CREST syndrome

CREST syndrome

doi: 10.61997/bjm.v15i2.501

Vitorino Modesto dos Santos[1], Kin Modesto Sugai[2], Rafael Campos Nunes[3]

Dear Editor

Systemic sclerosis (SSc) is a chronic autoimmune entity affecting the skin and internal organs with microvascular dysfunction, autoimmune dysregulation, and the uncontrolled fibroblast activation, causing skin and organ fibrosis; environmental factors (silica, solvent, ketones, and epoxy resins), and infectious agents (B19, cytomegalovirus, human herpesvirus 6, and Epstein-Barr virus) have been involved.[1-8]

We read in this journal with special interest the case study by Moralez OD et al.[5] about CREST syndrome, besides the very early diagnosis of systemic sclerosis (VEDOSS). The patient was a 42-year-old woman with inflammatory arthralgias in the hands, feet, and shoulders controlled by the non-steroidal anti-inflammatory drugs for three years. [5] She evolved with alopecia, Raynaud's phenomenon, skin thickening in extremities and trunk, marked weight loss, dysphagia for solid foods, anorexia, and significant asthenia. The routine laboratory exams revealed mild anemia, elevated inflammatory markers, a strongly positive anti-Scl-70 antibody (>200 U/mL) consistent with active SSc, positive ANA (1:160) with a homogeneous pattern, besides normal renal and liver functions.[5] She used mycophenolate mofetil until a maximum dose of 1.5gr BID; after 2 months without improvement, Rituximab was used (500mg IV STAT and every 6 months). Additional treatment included: Irbesartan (150mg PO QD), Sildenafil (20mg PO QD), Atorvastatin (10mg PO QD), Etoricoxib (90mg PO QD, PRN), Nifedipine (20mg PO BID), Esomeprazole (40mg PO QD), besides Vitamin D3 (100,000 IU, PO monthly). The authors highlighted the major role of individualized management and close care.[5] In this scenario, the aim is to present additional comments on novel literature data.[1-4,6-8]

[1]MD, PhD. Department of Medicine, Armed Forces Hospital and Catholic University of Brasília-DF, Brazil. ORCID: https://orcid.org/0000-0002-7033-6074. Correspondence: vitorinomodesto@gmail.com

[2]Postgraduate Course of Management, Technology, and Information Security. University of Brasília-DF, Brazil. ORCID: https://orcid.org/0000-0002-3777-0178

[3]Computer Science BSc Undergraduate. University of Brasília-DF, Brazil. ORCID: https://orcid.org/0000-0003-3769-6171

A 55-year-old man with previously known CREST syndrome was admitted presenting a severe epigastric pain radiating to the back and high lipase serum levels, besides CT images indicative of necrotizing pancreatitis.[1] He was clinically managed and with reintroduction of oral intake, showing a rapid clinical improvement and was discharged in a stable condition. The authors drew attention to the early recognition of some possible, although very rare, gastrointestinal or pancreatic complications of CREST syndrome due to vascular damage, immune dysregulation, or organ fibrosis.[1] Clinicians must maintain a high index of suspicion for atypical presentations of pancreatitis in the autoimmune patients, mainly when routine etiologies are excluded.[1] An 80-year-old woman with previous diagnosis of CREST syndrome in the past few months also experienced progressively worsening symptoms of severe dysphagia, heartburn, nausea, vomiting, abdominal pain, diarrhea, and fecal incontinence.[2] Laboratory results: positive ANA (1:1280) with an anti-centromere pattern, whereas the anti-double-stranded DNA (1:160) and the rheumatoid factor (36 IU) were positive.[2] She persisted presenting with minimal diuresis, and her respiratory symptoms did not improve, further necessitating the scheduled hemodialysis, which she did not accepted. Moreover, both the patient and her family finally decided to have a hospice care transition, based on the comfort and dignity, leading to the patient's peaceful passing.[2] It's very rare to have late-onset SLE, but there are also cases of overlap syndromes, and it would be necessary to rule out SLE according to the new ACR/ EULAR guidelines.

A 48-year-old woman with CREST syndrome presented progressive ischemia in all the extremities that caused the spontaneous auto-amputation of multiple fingers and toes.[3] The ANA and anti-Scl 70 antibody evaluations were positive, and the CT angiography revealed the obstruction of multifocal peripheral arteries; she was initially managed with nifedipine, along with aspirin and pentoxifylline, without success, and underwent some digit amputations before being submitted to the immunomodulatory therapy. Postoperatively, she was started on low-dose corticosteroids and methotrexate under rheumatology monitoring that revealed the stabilization without further progression.[3] The authors emphasized the

Creative Common License 4.0 (CC BY-NC)

seriousness of vascular complications in CREST syndrome; prompt diagnosis and treatment are necessary to avoid irreversible ischemic damages.[3] It would have been good if a capillaroscopy was also done on the patient. Moreover, this patient would benefit as well with prostacyclin analogues or endothelin receptor antagonists. A 54-year-old woman with progressive dyspnea, leg swelling, perioral puckering, telangiectasia, calcinosis, and sclerodactyly was diagnosed with the CREST syndrome.[4] As the echocardiography study suggested pulmonary arterial hypertension (PAH) and the tests showed positive antinuclear and anticentromere antibodies, she was referred to rheumatology and cardiology care for mycophenolate mofetil use and the PAH control.[4] The PAH medications may include endothelin receptor antagonists (ambrisentan, bosentan), PDE5 inhibitors (sildenafil), or Prostacyclin analogues (treprostinil), more indicated for cases with advanced disease.[4]

The authors emphasized the major diagnostic challenges of CREST syndrome and the importance of accurate clinical assessment, imaging studies, and antibody testing for early diagnosis confirmation, rapid multidisciplinary intervention, and good outcomes.[4] A 56-year-old woman had intermittent matinal hematemesis for eight months, on an empty stomach, and a weight loss of about 4 kg during this period; she presented with skin pallor, restricted mouth opening, dry skin with calcinosis and also sclerodactyly.[6] Laboratory tests revealed microcytic hypochromic anemia, positive ANA (1:640) with a centromere pattern, and the anticentromere antibody levels were significantly elevated. Telangiectasias in small blood vessels can develop in the stomach and esophagus of patients with CREST and may constitute a cause of bleeding, but the data are scarce.[6] The authors highlighted that endoscopy was unavailable due to the resource-limited medical center, and clinical acumen and autoimmune tests played a role in diagnosis.[6] A 44-year-old woman had a recent onset of Raynaud's phenomenon, sclerodactyly, esophageal disorder, telangiectasia, ANA (>1:1280), and anti-centromere antibodies.[7] One year later, she presented with calcinosis as a painful mass on her right foot, which characterized the rare, rapidly progressive, and complete manifestation of the CREST; following a referral of the patient to the podiatry care, the lesion was surgically excised. The authors emphasized the mean delay of over five years from the onset of Raynaud's phenomenon to the first other symptom in the female patients with CREST syndrome.[7] This atypical presentation with the full spectrum of diagnostic criteria within one year of initial evaluation highlights the role played by the early diagnosis, multidisciplinary management, and careful attention to the health of people with autoimmune diseases.[7] A 62-year-old woman with Raynaud's phenomenon for a decade presented with xerostomia, dysphagia, and multiple subcutaneous calcifications, and the laboratory determinations showed positive ANA (1:80) and negative anti-centromere antibodies.[8] Chest CT images revealed interstitial lung disease (ILD), and the radiographs of the right elbow, pelvis, and right femur showed multiple patchy soft tissue calcifications. With the diagnosis of CREST syndrome complicated by ILD, she underwent the treatment with prednisone, cyclophosphamide, and hydroxychloroquine sulfate.[8] Within two weeks of treatment, the response was optimal; both Raynaud's phenomenon and xerostomia improved, and three months later, the subcutaneous nodules had shrunk.

In conclusion, the single case reports of uncommon conditions may contribute to enhancing the clinical suspicion, early diagnosis, and prompt effective control.

REFERENCES

1. Al Hazzouri A, Attieh P, Ghaleb G, Khalil A, Chamchoum N, Karam K, et al. Necrotising pancreatitis in a patient with CREST syndrome: a rare autoimmune gastrointestinal complication. Eur J Case Rep Intern Med. 2025; 12(11):005812. https://doi.org/10.12890/2025_005812
2. Arbabi M, Garg B, Saghari S, Patel P. Gastrointestinal complications of systemic sclerosis: a case report. Cureus. 2025; 17(6):e86844. https://doi.org/10.7759/cureus.86844
3. Kumari S, Henna F, Alam U, Khattak F, Kamil KA. Beyond Raynaud's: atypical peripheral vascular manifestations in a case of CREST syndrome. Clin Case Rep. 2026; 14(1):e71815. https://doi.org/10.1002/ccr3.71815
4. Nahar NU, Lopez P, Ahmed F, Adegeye Y, Stanley F. Echoes of scleroderma: a case report unmasking CREST (Calcinosis, Raynaud's phenomenon, Oesophageal dysmotility, Sclerodactyly, and Telangiectasia) syndrome with point-of-care ultrasound in acute medicine. Cureus. 2025; 17(10):e95671. https://doi.org/10.7759/cureus.95671
5. Moralez OD, Hernández Guifarro FD. CREST syndrome: a patient with very early diagnosis of systemic sclerosis. (VEDOSS). Belize J Med. 2026; 15(1):1-6. https://doi.org/10.61997/bjm.v15i1.494
6. Ravikumar J, Sai Prudhvi T. Gastrointestinal hemorrhage in CREST syndrome: a case report. Cureus. 2025;17(6):e85978. https://doi.org/10.7759/cureus.85978
7. Schock GA, Simon D, Weitzman E, Weitzman R. An atypical case of CREST syndrome with early complete clinical manifestation. Cureus. 2025;17(6):e86500. https://doi.org/10.7759/cureus.86500
8. Xu L, Wu J, Liang S, Lu Y, Qin Y, Zhang C, et al. Medusas petrifying gaze: severe, diffused and refractory calcinosis from a patient with ACA-negative CREST syndrome. Rheumatol Immunol Res. 2025;6(2):114-116. https://doi.org/10.1515/rir-2025-0015

Creative Common License 4.0 (CC BY-NC)

Funding sources
This work did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration on the use of artificial intelligence
The authors declare that no artificial intelligence tools were used in the writing, analysis, or preparation of this manuscript.

Declarations of interest
None to disclaim.

Authorship
Vitorino Modesto dos Santos, Kin Modesto Sugai, and Rafael Campos Nunes made equally substantial contributions to: 1) the conception and design of the study, acquisition of data, and analysis and interpretation of data; 2) the drafting the article and revising it critically for important intellectual content; and 3) the final approval of the version to be submitted.

Received: March 6, 2026
Accepted: April 1, 2026

Creative Common License 4.0 (CC BY-NC)