Kaposi's sarcoma in a patient with psoriasis vulgaris

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SUMMARY

A 54-year-old woman presented with angiomatous lesions located on the upper extremities and right cruris. Histopathological findings were typical of Kaposi's sarcoma (KS). She had had mild to moderate psoriasis since she was 25 years old. She had been using cilazapril (an angiotensin-converting enzyme inhibitor) for the last 9 months. She had had similar lesions in the past while taking the same medication. Because our patient's KS lesions had developed during treatment with cilazapril, the drug was stopped. One month later, spontaneous regression of KS nodules was noted and after 4 months no KS lesions were seen.

KEY WORDS

Kaposi's sarcoma, psoriasis vulgaris, angiotensin-converting enzyme inhibitor, cilazapril

Introduction

We report a case of Kaposi's sarcoma (KS) possibly caused by cilazapril, which is an angiotensin-converting enzyme (ACE) inhibitor associated with psoriasis. In addition to its rare association between psoriasis and KS, this case is unusual because of the possible role of cilazapril in causing the KS.

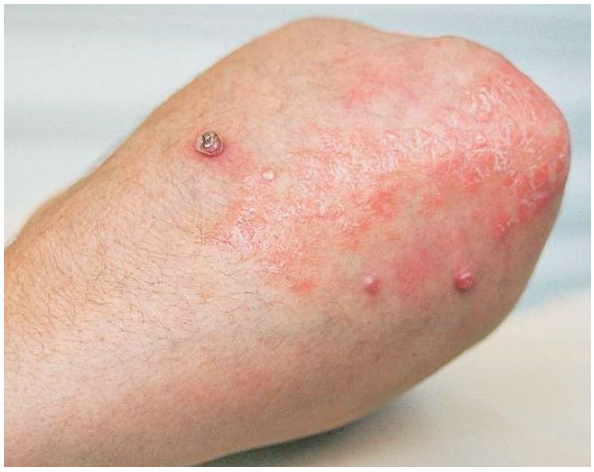
Case report

A 54-year-old woman presented with a 7-month history of seven nodular angiomatous lesions, 0.5 to 1 cm in diameter, and located on the upper extremities and right cruris (Fig. 1 a–b).

Two years earlier, she had had two similar lesions on her legs. Those lesions were completely excised at that time and their pathologic examination showed KS. Anti-HIV antibody and HIV antigen tests were found to be negative. She had had no new lesions throughout the 1 year, 5 month time period until her referral to our clinic.

The patient has had mild-to-moderate psoriasis since she was 25 years old. Psoriatic plaques were present on the extremities, localized to the knees and elbows, and a few guttate lesions were present on the trunk. She had previously been treated with topical corticosteroids and emollients, but had never taken systemic treatment. She had been using only moisturizers for the last 4 to 5 years. Her mouth and nail examination was normal and she had no problems with her joints.

The patient had essential hypertension and had been treated for 10 years with various antihypertensive drugs, mostly amlodipine besylate (a calcium channel blocker) and rarely carvedilol (an α-β blocker)



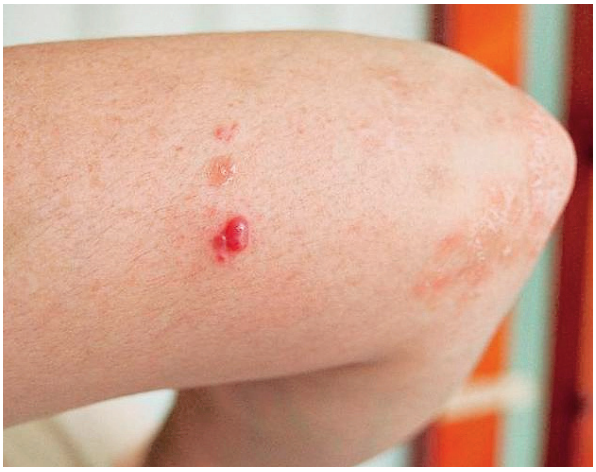


Figure 1 (a–b). Violaceous angiomatous nodules localized to the upper extremities

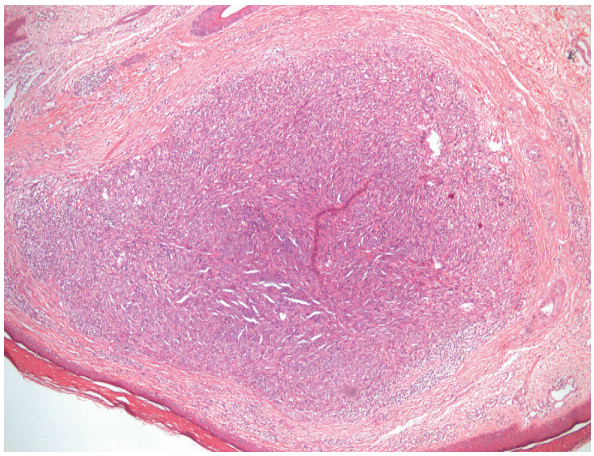


Figure 2. Tumoral nodular infiltration consisting of fusiform cells in dermis (HE 40×)

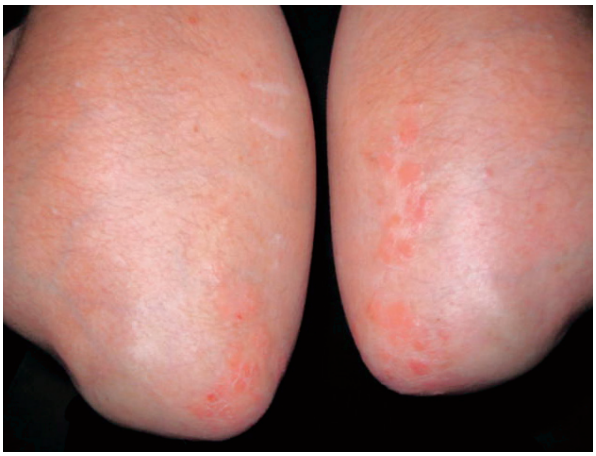


Figure 3. Desquamated erythematous plaques localized to the elbows; no KS lesions; 3 years after cessation of cilazapril

and cilazapril (an ACE inhibitor). She had been using cilazapril 5 mg/day for the last 9 months. She was taking no other medications.

A biopsy specimen was taken from the new angiomatous lesions. Histopathological findings were typical of KS (Fig 2). No fever, fatigue, anorexia, or lymphadenopathy was associated with the disease. Testing for anti-HIV antibody was done again and it was negative. The laboratory findings, including a blood chemistry, urinalysis, erythrocyte sedimentation rate, and full blood count, were normal. Testing for blood in the stool was negative. The thorax computed tomography and abdominal ultrasonography tests were normal. Human herpesvirus-8 (HHV-8) DNA sequences were detected in blood samples and KS tissue specimens using PCR.

When reviewing her previous treatments, we found out that the patient had had similar lesions 2 years earlier while taking cilazapril, and, thereafter, she no lesions while taking amlodipine besylate. Since our patient's KS lesions developed during treatment with cilazapril, the drug was stopped. One month later, spontaneous regression in the number and sizes of the KS nodules was noted and after 4 months no KS lesions were seen. The patient was informed about the relationship between her KS and cilazapril. She was seen just before this report was written and at that point she had been free of lesions for 3 years (Fig 3).

Discussion

KS is a multifocal endothelial proliferation predominantly involving the skin and other organs. There are currently four recognized clinical subsets of KS: classic, endemic, iatrogenic, and human immunodeficiency virus (HIV) related. The hypothesis now gain-

ing acceptance is that all forms of KS have a common etiology in human herpesvirus-8 (HHV-8) infection. However, HHV-8 infection alone is not sufficient for the development of KS, and additional cofactors—genetic, immunological, and environmental—are required elements (1).

In its early stage, KS is assumed to be a reactive disease characterized by the production of Th-1 type inflammatory cytokines that trigger reactivation of the HHV-8 infection, activation of endothelial cells, spindle cell formation, and the induction of angiogenesis. Disease progression requires deficient immune control of viral escape mechanisms (2).

In our patient, HHV-8 DNA sequences were detected in the blood and tissue. She had no history of immunosuppressive treatment, no malignancies, and was in a good, healthy condition. Simultaneous occurrence of psoriasis and secondary iatrogenic KS is very rare. KS has been reported in a few psoriasis patients who received methotrexate and corticosteroids (3, 4), but our patient had never taken systemic treatment, and she had been using only moisturizers for the last 4 to 5 years. Consequently, our patient was not at increased risk for KS. It is interesting that the lesions had begun during cilazapril treatment and disappeared after it was stopped, and that her history showed that she had had similar lesions in the past while taking the same medication. On account of these findings, the possibility of a cilazapril-induced form of KS was raised.

To our knowledge, this is the fourth such case reported in the literature, in which an ACE inhibitor could be a trigger mechanism leading to the development of KS. KS lesions in the other 3 cases (captopril in two cases and lisinopril in one case) also regressed after the ACE inhibitor was stopped (5–7).

There are some controversial reports that ACE inhibitors could lead to the development of KS. In Yasar's case of a patient with renal failure on hemodialysis, KS lesions had developed during treatment with captopril, but showed no evidence of regression after withdrawal of the drug (8).

In Vogt and Frey's case, captopril was reported to inhibit angiogenesis in KS, leading to a disappearance or regression of the lesions (9).

ACE inhibitors, in addition to their well-known beneficial effects in hypertension, have immmunomodulatory effects. The immunomodulatory action of ACE inhibitors has been attributed to several mechanisms including antiproliferative activity, inhibition of free radicals, inhibition of metalloproteases, and elevation of immunomodulatory prostaglandins. The ability of ACE inhibitors to inhibit the production of IL-12 is also well documented and IL-12 plays an essential role in cell-mediated immune reactions and stimulates the development of T-helper type 1 immune responses. Therefore suppression of IL-12 may contribute to the immunomodulatory effect of ACE inhibitors (10). Suppression of ACE itself may explain immune alteration (possible immunosuppression) because ACE has been shown to be involved in immune function and to be elevated in inflammatory conditions (10).

We believe that the possible immunosuppressive effects of cilazapril, immune alteration due to psoriasis, along with the presence of HHV-8, may have contributed to the pathogenesis of KS in our case.

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