

## CLINICAL VIGNETTE

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# COVID-19 Infection Induced Raynaud's Syndrome

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### **Abstract**

COVID-19 represents a global health challenge that world's health authorities have been struggling to control. As of 6th of September 2020 there were nearly 27 million laboratory confirmed infection of SARS-COV2 and more than 900,000 deaths.<sup>1</sup> Typical symptoms include: fever, anosmia, fatigue, myalgia, diarrhea, headache, cough and sometimes pneumonia which represent the most common cause of mortality. There is consensus that in severe COVID-19 infection, an exaggerated systemic inflammatory response occurs, associated with increased serum levels of inflammatory markers, including Erythrocyte Sedimentation Rate (ESR), C-reactive protein (CRP), ferritin, D-dimer, and IL-6 (among other interleukins). This may result in cytokine storm that usually correlate with acute respiratory syndrome associated with the severe form of the infection.<sup>2</sup> This hyperinflammatory response is observed in both ICU and non-ICU patients. Inflammatory markers were found to be higher in ICU patients of all ages. Several autoimmune conditions associated with COVID-19 infection have been reported with possible explanation of molecular mimicry between the virus and human proteins, which means the immune system reaction against the virus may cross-react with body proteins that share peptide sequences with SARS-COV-2 leading to autoimmune pathologic sequelae.<sup>3</sup> We report a case of 50-year-old female who developed Raynaud's syndrome following recent infection with SARS-COV2.

### **Case Presentation**

A 50-year-old female without remarkable past medical history presented with 10 days of constant hands violaceous discoloration most noticeable on distal phalanxes of both hands. This was triggered by physical activity and cold exposure. The patient initially developed skin discoloration over the proximal phalanx of her fingers, often pruritic, erythematous, and later painful with burning sensation on distal phalanxes associated with violaceous discoloration and edema. The patient works as a clerk has no prior history of Raynaud phenomenon, acrocyanosis, chilblains, photosensitivity, carpal tunnel syndrome, hypothyroidism, osteoarthritis, skin disorders, neurological conditions, autoimmune or rheumatological diseases. She has unremarkable family history and was not taking any regular medications. Physical exam was remarkable for cyanosis in-

volving the distal phalanxes of all fingers with livedo reticularis on both palms. She had no joint pain but reported possible exposure to SARS-COV-2 virus at work with upper respiratory symptoms one week prior to developing her hand symptoms. The symptoms included mild sore throat, non-productive cough, and low-grade fever. Nasopharyngeal PCR confirmed infection with SARS-COV-2 virus. Additional testing included normal prothrombin time, activated partial thromboplastin time, and thrombin time; D-dimer, comprehensive metabolic panel and thyroid function. CBC with differential showed lymphopenia which is often reported in COVID-19 patients and she had elevated inflammatory markers, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and ferritin. Doppler upper extremity imaging was consistent with Reynaud's. She was instructed to avoid cold exposure, sudden temperature changes, and to use hand emollient and avoid repetitive trauma. She reported no improvement and was started on Nifedipine 30 mg once daily and completely resolved her symptoms.

### **Discussion**

This patient's presenting symptoms, clinical exam and Doppler demonstrating decreased flow and a high velocity biphasic waveform on distal palmer arteries and palmer digital arteries were consistent with Raynaud's phenomenon. The timing suggests it was Raynaud's Syndrome secondary to COVID-19 that triggered the presentation, in the absence of personal or family history of Raynaud's phenomenon. However, the fixed discoloration is considered atypical. Other rheumatological conditions in the differential diagnoses include scleroderma. However, the lack of typical scleroderma cutaneous changes, esophageal dysmotility or respiratory involvement do not meet 2012 ACR/EULAR criteria.<sup>4</sup> Chilblain may cause pruritic discolored lesions in association with Raynaud's phenomenon, however, the patients skin lesions were not typical of Chilblain's lesions.<sup>5</sup> Cutaneous lesions associated with COVID-19 induced vasculitis have been recently reported including Chilblain but in this case, the imaging suggested Raynaud rather than Chilblain. Other differential diagnoses include: Osteoarthritis of small hand joints, Carpal tunnel syndrome and polyneuropathy, however, patient presentation and vascular imaging supported Raynaud's syndrome, not to

mention patient's symptoms complete resolution upon trial of calcium channel blocker. We believe this is the first report of Raynaud's syndrome triggered by infection with SARS-COV-2. It is unknown if the condition will recur. This case raises the possibility of delayed immune mediated reaction related to SARS-COV-2 in genetically predisposed patients. Raynaud's phenomenon has been triggered by other viral infections including Parvovirus B19<sup>6</sup>. COVID-19 related hyperinflammation and associated cytokines storm has been widely reported.<sup>2,3</sup> More studies are needed to clarify the association between COVID-19, autoimmunity and connective tissue disease.

## REFERENCES

1. **World Health Organization.** Coronavirus disease 2019 (COVID-19) weekly epidemiological update: 7 September 2020. [https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200907-weekly-epi-update-4.pdf?sfvrsn=f5f607ee\\_2\\_](https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200907-weekly-epi-update-4.pdf?sfvrsn=f5f607ee_2_)
2. **García LF.** Immune Response, Inflammation, and the Clinical Spectrum of COVID-19. *Front Immunol.* 2020 Jun 16;11:1441. doi: 10.3389/fimmu.2020.01441. PMID: 32612615; PMCID: PMC7308593.
3. **Ehrenfeld M, Tincani A, Andreoli L, Cattalini M, Greenbaum A, Kanduc D, Alijotas-Reig J, Zinserling V, Semenova N, Amital H, Shoenfeld Y.** Covid-19 and autoimmunity. *Autoimmun Rev.* 2020 Aug;19(8):102597. doi: 10.1016/j.autrev.2020.102597. Epub 2020 Jun 11. PMID: 32535093; PMCID: PMC7289100.
4. **van den Hoogen F, Khanna D, Fransen J, Johnson SR, Baron M, Tyndall A, Matucci-Cerinic M, Naden RP, Medsger TA Jr, Carreira PE, Riemekasten G, Clements PJ, Denton CP, Distler O, Allanore Y, Furst DE, Gabrielli A, Mayes MD, van Laar JM, Seibold JR, Czirjak L, Steen VD, Inanc M, Kowal-Bielecka O, Müller-Ladner U, Valentini G, Veale DJ, Vonk MC, Walker UA, Chung L, Collier DH, Csuka ME, Fessler BJ, Guiducci S, Herrick A, Hsu VM, Jimenez S, Kahaleh B, Merkel PA, Sierakowski S, Silver RM, Simms RW, Varga J, Pope JE.** 2013 classification criteria for systemic sclerosis: an American College of Rheumatology/European League against Rheumatism collaborative initiative. *Arthritis Rheum.* 2013 Nov;65(11):2737-47. doi: 10.1002/art.38098. Epub 2013 Oct 3. PMID: 24122180; PMCID: PMC3930146.
5. **Shima T, Yamamoto Y, Kanazawa N, Murata KY, Ito H, Kondo T, Yuan J, Hashiguchi A, Takashima H, Furukawa F.** Repeated hyperhidrosis and chilblain-like swelling with ulceration of the fingers and toes in hereditary sensory and autonomic neuropathy type II. *J Dermatol.* 2018 Nov;45(11):e308-e309. doi: 10.1111/1346-8138.14336. Epub 2018 Apr 27. PMID: 29701257.
6. **Harel L, Straussberg R, Rudich H, Cohen AH, Amir J.** Raynaud's phenomenon as a manifestation of parvovirus B19 infection: case reports and review of parvovirus B19 rheumatic and vasculitic syndromes. *Clin Infect Dis.* 2000 Mar;30(3):500-3. doi: 10.1086/313712. PMID: 10722434.