CASE REPORT

Localized cutaneous sclerodermoid changes secondary to human cytomegalovirus infection: An uncommon presentation in an immunocompetent host

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INTRODUCTION

Human cytomegalovirus (CMV) serology is positive in nearly two-thirds of individuals in the United States, but cutaneous manifestations of infection are exceedingly rare.[1-4] To our knowledge, few cases of CMV-induced cutaneous manifestations have been reported and most commonly occur in immunocompromised populations. Here we report a case of localized sclerodermoid skin changes in an immunocompetent patient with CMV infection.

Abbreviations used:

CMV: cytomegalovirus
PCR: polymerase chain reaction

CASE REPORT

A 27-year-old incarcerated African-American man with history of polysubstance abuse was transferred to a university medical center for pancytopenia workup with 5 weeks of fevers and abdominal pain. He was previously healthy and was previously treated with nonsteroidal anti-inflammatory drugs while in prison, which caused acute renal failure requiring intermittent hemodialysis before transfer. Fevers continued, and the patient noted approximately 2 weeks of asymmetric polyarthralgias with extreme suprapatellar tenderness and tightness bilaterally and an identical 2-day history involving the right lateral upper extremity. Examination found mildly hyperpigmented, tender, indurated suprapatellar and right lateral upper extremity dermal plaques (Fig 1). Review of systems was otherwise unremarkable with pertinent negatives including absence of weight loss, cough, dysphagia, heartburn, and numbness/pain in distal extremities when exposed to cold.

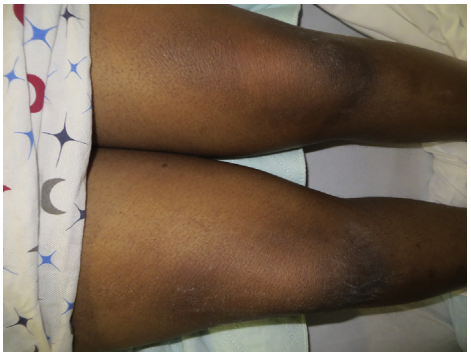

Fig 1. Hyperpigmented, tender, indurated suprapatellar dermal plaques on bilateral lower extremities.

On admission, the patient was pancytopenic with a white blood cell count of 4.66 K/μL, hemoglobin of 7.8 g/dL, hematocrit of 24.2%, and platelet count of 138 K/μL. An extensive rheumatologic, hematologic/oncologic, and infectious workup was positive for CMV by blood specimen allele-specific quantitative polymerase chain reaction (PCR) and an elevated erythrocyte sedimentation rate (37 mm/h) and C-reactive protein level (2.78 mg/dL). CMV by PCR

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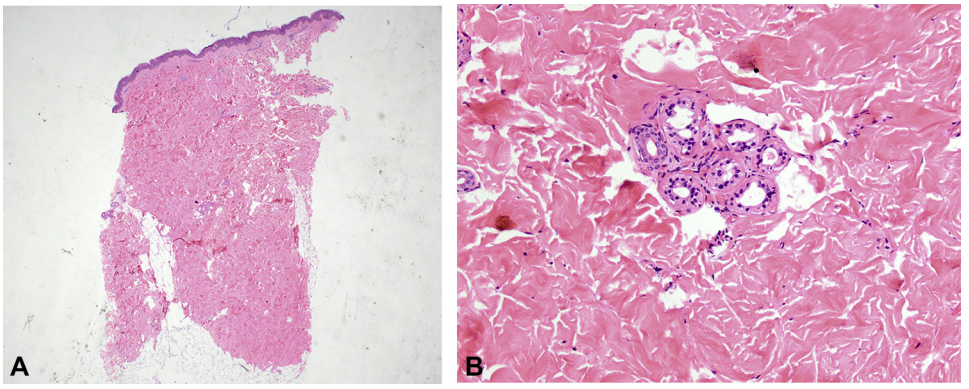

Fig 2. A, Sclerotic collagen bundles without evidence of granulomatous inflammation. **B**, Sclerotic collagen bundles with evidence of perivascular infiltration. (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A**, ×2; **B**, ×40.)

was retested and found to be positive a second time with nonreactive CMV IgM and reactive CMV IgG antibodies. Results of serologic testing for HIV, hepatitis B, hepatitis C, syphilis, Epstein-Barr virus, human T-cell lymphotropic virus, tick-borne illness, and parasitic infection were negative. Results for antinuclear antibodies and anti-Smith, anti—double stranded DNA, anticentromere, anti—SCL 70, anticyclic citrullinated peptide, and antineutrophil cytoplasmic antibodies were all negative. Immunoglobulins and C3 and C4 levels were within normal limits, and genetic testing by PCR for BCR-ABL and JAK2 V617F mutations were negative for chronic myelogenous leukemia and myeloproliferative disorders, including polycythemia vera, essential thrombocytopenia, and myelofibrosis. An angiotensin-converting enzyme level was mildly elevated, a chest radiograph was unremarkable, and chest/abdomen/pelvis computed tomography with contrast demonstrated mild mediastinal, axillary, inguinal, and external iliac lymphadenopathy, likely explained by active CMV infection.

A skin punch biopsy was performed at the right upper extremity dermal plaque. Hematoxylin-eosin staining found sclerosing dermatitis suggestive of localized sclerodermoid change (Fig 2, *A* and *B*). The upper dermis showed a sparse superficial lymphocytic infiltrate with few melanophages, but no evidence of granulomatous inflammation suggestive of cutaneous sarcoid or panniculitis was found (Fig 2, *A* and *B*). Immunoperoxidase staining of the specimen for CMV was negative. CMV PCR of the skin was not performed, as the positive serologic testing combined with the previously described sclerosis and perivascular infiltration were considered confirmatory.

Bone marrow biopsy found a normocytic, normochromic anemia with moderately hypocellular marrow (20% to 30%) and a universal decrease in hematopoiesis, which was nonsuggestive of a neoplastic or myelofibrotic process but rather favored infectious versus inflammatory etiology.

The patient started intravenous ganciclovir as an inpatient and transitioned to valganciclovir, 900 mg by mouth twice daily for 2 weeks as an outpatient. Follow-up 2 weeks postdischarge found complete resolution of the skin-related pain, while the hyperpigmentation and indurated plaques remained.

DISCUSSION

Cutaneous manifestations of CMV infection are uncommon but have been reported with wide variability as ulcers, purpura, nodules, maculopapular eruptions, necrotic papules, verrucous plaques, petechiae, pustules, and localized sclerodermoid change, as in this case report.[4-6] The association between CMV infection and the immunocompromised host has been clearly documented in the literature, and it is understood that the presence of CMV-induced cutaneous pathology portends a poor prognosis with mortality rates studied up to 85% within 6 months.[4,5,7,8] In immunocompetent individuals, case reports show an association between CMV infection and onset of cutaneous and systemic scleroderma in addition to the presentations above.[6,9]

CMV was initially low on our list of differential diagnoses because of our patient's immunocompetence.[2,8] Myelofibrosis, leukemia, and sarcoidosis were early considerations ruled out by peripheral blood smear as well as bone marrow and dermal plaque biopsies. Systemic sclerosis was eliminated from consideration because of a lack of systemic findings and negative antibody titers.

CMV is known to incite vascular pathology, which likely contributed to the localized skin findings in our patient. Previous studies indicate that CMV

interacts with proteins involved with the development of scleroderma, specifically human CMV late protein UL94 and NAG-2, which has been associated with sclerodermoid skin changes.[9-11] CMV also induces transforming growth factor beta to upregulate profibroblastic cytokines and increases tumor necrosis factor signaling pathway activity, thereby upregulating vascular endothelial growth, adhesion molecule function, vascular endothelial apoptosis, and fibroblast activity.[9,10]

Clinically significant CMV infections may arise in both immunocompromised and immunocompetent populations with variable cutaneous manifestations. Our report highlights a rare case of CMV-induced proximal extremity sclerodermoid skin changes in an immunocompetent host without signs of systemic sclerosis. Detailed history taking may be particularly helpful in elucidating this diagnosis, as with our patient, whose risk for contracting CMV and other immunocompromising conditions is increased because of incarceration. Nevertheless, antiviral treatment resulted in complete resolution of pain-related skin symptoms, although the dermal plaques remain.

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