- Image 11: *J Am Acad Dermatol.* 2011;65(1):1-12.

An Unusual Rash, a False alarm, and The Truth : CREST syndrome

Rusudan Tchigvaria, M.D. PGY-3, Baha Fayoumi M.D. PGY-3 Emad Hammode M.D.

Canyon Vista Medical Center-Midwestern University

Introduction

CREST syndrome—limited cutaneous systemic sclerosis (lcSSc)—is a subtype of systemic sclerosis (SSc) defined by **calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia**. Compared with diffuse cutaneous SSc, CREST shows more localized skin involvement but remains associated with **pulmonary arterial hypertension, calcinosis, and pulmonary fibrosis**.

Pathogenesis involves an **initial vascular insult**, platelet activation, and dysregulated thrombotic/fibrinolytic pathways, which trigger endothelial injury, autoimmunity, and progressive fibrosis. Early presentations (e.g., digital ischemia or painful rashes) can mimic infectious or vascular processes, delaying recognition

Literature review

False-positive HIV tests, particularly with 4th generation Ag/Ab combo assays, can occur in patients with autoimmune diseases, leading to significant clinical and psychosocial consequences. As illustrated in "Severe Lupus Flare in Disguise," a young woman in her 30s with fatigue, oral thrush, and a positive HIV Ag/Ab test was later diagnosed with systemic lupus erythematosus after confirmatory PCR was negative and an elevated ANA titer was identified.

A large study by Lin et al. demonstrated that false-positive HIV screens, though rare (~0.10% of samples), are more common with advancing age and can occur in the context of diverse underlying medical conditions, emphasizing the need for confirmatory testing and careful clinical evaluation rather than immediate clinical labeling.

Molecular mimicry, as described by Muta and Yamano, underlies this cross-reactivity, where the P24 HIV antigen shares epitopes with autoimmune antibodies, resulting in false-positive HIV screening. Autoimmune diseases cause chronic immune activation and B cell stimulation, leading to the production of non-specific antibodies. These antibodies can cross-react with HCV antigens in serological assays, resulting in false-positive HCV antibody tests.

Conclusion and Recommendations

This case highlights the diagnostic challenges of systemic sclerosis presenting with cellulitis-like features and false-positive HIV/HCV tests, emphasizing the need for thorough investigation and early recognition to ensure appropriate treatment. In atypical populations, such as elderly men, who fall outside the typical demographic profile of middle-aged women that the presentation may be overlooked or misattributed. Thus, recognition often relies on autoantibody testing (ANA, anticentromere antibodies) in the context of unexplained vascular or ischemic changes, underscoring the need for a broad differential and high clinical suspicion.

We recommend to maintain a broad differential, consider autoimmune testing in patients with atypical presentations, and confirm infectious disease screenings to avoid misdiagnosis.

Case Report

A **74-year-old man** with hypertension and a seizure disorder initially presented with progressive weakness and a **painful bilateral lower extremity rash**. Vital signs revealed mild tachycardia. Laboratory values: WBC 11.7 (neutrophilic), Na 126, and Cr 1.7 (from baseline 1.4). Working diagnoses included cellulitis, AKI, and hyponatremia. He received IV fluids and HCTZ was discontinued, improving renal function and sodium. **Augmentin** was started empirically, though vasculitis was considered.

Screening revealed **reactive HIV and HCV serologies**, but confirmatory testing was pending. The rash resolved, and the patient was discharged with follow-up. Post-discharge, **HIV and HCV confirmatory tests were negative**.

He returned days later with **confusion and bilateral second-digit pain**, showing **cyanosis, ulceration, and swelling**. Arterial ultrasound excluded peripheral arterial disease. Autoimmune workup revealed **positive ANA and anticentromere antibodies (>8)**, with all other autoantibodies negative—confirming **limited systemic sclerosis (CREST syndrome)**

Test	Result	Comment
Anti-centromere B abs	>8.0	High
Antichromatin Abs	0.7	Normal
Antiproteinase 3 Abs (PR3)	<0.2	Normal
Atypical pANCA	<1:20	Normal
Cytoplasmic (C-ANCA)	<1:20	Normal
Perinuclear (P-ANCA)	<1:20	Normal
Anti-DNA Ab Qn	<1	Normal
Anti-Jo-1	<0.2	Normal
Antiscleroderma-70 Abs	<0.2	Normal
RNP Abs	<0.2	Normal
Smith Abs	<0.2	Normal
antimyeloperoxide Abs	<0.2	Normal
Sjogrens Anti-SS A/B	<0.2	Normal
Antinuclear Abs (ANA) direct	Positive	Positive

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