International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2024: 7.101

An Interesting Case of Long Covid Vasculitis

Atluri Venkata Abhinav[1], Rajeswari Sankaralingam[2], Sudagar Singh[3], Divya Yanamadala[4], Nidhi Prabhu[5]

[1]Senior Resident, Department of Rheumatology, SRIHER
Corresponding Author Email: *abhiatluri2703[at]gmail.com*

[2]Professor & HOD, Department of Rheumatology, SRIHER

[3]Professor and Medical Director, Department of General Medicine, SRIHER

[4]DM Rheumatology Resident, Department of Rheumatology, SRIHER

[5]DM Rheumatology Resident, Department of Rheumatology, SRIHER

Abstract: ***SARS-CoV-2 virus was first identified in 2019 and affected approximately 775 million people worldwide[1]. COVID-19 can cause many complications, and one of the rarest and least known is large vessel vasculitis involving the aorta and myocardium. Few cases are reported with aortitis, but involvement of the myocardium is very rare. The pathophysiological observations in post-COVID-19 vasculitis have been studied[2], and certain observations have been made. SARS-CoV-2 infects the host organs, including the lung, heart, kidney, and intestine, using the angiotensin-converting enzyme 2 (ACE2) receptor. These ACE2 receptors are expressed in endothelial cells, as known by previous COVID-19 studies. Aortic endothelium, largely provided with angiotensin-converting enzyme-2 receptors, is directly attacked by virions, leading to an endotheliitis that could later be complicated by hypersensitive vasculitis.***

Keywords: COVID-19 vasculitis, large vessel vasculitis, post-COVID complications, ACE2 receptor pathology, myocardial aortitis

1. Case Report

A 77-year-old female presented to our hospital in September 2022 with complaints of fever for 10 days, severe myalgia, weight loss of 5 kg in 6 months, and decreased appetite with no other localizing signs of infection. She had recently recovered from COVID-19 in May 2022. There was no history of COVID-19 vaccination or past history of any other comorbid conditions. There was a probable contact with history of tuberculosis in her husband who recently succumbed. On examination, tachycardia and tachypnea were noted with otherwise normal general and systemic examinations. Hence, a provisional diagnosis of respiratory infection following post-COVID-19 state was made.

Laboratory parameters showed Hb 8.0 gm/dl, ESR 139 mm/hr, CRP 26.3 mg/dl, serum pro-calcitonin 2.7 ng/ml, serum iron 33, serum ferritin 748, serum albumin 2.4 mg/dl and vitamin D3 13.25 IU. Tropical panel for fever evaluation was negative. Urine and blood cultures were sterile. Sputum samples were analysed and tested negative for tuberculosis and other infections. Mantoux showed no induration and RT-PCR for covid-19 was negative. Chest X ray showed bilateral heterogeneous infiltrates in the lower zones. Ultrasonography of the abdomen was normal. High-resolution Computed Tomography of the thorax subtle ill-defined ground glass opacities in both lungs and bronchiectasis changes in right and left upper lobe. Bronchoscopy was done and AFB, CBNAAT for TB, gram stain and bacterial cultures were sterile. Cytology was reported negative for malignancy. Later MGIT culture showed no growth.In view of high ESR, CRP, fever history, weight loss. The possibility of vasculitis/ underlying malignancy was entertained. PET CT was done which showed increased FDG uptake along walls of the right atrium, left ventricle, ascending aorta, and origin of great vessels suggestive of vasculitis. Carotid artery doppler showed common carotid wall artery thickening around 1.4 mm, and temporal artery doppler showed no significant abnormality. IL 6 and IgG4 were abnormal with values 98.58 and 2.31 respectively. ANCA and ANA by LIA 17 were negative.

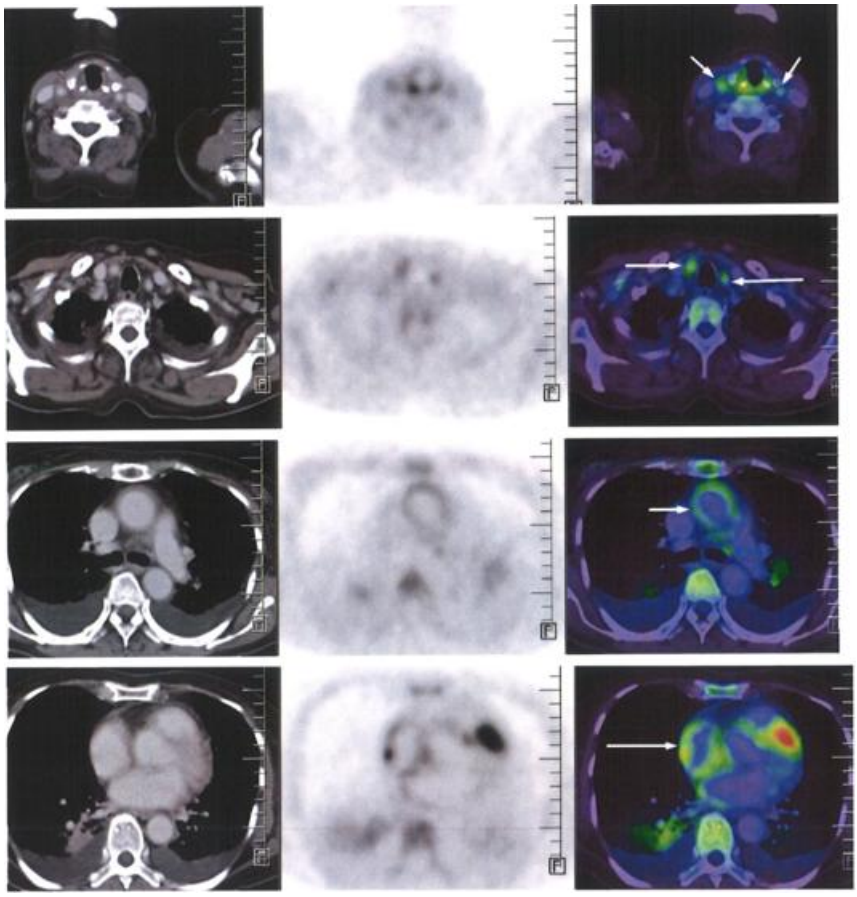

Figure 1: PET CT showing Increased FDG uptake along the walls of right atrium, interatrial septum, left ventricle, ascending aorta, origin of great vessels from the aorta and bilateral common carotid arteries.

Treatment Given:
The patient was given steroids in the dose of 1 mg/kg body weight The patient improved dramatically and became afebrile. However, she was lost to followup.

2. Discussion

This case highlights a complex presentation in a 77-year-old lady with acute complaints of fever, weight loss, and myalgia, with a past history of COVID-19. The possibility of epidimeologically relevant acute infections were ruled out. Additionally aerobic blood cultures were sterile. Tuberculosis and malignancy were initially suspected, considering her age and contact history with her husband. Mantoux, sputum, BAL samples for AFB ,GeneXpert and MGIT culture for tuberculosis were negative. Cytology for malignant cells was negative. The markedly elevated ESR and CRP levels, combined with systemic symptoms and PET-CT[3,4] findings of increased FDG uptake in large vessels (as shown in Fig. 1), pointed towards an inflammatory or autoimmune process involving large vessels.

The two most common large vessel vasculitides are Giant cell arteritis(GCA)[5,6] and Takayasu arteritis[7,8]. Cranial GCA was unlikely as there was no headache, or other relevant neurological deficit, and MRI brain was normal. Temporal artery ultrasonography with Doppler was normal, and therefore a biopsy was not done. Carotid artery Doppler showed common carotid artery wall thickening with an increased intimal medial thickness around 1.4 mm respectively but there were no features of stenosis. The pattern of involvement of large vessels and myocardium in PET-CT[3,4] clearly was not suggestive of large vessel Giant cell arteritis, prompting the need to rule out other possibilities. The trigger for vasculitis was unknown at this point, so we proceeded with further evaluation and ruled out ANCA vasculitis[6], IgG4 disease[6] and syphilis[6] as relevant serology was negative and additionally the patient's clinical presentation was not suggestive of relapsing polychondritis[6], Cogan's syndrome[6] or Behcet's disease[6,9,10], precluding the need for further workup.

Involvement of the myocardium[11] and right atrial wall uptake was unusual and atypical in our case. The close differentials include Takayasu arteritis [11], Giant cell arteritis[12], sarcoidosis[6,13,14], Q fever[15], other vasculitidis like Polyarteritis nodosa and eosinophilic granulomatosis with polyangitis[16].

Takayasu arteritis[7,8,17] can be a rare cause of myocarditis related cardiac dysfunction and was studied in 139 takayasu patients [11] ,out of which only 2.8 percent reported to have myocarditis.Cardiovascular magnetic resonance (CMR) and FDG PET -CT[18] scans play a role in the diagnosis of myocarditis. In our case ,Takayasu arteritis was ruled out due to lack of history of claudication, asymmetric pulse, renal artery involvment and valvular involvment commonly aortic regurgitation.Sacroidosis[6,13,14] was ruled out as there was no evidence of AV block , arhythmias ,syncope , orthopnea and serum ACE levels were normal. No imaging findings suggestive of sarcoidosis were found. Myocarditis is a rare manifestation of acute Q fever caused by Coxiella

burnetii[15,19]. Similarly ,in our case, there was no history of exposure to live stock, cats, dogs or consumption of unpasteurized mild products. Electrocardiogram and echocardiogram findings were normal, and Q fever serology was negative. Eosinophilic granulomatosis with polyangitis (E-GPA) affects small and medium vessels . It can cause eosinophilic myocarditis also known as Loeffler myocarditis. However , in our case,there was no eosinophilia , sinusitis , hearing loss or other clinical features that would suggest E-GPA.

Giant cell arteritis ocassionally presents as myocarditis[12,20], most commonly manifesting as myocardial infarction , stroke , thoracic aortic aneurysm. In our case, CT thorax (as shown in Fig. 2) and the PET-CT[21] showed multiple ground-glass opacities suggesting an infective ethology. A few published case reports in the literature have mentioned the possibility of COVID-19 infection triggering large vessel vasculitis. The underlying pathophysiologic mechanism [2]involves a cytokine storm due to the release of mainly interleukin-1β, interleukin-6, and tumor necrosis factor (TNF)-alpha, resulting in endothelial dysfunction and damage. In our case serum IL-6 levels were high.

We reviewd three recently published case reports[22–24] on post covid large vessel vasculitis and compared the presentation and findings with our case .In the first case report [22], a 71 year old male with history of covid 19 two months prior presented with elevated inflammatory markers , a negative SARS-CoV-2 polymerase chain reaction and postive SARS-CoV-2 antibodies . CT thorax abdomen pelvis revealed inflammatory change surrounding the aortic arch extending all the way down the aorta in keeping with a florid inflammatory aortitis with no aneurysms. The patient responded well to steroids and repeat imaging showed resolution.

In the second case [25] published in 2023 , a 71 year old japanese man presented with persistent spiking fever and a productive cough showing bilateral ground glass opacties in CT thorax , elevated infllammatory markers turned out positive for SARS-CoV-2 polymerase chain reaction , Contrast-enhanced CT on day 8 showed increased contrast enhancement of the vessel wall, ranging from the abdominal aorta to the bilateral common iliac arteries and 18F-fluorodeoxyglucose positron emission tomography (18F-FDG PET/CT) showed elevated 18F-FDG uptake in the arterial wall with increased contrast enhancement. Treatment was given with only NSAIDS and repeat imaging features showed resolution of uptake.

In the third case [23] published in 2020 , a 71 year old male with a history of SARS-CoV-2 presented with cough , fever , dyspnea and diarrhoea . He later developed extreme fatigue , weight loss of 5 kg after 2 months,along with elevated inflammatory markers. Computed tomography (CT) thorax, abdomen, and pelvis demonstrated a diffuse inflammatory aortitis from the subclavian arteries to the iliac bifurcation. A nasopharygeal swab was negative for SARS-CoV-2 but positive IgG antibody serology proved recent infection. Patient was treated with steroids and subsequent CT scans showed resolution of uptake.

In contrast to our case ,all other cases had varied presentation in imaging and the timeline after covid 19 infection varied from simultaneous to 2 months later. All cases showed a good response to treatment with steroids. However, the involvment of myocardium , right atrium , interatrial septum , ascending aorta and common carotid arteries with increased IL-6 levels as seen in our case is the first reported case to the best of our knowledge.

3. Conclusion

Recently, many cases are being reported with vasculitis post-COVID-19. This case is a rare presentation with the involvement of myocardium and is reported to raise awareness among clinicians for early imaging and aggressive management with steroids that will benefit the patients.

Conflicts of Interest:
None

Funding:
None

Data Availability Statement:
Not applicable

Consent:
Ethical approval: Not required Consent: Written consent is obtained from the patient and is available on request

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