil/mm3)	2.93
Hemoglobin (g/dl)	9.5
Hematocrit (%)	27.8
MCV (fL)	94.9
MCH (pg)	32.4
MCHC (g/dL)	34.2
RDW_CV (%)	14.8
Blood sugar (mg/dl)	81
Blood urea nitrogen(mg/dl)	30
Creatinine(mg/dl)	1.2
ALT (U/l)	12
AST (U/l)	13
ALP (U/l)	110
Lactate dehydrogenase (U/l)	248
Rheumatoid factor (RF) (IU/ML)	60
LDH (mg/dl)	268

Abbreviations: ESR: Erythrocyte sedimentation rate, WBC: White Blood Cell, RBC: Red Blood Cell, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin concentration, RDW: Red Cell Distribution Width, ALT: Alanine transaminase, AST: Aspartate transaminase, ALP: Alkaline phosphatase LDH: lactate dehydrogenase.

some tender purplish lesions **(Figure 5 & Table 2)**.

Her physical examination revealed several purplish patches located on the dorsal side of her left hand, ventral side of both feet and some erythematous nodules on her trunk **(Figures 3-4)**. There were deformities in her feet due to RA and tenderness of her both wrists. There was no family history of rheumatoid, hematologic or skin diseases. Punch biopsies were performed on her feet and trunk lesions. There were three major different diagnoses for her skin biopsy: KS, vasculitis, and metastasis. Based on further pathological studies and immunohistochemistry (IHC) studies, KS was ascertained. Histopathologic examination of the skin biopsy revealed proliferation of vascular channels and spindle cells in dermis. Scattered groups of perivascular lymphocytes and plasma cells are also present. The stromal spindle cells showed positive staining for antibody against HHV8 latent nuclear antigen 1 by immunohistochemistry. As a result, KS diagnosis was ascertained **(Figure 6-8)**.

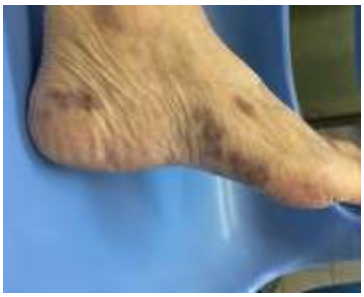

Figure 4 Erythematous purple red patches on both legs.

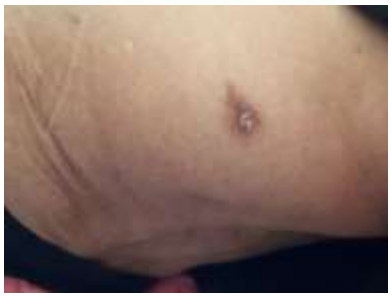

Figure 5 Purplish patch of trunk the arrow places the biopsy.

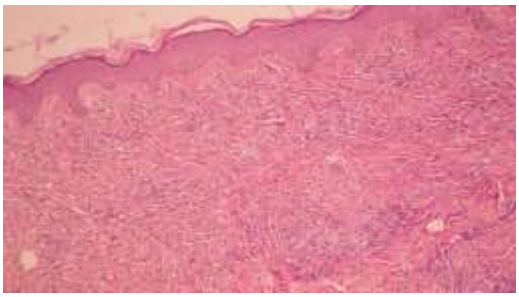

Figure 6 Vascular spaces and spindle shaped cells are seen in dermis. (×100), the inset shows more detail (×400).

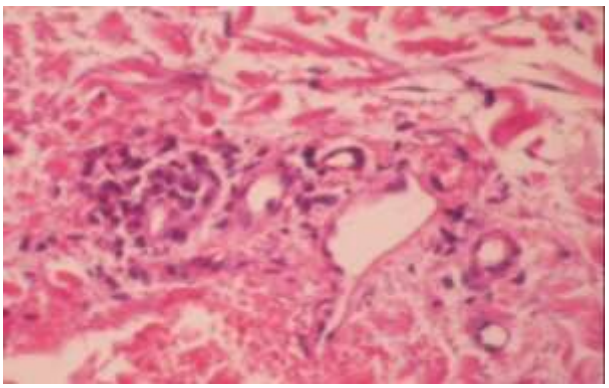

Figure 7 Lymphocytes and plasma cells are present in the stroma adjacent to a vessel (H&E , ×400).

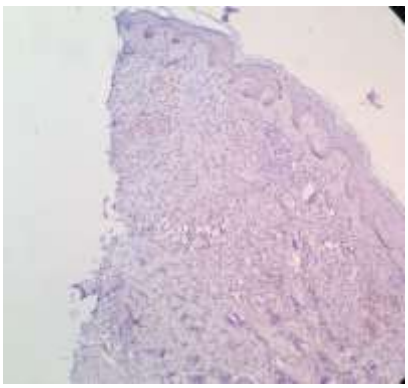

Figure 8 Stromal spindle cells stain with antybody to HHV8 latent nuclear antigen 1 (LNA_1)(×100).

Table 2 Laboratory findings after skin lesions development

Biochemical Test	*Values*
ESR (mm)	140
WBC (/mm3)	4070
Neutrophils (%)	63.4
Lymphocytes (%)	24.5
Monocyte (%)	8.1
Platelet (/mm3)	301000
RBC (Mil/mm3)	4.77
Hemoglobin (g/dl)	13.4
Hematocrit (%)	38.4
MCV (fL)	80.5
MCH (pg)	28.1
MCHC (g/dL)	34.9
RDW_CV (%)	10.8
Blood sugar (mg/dl)	93
Blood urea nitrogen (mg/dl)	28
Creatinine (mg/dl)	1.1

Abbreviations: ESR: Erythrocyte sedimentation rate, WBC: White Blood Cell, RBC: Red Blood Cell, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin concentration, RDW: Red Cell Distribution Width

Discussion

We reported a rare association of KS, RA and MM. Our patient had been under treatment for RA for 10 years and recently diagnosed with MM and KS. Former studies have indicated an increased risk of developing malignancies such as melanoma, non-Hodgkin's lymphoma, and lung cancer among RA patients treated with methotrexate,[3] but our patient developed MM. Studies in Finland indicate a higher chance of developing MM in RA patients and that such higher chance could be due to immunosuppressive therapies for RA.[4] Sekiguchi and colleagues also report a case of Epstein-Barr virus-positive multiple myeloma in an immunosuppressed RA patient.[5] These results and cases are similar to our case that was immunosuppressed with corticosteroid and methotrexate. Furthermore, laboratory tests of patient indicated negative results for HIV Ab and as a result her KS development can be

determined due to RA immunosuppressive therapies. It should also be noted that KS is mostly associated with Kaposi's sarcoma herpesvirus/human herpesvirus 8 (KSHV/HHV-8) infections.[6] The correlation between KS and human herpes virus 8 has been documented,[7] but as Sadeghian and colleagues reported in their systematic review, no documented correlation was reported between MM and human herpesvirus 8,[8] and the presence of MM and positive results for human herpesvirus 8 could be a coincidence. Association of KS and RA is reported in different literature[6,9] and mainly, the use of corticosteroids is accused as the cause of KS development. Recently, Olivo and colleagues[10] reported a case of KS in a patient with RA, treated with abatacept, a biologic agent, targeting specific T-cell costimulation. Similar to our case, most of KS cases which developed in RA patients were in those under treatments with immunosuppressive drugs. The prognosis of KS following corticosteroid treatments is unpredictable. Bergler-Czop and colleagues[6] reported a case of KS in an immunosuppressed RA patient. They also report that half of iatrogenic KS cases ameliorate after discontinuation of corticosteroids, but the other half face progression. There was also a case report of association of KS and MM reported by Cohen and colleagues.[11] As mentioned above, MM can occur in patients with RA who are treated with immunosuppressive drugs[4] and also KS can occur in RA patients as a result of corticosteroid treatments[9] but so far, the presence of RA, MM and KS has not been reported except in our study which is the first reported case of association of RA, MM and KS. Such association is rare and the cause is thought to be immunosuppression. Therefore, we suggest that any suspicious skin lesion in RA or immunosuppressed patients should be followed by skin biopsy.

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