Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Autoimmunity Reviews 20 (2021) 102883

Contents lists available at ScienceDirect

Autoimmunity Reviews

journal homepage: www.elsevier.com/locate/autrev

Review

Rheumatological complications of Covid 19

Hannah Zacharias [a], Shirish Dubey [a,b,*], Gouri Koduri [c], David D'Cruz [d]

[a] Dept of Rheumatology, Oxford University Hospitals NHS FT, Windmill Road, Oxford OX3 7LD, UK
[b] Nuffield Department of Musculoskeletal Sciences, University of Oxford, Windmill Road, Oxford OX3 7LD, UK
[c] Dept of Rheumatology, Southend University Hospitals NHS FT, Prittlewell Chase, Southend-on-Sea SS0 0RY, UK
[d] Louise Coote Lupus Unit, Guy's Hospital, London SE1 9RT, UK

ARTICLE INFO

Keywords:
COVID-19
Chronic fatigue
Cytokine storm
Inflammatory arthritis
Long COVID
Systemic Lupus Erythematous
Vasculitis
Vasculopathy
Viral arthritis

ABSTRACT

Introduction: COVID-19 has caused unprecedented hardships in the 21st century with more than 150 million infections. Various immunological phenomena have been described during the course of the infection, and this infection has also triggered autoimmunity. Rheumatological illnesses have been described following resolution of the acute infection; hence we sought to conduct a review of the rheumatological complications of COVID-19.
Methods: We conducted a literature search for articles relating to sequelae of COVID-19 from Jan 2020 to 30th April 2021.
Results: We found a number of reports of inflammatory arthritis after SARS-CoV-2 infection. SLE and renal disease have been described, and vasculitis also appears to be a common complication. Rhabdomyolysis and myositis has also been reported in a number of patients. We also found some evidence of large vessel vasculitis in 'long COVID' patients.
Conclusions: This review highlights a number of important complications such as inflammatory arthritis, lupus-like disease, myostis and vasculitis following SARS-CoV-2 infection.

1. Introduction

COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a new illness first described in January 2020 characterised by fever, dry cough, interstitial pneumonia, fatigue, headache, loss of taste and smell [1]. While the majority of patients with COVID-19 have a favourable outcome, some develop severe pneumonia eventually leading to acute respiratory distress syndrome (ARDS) and respiratory failure [2]. This illness has been declared a pandemic and at the time of writing this article, the global caseload had crossed 150 million, with more than 3 million deaths [3]. Recent immunological studies have provided further evidence that massive production and release of pro-inflammatory cytokines is the crux of the "cytokine storm". This can result in a destructive immune response and can eventually lead to ARDS and multi-organ dysfunction syndrome (MODS) [4,5]. Cytokine storm is also the result of activation of coagulation pathways during the immune response to infection, which leads to an imbalance between pro- and -anticoagulant factors and results in micro thrombosis, disseminated intra vascular coagulation, and multiorgan failure [6]. It also leads to a number of autoimmune phenomena and molecular mimicry appears to be the underlying issue leading to autoimmunity [7].

This pandemic has taken a heavy toll on the healthcare system across the world with lockdowns in various countires. Recent vaccination programmes have offered hope, and several countries including Israel, United Kingdom and United States have led the way with vaccine delivery [8]. Patients with systemic inflammatory conditions and immunomodulatory therapies are generally considered to be more prone to infections and the initial concern was that these patients would develop a severe or even life-threatening course of COVID-19 infection. Evidence so far has not suggested a strikingly increased risk of infection [9–11].

The effects of SARS-CoV-2 on the immune system and cytokine profiles are still unclear. Several reports have been published describing the immunological alterations seen with COVID-19. These range from a maladaptive immune response and abnormal cytokine production, to hyperactivation of T cells and increased numbers of activated monocytes, macrophages and neutrophils, which may ultimately result in untoward consequences [12–14]. The emergence of several autoimmune/autoinflammatory phenomena has been described such as Guillian-Barré syndrome, immune thrombocytopenia, Miller Fischer syndrome and type 1 diabetes mellitus – see Table 1 for full details [15].

* Corresponding author at: Dept of Rheumatology, Oxford University Hospitals NHS FT, Windmill Road, Oxford OX3 7LD, UK.
E-mail addresses: Hannah.zacharias@ouh.nhs.uk (H. Zacharias), shirish.dubey@ouh.nhs.uk (S. Dubey), gouri.koduri@southend.nhs.uk (G. Koduri), david.d'cruz@kcl.ac.uk (D. D'Cruz).

https://doi.org/10.1016/j.autrev.2021.102883
Received 26 April 2021; Accepted 3 May 2021
Available online 5 July 2021

Table 1
List of autoimmune conditions described with COVID-19.

Autoimmune conditions described with COVID-19
Guillain-Barré syndrome
Miller Fisher Syndrome (MFS)
Antiphospholipid syndrome
Immune thrombocytopenic purpura
Evans syndrome
Systemic lupus erythematosus (SLE)
Kawasaki disease
Cold agglutinin disease & autoimmune haemolytic anaemia
Neuromyelitis optica
NMDA-receptor encephalitis
Myasthenia gravis
Myositis
Type I diabetes
Large vessel vasculitis
Medium vessel vasculitis
Small vessel vasculitis
Psoriasis
Subacute thyroiditis
Graves' disease
Sarcoidosis
Inflammatory arthritis

Rheumatological manifestations these include inflammatory arthritis (viral arthritis, reactive arthritis, chronic arthritis, rheumatoid arthritis), lupus like syndromes, vasculopathy (Kawasaki-like disease, chilblain lesions, vasculitis) and a chronic fatigue spectrum disorder.

In this narrative review, we describe the rheumatic manifestations during and after the illness as well as the pathophysiologic mechanisms of autoimmune problems which may enable these illnesses following COVID-19 infection.

2. Methods

Our objective was to narrate the rheumatic manifestations that are associated with or follow COVID-19 infection. We conducted a literature search for articles since the inception of the pandemic and published until 30th April 2021. We included original articles, reviews, viewpoints, commentaries, case series and case reports. The references and related citations for the resulting articles were also reviewed for inclusion.

The primary databases used to retrieve the medical literature presented in this review were PubMed, NCBI Lit COVID, MedRxiv, Embase and Medline.

The search terms, used both separately and in combination, included: "transmission," "COVID-19," "coronavirus," "SARS-CoV-2," "reactive", "viral", "arthritis, "ANCA", "vasculitis", "long haul", "long COVID" "chronic fatigue" (long COVID), "Lupus", "SLE" "Kawasaki", "Paediatric Inflammatory Multisystem Syndrome temporally related with COVID-19", "PIMS-TS", "Multisystem Inflammatory Syndrome in Children", "MIS-C", "rheumatic", "autoimmune", "musculoskeletal", "myositis", "scleroderma".

3. Results

We have divided the results into various sections for ease of understanding and based on pathological groupings. These include inflammatory arthritis, connective tissue disorders including SLE/lupus-like disease and myositis, renal disease and vasculitis.

3.1. Inflammatory arthritis

Viral infections can cause arthritis and the spectrum of symptoms can range from mild arthralgia to spurious and chronic arthritis [16]. Chronic arthritis has been reported in association with hepatitis C and several endemic alphaviruses such as Chikungunya, whereas self-limited arthritis can occur with parvovirus B19, rubella or hepatitis B virus. By contrast, coronaviruses seem to typically cause arthralgia and myalgia rather than a true inflammatory arthritis [1,17–21]. Arthralgia is reported in 15% of patients with COVID-19, and myalgia has been reported in 44% of patients [1,16]. Musculoskeletal symptoms, however, do not seem to be associated with COVID-19 severity [1]. Respiratory viral infections have also been associated with an increased number of cases of rheumatoid arthritis (RA) [20]. Our literature search revealed a few cases of reactive arthritis following SARS-CoV-2 infection alongside five cases of RA and two cases of seronegative spondyloarthropathy. These cases were in different age groups with varied disease courses, as well as presentations in the joints of the upper and lower extremities.

The first case involved a male patient in his 50s who was admitted with COVID-19 pneumonia. On day 21, he developed acute bilateral ankle arthritis with mild enthesitis in his right Achilles tendon, but without any other features of reactive arthritis [22]. The second case was a 73-year-old man who developed acute arthritis of the small joints of the hands and feet after 8 days of completion of COVID-19 treatment [23]. The third case was a 47-year-old man who presented with a three-day history of progressive right knee pain and swelling and pain in his glans penis. Investigations for HIV, syphilis, chlamydia, and gonorrhoea were negative as well as arthrocentesis [24]. A 65-year-old woman with HLA B27 positivity developed symmetrical arthritis of ankles, knees and wrists and a cutaneous vasculitis 10 days after resolution of all COVID-19-related symptoms [25]. Another patient developed inflammatory arthralgia with cyclic citrullinated peptide (CCP) antibodies which resolved with a short course of oral corticosteroids [26]. Furthermore, a 39-year-old Saudi Arabian woman, developed synovitis in the PIP and DIP joints, 2 weeks after recovery from COVID-19 infection [27]. Two cases of monoarthritis were also described after resolution of COVID-19. A report described a patient with elbow arthritis associated with psoriatic skin lesions with no previous history of dactylitis or arthritis [28] and another report described a patient with severe right wrist pain and swelling 2 weeks after COVID-19 [29]. A young healthy 16-year-old girl developed dactylitis of the left toes after 3 weeks of contracting COVID-19 which resolved with NSAIDs [30]. Yokogawa and colleagues described a man with knee arthritis occurring during COVID-19, resolving spontaneously, suspected to be a viral arthritis [31]. Langhoff Hønge et al. describe a case that presented with acute polyarthritis and fever a few days after discharge from hospital with COVID-19 and responded well to treatment as reactive arthritis [32].

Baimukhamedov et al. describe a case with new onset of RA with polyarticular presentation 3 weeks after diagnosis of COVID-19 initially with only rheumatoid factor positivity but subsequently also CCP positivity as well. This patient was treated with Methotrexate and corticosteroids [33]. Derksen et al. report 3 patients who developed seropositive RA on average 6.6 weeks after Covid-19 infection [34]. Another patient was reported by Roongta et al. who describe a 56 year old woman who developed seropositive RA with joint symptoms starting 2–3 weeks after recovery from Covid-19 [35]. To date there is only one paediatric case described in the literature; a 10-year-old boy presented with oligoarthritis, fever and urticaria [36].

The first case of Spondyloarthropathy triggered by SARS-CoV-2 infection was reported in a genetically predisposed (family history of psoriasis, HLA B27 negative) woman [37]. Another case was reported of a 53 year old man who developed inflammatory back pain with sacroilitis on MRI following asymptomatic COVID-19 infection [38]. A Spanish study noted that in their cohort of 306 patients with proven COVID-19, eighty-one (26.4%) complained of muscle and joint pains at presentation but only four (1.3%) developed acute arthritis during hospitalisation and all were proven crystal arthropathy [39].

Indeed, the majority of cases are in keeping with reactive arthritis generally developing between 1 and 3 weeks after the infection. Interestingly, the cases of RA reported from Holland were about 6 weeks after the infection [34]. The exact mechanisms for joint inflammation are not fully understood, however, SARS-CoV-2 infection leads to stimulation of

macrophages which in turn causes release of high levels of cytokines and chemokines which enhance the inflammatory process [40]. Molecular mimicry appears to play a major role in the pathogenesis [7]. Although viral infections are known to potentially induce reactive arthritis [41], viremia was documented in only 15% of cases of COVID-19 [42]. Interleukin 17 A has been involved in the pathogenesis of both reactive arthritis and spondyloarthritis in general [41] and also in the hyper inflammatory state of COVID-19 [43].

A plausible explanation for the lower incidence of musculoskeletal inflammation is corticosteroid based COVID-19 treatment which probably dampened the musculoskeletal manifestations. Overall, COVID-19 seems to present mild-to-moderate musculoskeletal symptoms, which are indistinguishable from those associated with other respiratory viruses, such as influenza infection.

3.2. Connective tissue disorders

SLE is a disease of immune dysregulation leading to multisystem inflammation. Genetic predisposition, environmental triggers, and the hormonal milieu contribute to disease development and activity [44,45]. COVID-19 infection causes a dysregulated cytokine response with high resultant expression of pro-inflammatory cytokines, such as IL-1, IL-6, and TNF-alpha, which in turn could potentially be exacerbated by the shift in Th1 to Th2 response seen in SLE. It is commonly recognised that SLE, antiphospholipid syndrome (APS) and antiphospholipid antibodies (aPL) can be triggered by viral illnesses [46–48]. There are a small number of cases of Systemic Lupus Erythematous (SLE) that have been reported in association with COVID-19 [49–53] (Table 2). All these patients responded well to immunosuppression except the first patient in this series who died.

There are several reports of the association of COVID-19 with antiphospholipid antibodies (aPL) and thrombosis [54–56]. It remains to be determined whether aPL are associated with an autoimmune rheumatic disease, or they indicate a viral-induced secondary APS [57]. These antibodies can also arise transiently in patients with critical illness and infectious diseases through molecular mimicry between bacteria or viruses and beta2-glycoprotein-1, hence the importance of repeat testing at 12 weeks which is part of the APS classification criteria. It is also important to note that increasing age, immunosenescence and the presence of atherosclerosis are factors contributing to the development of aPL [58]. The significance of aPL in COVID-19 patients remains to be clarified. Recent reports of very rare venous sinus thrombosis and

Table 2
Cases of SLE with Covid 19 - their clinical, laboratory features and management.

Author	Age	Sex	COVID symptoms	Testing	Timing of symptoms	SLE symptoms	SLE serology	Treatment
Cardoso et al. [49]	18	F	Cough, shortness of breath, fever Malaise	SARS- Cov-2 PCR positive	1 month	Pericardial tamponade ARDS DVT	ANA (1:2560) dsDNA 943 LAC +, aPL +, B2GP1 positive Low C3/C4	Pulsed methylprednisolone, Azathioprine, Hydroxychloroquine, ECMO, plasmapheresis (discontinued when PCR positive) Tocilizumab (COVID protocol)
Slimani et al. [50]	23	F	Fever, fatigue, dry cough, dyspnoea Bilateral pulmonary infiltrates Erythematous papules on trunk (negative DIF)	RT-PCR Nasopharyngeal swab	13 days		Lymphopenia, elevated PT and APTT, ANA, dsDNA antibodies, triple positive aPL antibodies Low C3/C4 levels, positive direct Coombs test and proteinuria (0.7 g/24 h)	Methylprednisolone
El Aoud et al. [51]	62	M	Fever, cough, myalgia	Positive nasopharyngeal swab	17 days	Shortness of breath, AKI, confusion,	Lymphopenia, AKI, proteinuria, ANA 1:160, negative dsDNA, normal complement	Methylprednisolone, Tocilizumab, Corticosteroids
Hali et al. [52]	25	F	Fever, myalgia, asthenia Bilateral pulmonary infiltrates	RT PCR Nasopharyngeal swab	15 days	Diffuse maculopapular exanthema (palmar-plantar), periorbital edema infiltrated purpuric lesions of lower limbs, multiple labial and palatal erosions Mitral insufficiency without pericardial effusion	Anaemia, neutropenia and lymphopenia. Positive ANA, and dsDNA, low complement levels, Proteinuria *MAS Day 19* Ferritinemia, hypofibrinemia, LDH 510, high liver enzymes, hypertriglyceridemia Skin biopsy – leucocytoclastic vasculitis	Methylprednisolone
Gracia-Ramos et al. [53]	45	M	Fever, dry cough, myalgia, arthralgia	RT PCR Nasopharyngeal swab	21 days	Bilateral pleural effusion, ascites, splenomegaly, and renal failure (proteinuria and hematuria)	Severe thrombocytopenia, anaemia, prolonged APTT and elevated fibrinogen ANA 1:1280, ds DNA 23 IU/mL, positive anti-SSA and anti-SSB, low complement	Pulsed methylprednisolone Chloroquine IV immunoglobulin Rituximab Splenectomy

Acronyms: AKI - acute kidney injury, ANA - Anti-nuclear antibody, ANCA - Anti-neutrophil cytoplasmic antibodies, aPL - Antiphospholipid antibody, APPT - Activated partial thromboplastin time, ARDS - Acute respiratory distress syndrome, B2GP1 – Beta-2-Glycoprotein 1, C3/C4 - complements C3 and C4, DIF - Direct immunofluorescence, DVT - Deep vein thrombosis, ECMO - extracorporal membrane oxygenation, LAC - Lupus Anticoagulant, LDH - Lactate dehydrogenase, PCR - Polymerase chain reaction, PT - prothrombin time.

venous thromboembolic events related to COVID-19 vaccinations lend support to the concept that these events are due to immune mediated thrombosis linked to the vaccine [59,60]. These reports clearly need further study, but also open up new possibilities of pathogenesis of thromboembolic phenomena with COVID-19.

Whilst the cases of SLE published at this time fulfil classification criteria, it remains unclear with this small volume of reports as to whether this is a transient phenomenon and what the longer term outcomes are. Lymphopenia is a major immunological abnormality in severe COVID-19, and is strongly associated with increased mortality rates [61,62]. Lymphopenia is a haematological component in the ACR/EULAR criteria for classification of SLE and was reported in all four case reports although it is not possible to distinguish this from a viral cause.

There are 2 case reports where SLE developed after SARS-CoV-2 infection [63,64]. These cases fulfil the classification criteria for SLE, and have needed treatment with immunosuppression. The first is an 85 year old woman with positive SARS-CoV-2 antibodies, but unknown primary infection presenting with digital infarction, thrombocytopenia, pleural effusion, proteinuria and low complement. The second report is of a 35 year old man who had COVID-19 2 months prior to presentation with fever, rash and proteinuria with ANA, dsDNA, Ro and La antibodies. Renal biopsy showed class 1 lupus nephritis. The pathophysiology of severe COVID-19 mimics the B cell responses seen in SLE [65] and there is a possibility – so far unproven, that patients with COVID-19 will be more at risk of developing SLE in the future.

A number of patients with COVID-19 have myalgia, and MDA5 (melanoma differentiation association protein 5) antibodies are also found in a number of patients [40]. There are a number of reports of rhabdomyolysis, presumably secondary to viral myositis [66,67]. Beydon et al. reported myositis in one of their patients with good response to corticosteroids [68]. Mehan et al. reported that out of 641 patients in their centre, 9 patients had spinal MRI and 7 of these showed features consistent with myositis [69]. Shabbir et al. report a patient who developed myopericarditis and myositis as presenting feature of COVID-19, and responded well to Prednisolone, Colchicine and Ibuprofen [70]. Almadani et al. report a patient who presented with compartment syndrome secondary to viral myositis [71]. A case of unilateral orbital myositis has also been reported [72]. Sacchi et al. report a 77 year old woman who developed myositis with Anti-Ku and anti-MI-2β antibodies 2 weeks after being admitted with COVID-19 and having negative ANA on admission which had risen to 1:320 at the time of diagnosis of myositis. This patient was treated with high dose corticosteroids and responded well [73]. Zhang et al. report a 58 year old woman who presented with weakness and high muscle enzymes and gradually worsened and also developed bulbar weakness. She was found to have Ku, anti–SAE 1 IgG and anti–SS-A antibodies and was treated with IV Methyl prednisolone with good response [74].

Lokineni et al. describe a patient who developed autoimmune necrotising myopathy about 3 months after COVID-19 infection and this was treated with Prednisolone and Azathioprine [75]. Tawfeeq et al. report 2 cases of calcific myositis as a complication of COVID-19 induced viral myositis with creatinine kinase values more than 10 times the upper limit of normal in both cases associated with peak of inflammation. The first case is a 62 year old manual worker who was ventilated for COVID-19 and developed viral myositis but this was then complicated by calcific myositis with significant impairment of shoulder movements. The second case was similar with prolonged prone ventilation and high muscle enzymes initially complicated later by calcific myositis visible on X-rays [76].

Renal involvement is well documented in COVID-19; with acute kidney injury, proteinuria, haematuria [77,78] as well as acute proximal tubular injury and severe endothelial injury at autopsy [79]. Rare cases of glomerulonephritis in patients with COVID-19 have also been described [80]. In addition to direct virus mediated injury, kidney involvement with a COVID-19 infection could be due to systemic hypoxia, hypercoagulability, microangiopathy, rhabdomyolysis, sepsis, cytokine storm, and angiotensin II pathway activation [81].

In the patient described by Cardoso et al. again there is an overlap between findings consistent with SLE and COVID-19, such as myopericarditis and pulmonary compromise [49]. Pericardial effusion is common in SLE (10–54%) [82], while it is rare in COVID-19 [83]. Cardiac tamponade is uncommon but reported in both conditions [84–87]. COVID-19 viral myopericarditis is increasingly being recognised and cardiac MRI is helpful in documenting these changes [88]. A recent study by Zhou et al. showed that autoimmune phenomena exist in some patients with COVID-19. Among 20 subjects with critical COVID-19, the authors report a prevalence of between 20% and 50% of autoimmune disease related autoantibodies [89].

There are limited reports of SLE type illnesses associated with COVID-19 and currently the co-presentation may represent coincidence. Myositis is rare, although myalgia is common and there are limited reports of COVID-19 triggering autoimmune myositis. COVID-19 patients are complex, often with multiorgan involvement; close follow-up becomes imperative if autoimmune phenomena have been triggered. Longer term follow-up data are needed to understand the progression towards a chronic SLE type and chronic myositis type conditions.

3.3. Vasculitis

A series of publications have reported the development of a vasculitis-like illness in COVID-19 patients, with presentations ranging from vasculitis syndromes [90] to histologic findings of vasculitis seen on postmortem examination [91]. Histologic evidence of COVID-19 induced vasculitis has also been reported in several organs including the lung, liver, kidney, or skin [92,93]. Manenti et al. describe pathophysiologic observations in small/medium sized arteries in COVID-19; first is an acute endotheliitis, followed by *peri*−/pan-arteritis with deposition of polyclonal antigen-antibody immune complexes, suggesting a type III hypersensitive acute vasculitis [94,95]. Many of the predisposing comorbid conditions for COVID-19, including advanced age, diabetes mellitus, hypertension and obesity are also associated with vascular dysfunction and altered endothelial cell metabolism [96]. There is growing recognition that states of heightened innate immune response and a prothrombotic state elicited by innate immune mediators such as that seen in COVID-19 lead to an escalating cascade of inflammatory pathways that promote profound micro and macrovascular EC dysfunction and damage, with impairment of other important functions of the endothelium [97].

3.3.1. Cutaneous manifestations

The spectrum of dermatological manifestations has been well documented and Casas et al. have classified the dermatological manifestations of COVID- 19 as acral areas of erythema with vesicles or pustules (pseudo-chilblain) (19%), other vesicular eruptions (9%), urticarial lesions (19%), maculopapular eruptions (47%) and livedo or necrosis (6%) [98]. COVID-19 toes/pseudo-chilblains are reported predominantly in children and young adults and appear to be a relatively late feature of COVID-19 [99–101]. Livedo or necrosis, with lesions suggesting occlusive vascular disease usually affects people with more severe COVID-19 with no association with the duration of infection. A French retrospective study suggested that chilblains are common sequelae of COVID-19 and are associated with microthrombi on biopsy [102].

There are case reports documenting the presence of COVID-19 with cutaneous vasculitis - severe respiratory failure with ARDS developed in a patient with lower limb vasculitic purpura [103,104], a bullous haemorrhagic rash that progressed to necrotic lesions with histopathology confirmed vasculitis of small- and medium-sized cutaneous vessels [105], purple palpable papules and haemorrhagic blisters characterised histologically as leucocytoclastic vasculitis [106], and cutaneous vasculitic lesions and gangrene [107]. Camprodon Gómez et al. [108] and Mayor-Ibarguren [105] both described patients with leucocytoclastic

vasculitis with positive SARS-CoV-2 PCR in skin biopsies with positive serum IgM and IgG against SARS-CoV-2 but negative oropharyngeal swab PCR. This could indicate that leucocytoclastic vasculitis develops as a late manifestation of COVID-19 infection.

3.3.2. Central nervous system (CNS) involvement

Oxley et al. reported 5 cases of stroke involving large vessels in under-50s reported with COVID-19 [109]. However, Varatharaj et al. report a UK wide surveillance study in which 125 patients presented with a cerebrovascular event, of whom only one (1%) had CNS vasculitis [110]. Hanafi et al. report CNS vasculitis as a complication of COVID-19 in a patient who had extensive cerebral small-vessel ischemic lesions resembling cerebral vasculitis in a characteristic combined imaging pattern of ischemia, haemorrhage, and punctuate postcontrast enhancement with a characteristic lower extremity skin rash [111].

De Sousa et al. reported a 28-year-old male (SARS-CoV-2 IgM positive) presenting with intense headache, dysarthria and deviation of lip having MRI findings of cerebral vasculitis [112]. Bilateral trochlear nerve palsy due to cerebral vasculitis related to COVID-19 infection presenting with headache is also reported [113]. Dixon et al. have also reported a case of stroke secondary to CNS vasculitis from Covid-19 with good response to Tocilizumab [114].

These cases lend support to the suspected mechanism of "endotheliitis" associated with this novel coronavirus. It is presumed that SARS-CoV-2 infects vascular endothelial cells and causes inflammation through angiotensin converting enzyme inhibitor 2 (ACE2) expressed in vascular endothelial cells. The expression of the ACE2 receptor in neurons and cerebral endothelial cells indicates a high level of invasiveness for the SARS-CoV-2 in comparison with other coronaviruses [115]. Activation of the vascular endothelium is likely to lead to development of vasculitis with another insult or injury for other types of vasculitis as well.

3.3.3. Large vessel vasculitis (LVV)

Inflammation of aorta has been described but attributed to infection with SARS-CoV-2 rather than vasculitis [94]. A reported case of large vessel vasculitis diagnosed on PET CT with associated Covid pneumonia presents the same dilemma [116]. Another case has been reported as LVV but with spontaneous resolution suggesting an infectious aortitis [117]. There is an inherent difficulty in differentiating 'infectious aortitis' from autoimmune vasculitis during an acute infection, the challenges of performing (due to risk of spread of infection) and interpreting PET CT contributes further to this problem. However, LVV could be a complication of COVID-19 – an Italian study on patients with persistent symptoms after recovery from COVID-19 (so called long COVID) demonstrated 6/10 patients with large vessel vasculitis seen on PET CT imaging [118]. The smooth linear pattern seen in the aorta of these patients could not be differentiated from the similar patterns in patients with large vessel vasculitis. The ascending aorta, arch of aorta, descending aorta and ilio-femorals were the common arteries showing increased uptake in these patients.

3.3.4. Small vessel vasculitis

Hussein et al. report a case of granulomatosis with polyangiitis with proteinase 3 antibodies that presented with alveolar haemorrhage associated with a 4-day history of COVID-19 infection. This patient was treated and recovered with pulse intravenous corticosteroids, plasmapheresis and intravenous immunoglobulin [119]. She was not given further immunosuppression because of coexisting COVID-19. Although acute tubular injury is the most common kidney pathology seen with SARS-CoV-2 infection, ANCA-associated glomerulonephritis can be associated with COVID-19. Uppal et al. report 2 cases of pauci immune GN (one MPO, one PR3) with SARS-CoV-2 infection, who clinically improved with treatment of COVID-19 and immunosuppressants (methylprednisolone/Rituximab) [120]. A further case report of c-ANCA positive crescentic GN with alveolar haemorrhage is also reported [121]. Bressler et al. report a 46 year old man who developed renal involvement as part of AAV concomitant with COVID-19 and was treated with corticosteroids and Rituximab [122]. Weston et al. report a 12 year old girl with likely previous asymptomatic infection with SARS-CoV-2 who developed biopsy proven vasculitis associated with myeloperoxidase antibodies and needing aggressive management through corticosteroids, Rituximab and Cyclophosphamide [123]. A case of bowel perforation secondary to gut vasculitis has been reported [124] and another who eventually died following bowel inflammation and perforation [125]. Another case with medium vessel vasculitis was not given any treatment and resolved spontaneously highlighting the challenges around management of these patients [126].

Both MPO and PR3 associated vasculitis can lead to pauci-immune GN and there is evidence that neutrophil extracellular traps (NETs) serve as a source of autoantigens presenting MPO and PR3 to the immune system. The presence of NETs has been observed on kidney biopsy samples of patients with AAV [127] and is postulated to be involved in COVID-19 pathogenesis. Immunosuppression is the mainstay of ANCA associated vasculitis (AAV) treatment and if left untreated, mortality is high. The patients who developed ANCA associated glomerulonephritis in association with COVID-19 responded well to immunosuppressive agents including rituximab, and none had deterioration of SARS-CoV-2 – related disease. There is limited knowledge on the outcomes of COVID-19 in patients commenced on Cyclophosphamide and Rituximab for treatment of vasculitis but emerging reports of COVID-19 patients who had been receiving rituximab for their underlying immune-mediated conditions have demonstrated no worse course or outcome compared with those in the general population, with some suggestion that rituximab may affect the cytokine storm seen in COVID-19 and may improve outcomes [128,129]. Data from United Kingdom registry for vasculitis suggests that AAV patients and patients already on corticosteroids prior to developing COVID-19 have worse outcomes [130].

3.3.5. IgA vasculitis

Recently, four cases have highlighted SARS-CoV-2 as a trigger for IgA vasculitis, three of which had renal involvement [131–134]. Anti- SARS-CoV-2 IgA is the first immunoglobulin to be detected in COVID-19 as early as 2 days after onset [135]. In children with chilblain lesions, IgA antibodies to SARS-CoV-2 spike protein S1 domain are observed, suggesting that their immune response represents mucosal protection that lessens the likelihood of triggering an IgG response [136]. Furthermore, chilblain like lesions with possible vascular damage linked to COVID-19 infection with positive anti–COVID-19 serologic testing reveal IgA but no IgG antibodies in several patients [101].

Allez et al. report a patient who developed IgA vasculitis on a background of Crohn's disease treated with Adalimumab and suggest that disrupted intestinal barrier function may play a role in the development of IgA vasculitis [131,137]. Mucosal infections result in upregulation of IL-6 as in COVID-19, may trigger immune complexes containing galactose-deficient (Gd-)IgA1 and subsequent renal damage [138].

3.4. Kawasaki-like disease

Several studies have demonstrated that COVID-19 in children is a relatively mild disease [139]. However, recently a more serious condition characterised by systemic inflammation with clinical or microbiological evidence of exposure to SARS-CoV-2 has been reported [140]. This syndrome is now known as either "Pediatric Inflammatory Multisystem Syndrome temporally related with COVID-19" (PIMS-TS) [141], or Multisystem Inflammatory Syndrome in Children (MIS-C) [142,143] and is currently considered a rare post-COVID-19 complication which, in a minority of cases, can lead to death.

Kawasaki disease (KD) is an acute systemic inflammatory disease of medium- and small-sized vessels that mostly involves children under 5 years old with higher prevalences in Asian countries like Japan [143].

Verdoni et al. report a 30-fold increased incidence of Kawasaki-like disease after the spread of SARS-CoV-2 to Bergamo, Italy [144]. Researchers from France [145], United Kingdom [146], and the USA [141] also described clusters of children with systemic inflammatory disorders without an alternative diagnosis and with clinical or microbiological evidence of exposure to SARS-CoV-2. Interestingly the effect of COVID-19 on patients with KD in Japan seems to be small, Lio et al. revealed only one patient with PIMS-TS with Kawasaki-like presentations [147]; PIMS-TS apparently shows a predilection for individuals of black or Hispanic descent [146,148], suggesting that genetic factors may contribute to its uneven distribution.

The first reported case was in a 6-month-old infant who was admitted as a classical Kawasaki and later tested positive for COVID-19; she was treated with aspirin and intravenous immunoglobulin (IVIG) [140]. Children with the symptoms and signs of Kawasaki-like disease diagnosed during the SARS-CoV-2 pandemic and showing evidence of immune response to the virus were older, had a higher rate of cardiac involvement, gastrointestinal symptoms, shock syndrome and features of macrophage activation syndrome (MAS) [144,146,149–150]. Myocarditis is a distinguishing feature of PIMS-TS, at times requiring mechanical circulatory support [145]. Many of these cases occurred after several weeks of quarantine, and it is possible that these subjects suffered from a mild form of COVID-19 after intrafamilial transmission and severe complications appeared weeks later [151].

There are a small number of adult-onset Kawasaki Disease Shock Syndrome cases reported; one complicated by coronary aneurysms occurred in a 20-year-old man of East Asian ancestry [152], a 36-year old Hispanic woman [153] and a 45-year old Hispanic man [154]. Immunomodulatory therapeutic strategies have been shown to be effective for PIMS-TS, including intravenous immunoglobulin (IVIG) and steroids [141,144–146].

KD is an inflammatory vascular disease with an unknown etiology, an association between Kawasaki disease and viral respiratory infections has been suspected [155–157]. PIMS-TS appears to be a post-acute immunological reaction to an initial SARS-CoV-2 infection, as the majority are asymptomatic during the initial SARS-CoV-2 infection and do not have positive nasopharyngeal swabs but have serological evidence of a previous infection, showing positive IgG against SARS-CoV-2 in most cases [141,144–146]. There is also speculation that the SARS-CoV-2 protein could act as a superantigen, similarly to mechanisms widely described for toxic shock syndrome (TSS) [158–160].

4. Limitations

The information presented in this literature review must be considered along with important limitations, much is yet to be validated using robust statistical methods. The wide diversity of study methodologies, statistical approaches, sample sizes, population characteristics, geographic sites, and quality of publications may have confounded our interpretation of the data. There is also the problem of left censorship bias where patients who died or were lost to follow-up were not reported. However, in the context of a severe pandemic caused by a novel virus, it is vital to address the emerging data and identify gaps in current knowledge.

5. Summary

Identification of complications of COVID-19 is vital for guiding clinical care, improving patient outcomes, and allocating resources. In this review we primarily aimed to understand the rheumatological manifestations during and after COVID-19 infection. We describe a number of complications including inflammatory arthritis (with some patients developing RA), SLE and myositis among the CTD spectrum being commoner and vasculitis. Vasculitis appears to have a significant role in the initial infection as well as a complication of it. Further studies are necessary to understand the pathogenesis of COVID-19 and its different clinical phenotypes. Follow-ups in the coming months will determine chronicity of these inflammatory conditions. A better understanding of the immune consequences that accompany SARS-CoV-2 infection is required to determine the immunopathogenic mechanisms capable of promoting or contrasting the development of rheumatic manifestations.

Key messages

Important complications of COVID-19 such as inflammatory arthritis, lupus-like disease, rhabdomyolysis/myositis and vasculitis are reported.

Identifying sequelae of COVID-19 is vital for improving patient outcomes, clinical care and allocating resources.

Long Covid seems to be associated with large vessel vasculitis.

Disclosures

No conflicts or relevant disclosures.

References

[1] Guan W, Ni Z, Hu Y. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382:1708–20.

[2] Wang L, Wang Y, Ye D, Liu Q. Review of the 2019 novel coronavirus (SARS-CoV-2) based on current evidence. Int J Antimicrob Agents 2020 Jun;55(6):105948.

[3] 3. Nile SH, Nile A, Qiu J, Li L, Jia X, Kai G. COVID-19: pathogenesis, cytokine storm and therapeutic potential of interferons. Cytokine Growth Factor Rev 2020; 53:66–70 [PMC free article] [PubMed] [Google Scholar] [Ref list].

[4] Zhou Y, Fu B, Zheng X, Wang D, Zhao C, Qi Y. Pathogenic T cells and inflammatory monocytes incite inflammatory storm in severe COVID-19 patients. Natl Sci Rev 2020;7(6):998–1002. nwaa041. [Google Scholar] [Ref list].

[5] Jose RJ, Manuel A. COVID-19 cytokine storm: the interplay between inflammation and coagulation. Lancet Respir Med 2020;20:S2213–600. https://doi.org/10.1016/S2213-2600(20)30216-2 [PMC free article] [PubMed] [CrossRef] [Google Scholar] [Ref list].

[6] Kanduc D, Shoenfeld Y. Molecular mimicry between SARS-CoV-2 spike glycoprotein and mammalian proteomes: implications for the vaccine. Immunol Res 2020;68(5):310–3. https://doi.org/10.1007/s12026-020-09152-6.

[7] World Health Organisation Covid 19 dashboard. https://covid19.who.int/. Last accessed 19/04/21.

[8] Shoenfeld Y. Corona (COVID-19) time musings: our involvement in COVID-19 pathogenesis, diagnosis, treatment and vaccine planning. Autoimmun Rev 2020 Jun;19(6):102538. https://doi.org/10.1016/j.autrev.2020.102538.

[9] Pablos JL, Abasolo L, Alvaro-Gracia JM, et al. RIER investigators group. Prevalence of hospital PCR-confirmed COVID-19 cases in patients with chronic inflammatory and autoimmune rheumatic diseases. Ann Rheum Dis 2020 Sep;79 (9):1170–3.

[10] Michelena X, Borrell H, López-Corbeto M, et al. Incidence of COVID-19 in a cohort of adult and paediatric patients with rheumatic diseases treated with targeted biologic and synthetic disease-modifying anti-rheumatic drugs. Semin Arthritis Rheum 2020 Aug;50(4):564–70.

[11] Stradner MH, Dejaco C, Zwerina J, Fritsch-Stork RD. Rheumatic musculoskeletal diseases and COVID-19, a review of the first 6 months of the pandemic. Front Med (Lausanne) 2020;7:562142. Published online 2020 Oct 9, https://doi.org/10.3389/fmed.2020.562142.

[12] Zuo Y, Yalavarthi S, Shi H, et al. Neutrophil extracellular traps (NETs) as markers of disease severity in COVID-19. MedRxiv 2020. https://doi.org/10.1101/2020.04.09.20059626.

[13] Long Q-X, Liu B-Z, Deng H-J, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. Nat Med 2020. https://doi.org/10.1038/s41591-020-0897-1.

[14] Du SQ, Yuan W. Mathematical modelling of interaction between innate and adaptive immune responses in COVID-19 and implications for viral pathogenesis. J Med Virol 2020. https://doi.org/10.1002/jmv.25866. In press jmv.25866.

[15] Ehrenfeld M, Tincani A, Andreoli L, et al. Covid-19 and autoimmunity. Autoimmun Rev 2020;19(8):102597. https://doi.org/10.1016/j.autrev.2020.102597.

[16] Marks M, Marks JL. Viral arthritis. Clin Med 2016;16:129–34.

[17] Friedman N, Alter H, Hindiyeh M, Mendelson E, Shemer Avni Y, Mandelboim M. Human coronavirus infections in Israel: epidemiology, clinical symptoms and summer seasonality of HCoV-HKU1. Viruses 2018 Sep 21;10(10):515. https://doi.org/10.3390/v10100515.

[18] Christian MD, Poutanen SM, Loutfy MR, Muller MP, Low DE. Severe acute respiratory syndrome. Clin Infect Dis 2004;38:1420–7.

[19] Li S, Wang R, Zhang Y, et al. Symptom combinations associated with outcome and therapeutic effects in a cohort of cases with SARS. Am J Chin Med 2006;34: 937–47.

[20] Joo YB, Lim YH, Kim KJ, Park KS, Park YJ. Respiratory viral infections and the risk of rheumatoid arthritis. Arthritis Res Ther 2019 Aug 30;21(1):199.

[21] Joob B, Wiwanitkit V. COVID-19 can present with a rash and be mistaken for dengue. J Am Acad Dermatol 2020;82. p. e177.
[22] Ono K, Kishimoto M, Shimasaki T, et al. Reactive arthritis after COVID-19 infection. RMD Open 2020 Aug;6(2).
[23] Saricaoglu EM, Hasanoglu I, Guner R. The first reactive arthritis case associated with COVID-19. J Med Virol 2020 Jul;11.
[24] Liew IY, Mak TM, Cui L, Vasoo S, Lim XR. A case of reactive arthritis secondary to coronavirus disease 2019 infection. J Clin Rheumatol 2020 Sep;26(6):233.
[25] Schenker HM, Hagen M, Simon D, Schett G, Manger B. Reactive arthritis and cutaneous vasculitis after SARS-CoV-2 infection. Rheumatology Nov 2020;18. p. [Epub ahead of print].
[26] Talarico RM, Stagnaro C, Ferro F, Carli L, Mosca M. Symmetric peripheral polyarthritis developed during SARS-CoV-2 infection. Lancet Rheumatol 2020: e518–9.
[27] Jali I. Reactive arthritis after COVID-19 infection. Cureus 2020;12(11):e11761. Published 2020 Nov 28, https://doi.org/10.7759/cureus.11761.
[28] De Stefano L, Rossi S, Montecucco C, Bugatti S. Transient monoarthritis and psoriatic skin lesions following COVID-19. Ann Rheum Dis August 2020. https://doi.org/10.1136/annrheumdis-2020-218520 [Epub ahead of print].
[29] Danssaert Z, Raum G, Hemtasilpa S. Reactive arthritis in a 37-year-old female with SARS-CoV2 infection. Cureus 2020 Aug 12;12(8):e9698.
[30] Salvatierra J, Martínez-Peñalver D, Salvatierra-Velasco Lucia. Covid-19 related dactyitis. Published online. 2020 Jul 1. https://doi.org/10.1016/j.jbspin.2020.06.009.
[31] Yokogawa N, Minematsu N, Katano H, Suzuki T. Case of acute arthritis following SARS-CoV-2 infection. Ann Rheum Dis June 2020. p. [Epub ahead of print].
[32] Hønge BL, Hermansen MF, Stogaard M. Reactive arthritis after COVID-19. BMJ Case Reports CP 2021;14(3):e241375. https://doi.org/10.1136/bcr-2020-241375.
[33] Baimukhamedov C, Barskova T, Matucci-Cerinic M. Arthritis after SARS-CoV-2 infection. Lancet Rheumatol 2021 May;3(5):e324–5. https://doi.org/10.1016/S2665-9913(21)00067-9.
[34] Derksen VFAM, Kissel T, Lamers-Karnebeek FBG, et al. Ann Rheum Dis Feb 2021. https://doi.org/10.1136/annrheumdis-2021-219859. Epub ahead of print.
[35] Roongta R, Chattopadhyay A, Ghosh A. Correspondence on 'Onset of rheumatoid arthritis after COVID-19: coincidence or connected?'. Ann Rheum Dis 27 April 2021. https://doi.org/10.1136/annrheumdis-2021-220479. Published Online First:.
[36] Houshmand H, Abounoori M, Ghaemi R, Bayat S, Houshmand G. Ten-year-old boy with atypical COVID-19 symptom presentation: a case report. Clin Case Rep November 2020;9(1):304–8. p. [Epub ahead of print].
[37] Novelli L, Motta F, Ceribelli A, et al. A case of psoriatic arthritis triggered by SARS-CoV-2 infection. Rheumatology (Oxford) 2021;60(1):e21–3. https://doi.org/10.1093/rheumatology/keaa691.
[38] Coath FL, Mackay J, Gaffney JK. Axial presentation of reactive arthritis secondary to Covid-19 infection. Rheumatology (Oxford) 2021 Jan 20:keab009.
[39] López-González M, Peral-Garrido ML, Calabuig I, et al. Case series of acute arthritis during COVID-19 admission. Ann Rheum Dis 2020:1–2. https://doi.org/10.1136/annrheumdis-2020-217914.
[40] Halpert G, Shoenfeld Y. SARS-CoV-2, the autoimmune virus. Autoimmun Rev 2020;19(12):102695. https://doi.org/10.1016/j.autrev.2020.102695.
[41] Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497–506.
[42] Wendling D, Prati C, Chouk M, et al. Reactive arthritis: treatment challenges and future perspectives. Curr Rheumatol Rep 2020;22:29.
[43] Coskun Benlidayi I, Kurtaran B, Tirasci E, Guzel R. Coronavirus disease 2019 (COVID-19) in a patient with ankylosing spondylitis treated with secukinumab: a case-based review. Rheumatol Int 2020;40(10):1707–16. https://doi.org/10.1007/s00296-020-04635-z.
[44] D'Cruz DP, Khamashta MA, Hughes GR. Systemic lupus erythematosus. Lancet 2007 Feb 17;369(9561):587–96. https://doi.org/10.1016/S0140-6736(07)60279-7. 17307106.
[45] Tsokos GC. Systemic lupus erythematosus. N Engl J Med 2011;365(22):2110–21.
[46] Perl A. Mechanisms of viral pathogenisis in rheumatic disease. Ann Rheum Dis 1999;58(8):454–61.
[47] Uthman IW, Gharavi AE. Viral infections and antiphospholid antibodies. Semin Arthritis Rheum 2002;31(4):256–63.
[48] Caso F, Costa L, Ruscitti P, Navarini L, Del Puente A, Giacomelli R, et al. Could Sars-coronavirus-2 trigger autoimmune and/or autoinflammatory mechanisms in genetically predisposed subjects? Autoimmun Rev 2020 May;19(5):102524. https://doi.org/10.1016/j.autrev.2020.102524. Epub 2020 Mar 24. PMID: 32220633; PMCID: PMC7271072.
[49] Cardoso ME, Hundal J, Feterman D, et al. Concomitant new diagnosis of systemic lupus erythematosus and COVID-19 with possible antiphospholipid syndrome. Just a coincidence? A case report and review of intertwining pathophysiology. Clin Rheumatol 2020:39. https://doi.org/10.1007/s10067-020-05310-1.
[50] Slimani Y, Abbassi R, El Fatoiki F-Z, Barrou L, Chiheb S. Systemic lupus erythematosus and varicella-like rash following COVID-19 in a previously healthy patient. J Med Virol 2021;93:1184–7.
[51] El Aoud S, Morin C, Lorriaux P, Obert J, Sorial D, Chaabouni T, et al. COVID-19 presenting as lupus erythematosus-like syndrome. Disaster Med Public Health Prep 2020:1–4.
[52] Hali F, Jabri H, Chiheb S, Hafiani Y, Nsiri A. A concomitant diagnosis of COVID-19 infection and systemic lupus erythematosus complicated by a macrophage activation syndrome: a new case report. Int J Dermatol 2021 Apr;17.
[53] Gracia-Ramos AE, Saavedra-Salinas MÁ. Can the SARS-CoV-2 infection trigger systemic lupus erythematosus? A case-based review. Rheumatol Int 2021;41(4):799–809. https://doi.org/10.1007/s00296-021-04794-7.
[54] Zhang Y, Xiao M, Zhang S, et al. Coagulopathy and Antiphospholipid Antibodies in Patients with Covid-19. N Engl J Med 2020;382(17).
[55] Yasri S, Wiwanitkit V. COVID-19, antiphospholipid syndrome and thrombosis. Clin Appl Thromb Hemost January 2020. https://doi.org/10.1177/1076029620931927.
[56] Harzallah I, Debliquis A, Drenous B. Lupus anticoagulant is frequent in Patients with Covid-19. J Thromb Haemost 2020;18(8):2064–5. https://doi.org/10.1111/jth.14867.
[57] Cavalli E, Bramanti A, Ciurleo R, et al. Entangling COVID-19 associated thrombosis into a secondary antiphospholipid antibody syndrome: diagnostic and therapeutic perspective. Int J Mol Med 2020;46(3):903–12.
[58] Montoya-Ortiz G. Immunosenescence, aging, and systemic lupus erythematous. Autoimmune Dis 2013;2013:267078. https://doi.org/10.1155/2013/267078.
[59] Greinacher A, Thiele T, Warkentin TE, Weisser K, Kyrle PA, Eichinger S. Thrombotic thrombocytopenia after ChAdOx1 nCov-19 vaccination. N Engl J Med 2021 Apr 9. https://doi.org/10.1056/NEJMoa2104840. Epub ahead of print.
[60] Scully M, Singh D, Lown R, Poles A, Solomon T, Levi M, et al. Pathologic antibodies to platelet factor 4 after ChAdOx1 nCoV-19 vaccination. N Engl J Med 2021 Apr 16. https://doi.org/10.1056/NEJMoa2105385. Epub ahead of print.
[61] Zheng M, Gao Y, Wang G, et al. Functional exhaustion of antiviral lymphocytes in COVID-19 patients. Cell Mol Immunol 2020:533–5.
[62] Qin C, Zhou L, Hu Z, et al. Dysregulation of immune response in patients with COVID-19 in Wuhan, China. Clin Infect Dis 2020;71:762–8.
[63] Bonometti R, Sacchi MC, Stobbione P, Lauritano EC, Tamiazzo S, Marchegiani A, et al. The first case of systemic lupus erythematosus (SLE) triggered by COVID-19 infection. Eur Rev Med Pharmacol Sci 2020;24(18):9695–7. https://doi.org/10.26355/eurrev_202009_23060.
[64] Zamani B, Moeini Taba SM, Shayestehpour M. Systemic lupus erythematosus manifestation following COVID-19: a case report. J Med Case Reports 2021;15:29. https://doi.org/10.1186/s13256-020-02582-8.
[65] Woodruff MC, Ramonell RP, Nguyen DC, et al. Extrafollicular B cell responses correlate with neutralizing antibodies and morbidity in COVID-19. Nat Immunol 2020;21:1506–16. https://doi.org/10.1038/s41590-020-00814-z.
[66] Paliwal VK, Garg RK, Gupta A, Tejan N. Neuromuscular presentations in patients with COVID-19. Neurol Sci 2020;41(11):3039–56.
[67] Mughal MS, Kaur IP, Alhashemi R, Rehman R, Du D. Acute viral myositis complicated by rhabdomyolysis: a sole manifestation of COVID-19 infection. J Commun Hosp Intern Med Perspect 2021;11(2):289–91. https://doi.org/10.1080/20009666.2021.1878601.
[68] Beydon M, Chevalier K, Al Tabaa O, Hamroun S, Delettre AS, Thomas M, et al. Myositis as a manifestation of SARS-CoV-2. Ann Rheum Dis 2021;80:e42. https://doi.org/10.1136/annrheumdis-2020-217573.
[69] Mehan WA, Yoon BC, Lang M, Li MD, Rincon S, Buch K. Paraspinal myositis in patients with COVID-19 infection. Am J Neuroradiol 2020;41:1949–52. https://doi.org/10.3174/ajnr.A6711.
[70] Shabbir A, Camm CF, Elkington A, Tilling L, Stirrup J, Chan A, et al. Myopericarditis and myositis in a patient with COVID-19: a case report. Eur Heart J Case Rep 2020 Oct 30;4(6):1–6. https://doi.org/10.1093/ehjcr/ytaa370.
[71] Almadani M, Shiferson A, Swearingen B, Shih M, Jacob T, Rhee R. Compartment syndrome secondary to viral myositis as initial presentation in COVID-19 patient. J Vasc Surg Cases Innov Tech 2020 Dec;6(4):524–7. https://doi.org/10.1016/j.jvscit.2020.08.021.
[72] Mangan MS, Yildiz E. New onset of unilateral orbital myositis following mild COVID-19 infection. Ocul Immunol Inflamm 2021 Apr;2:1–2. https://doi.org/10.1080/09273948.2021.
[73] Sacchi MC, Tamiazzo S, Lauritano EC, Bonometti R. Case report of COVID-19 in an elderly patient: could SARS-CoV2 trigger myositis? Eur Rev Med Pharmacol Sci 2020;24(22):11960–3. https://doi.org/10.26355/eurrev_202011_23857.
[74] Zhang H, Charmchi Z, Seidman RJ, Anziska Y, Velayudhan V, Perk J. COVID-19-associated myositis with severe proximal and bulbar weakness. Muscle Nerve 2020 Sep;62(3):E57–60. https://doi.org/10.1002/mus.27003.
[75] Lokineni S, Mortezavi M. Delayed-onset necrotizing myositis following COVID-19 infection. Eur J Case Rep Intern Med 2021;2. https://doi.org/10.12890/2021_002461.
[76] Tawfeeq H, Witham F, Dulay GS. COVID-19 related calcific myositis cases. BJR Case Rep 2021;7:120200120.
[77] Hong KS, Lee KH, Chung JH, et al. Clinical features and outcomes of 98 patients hospitalized with SARS-Cov-2 infection in Daegu, South Korea: a brief descriptive study. Yansei Med J 2020;61(5):431–7.
[78] Cheng Y, Luo R, Wang K, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney Int 2020;97(5):829–38.
[79] Su H, Yang M, Wan C, et al. Renal histopathological analysis of 26 post-mortem findings of patients with COVID-19 in China. Kidney Int 2020;98(1):219–27.
[80] Peleg Y, Kudose S, D'Agati V, et al. Acute kidney injury due to collapsing glomerulopathy following COVID-19 infection. Kidney Int Rep 2020;5(6):940–5.
[81] Batlle D, Soler MJ, Sparks MA, et al. COVID-19 and ACE2 in cardiovascular, lung, and kidney working group. Acute injury in COVID-19: emerging evidence of a distinct pathophysiology. J Am Soc Nephrol 2020;31(2020):1380–3.
[82] Tincani A, Rebaioli CB, Taglietti M, Shoenfeld Y. Heart involvement in systemic lupus erythematosus, anti-phospholipid syndrome and neonatal lupus. Rheumatology (Oxford) 2006 Oct;45(Suppl. 4):iv8–13. https://doi.org/10.1093/rheumatology/kel308. 16980725.

[83] Inciardi RM, Lupi L, Zaccone G, et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). JAMA Cardiol 2020;5(7):819–24. https://doi.org/10.1001/jamacardio.2020.1096.

[84] Castier MB, Albeuquerque EMN, Menezes MEFCC, et al. Cardiac tamponade in systemic lupus erythematosus. Report of four cases. Arq Bras Cardiol 2000;75:446–8.

[85] Kahl LE. The spectrum of pericardial tamponade in systemic lupus erythematosus: report of ten Patients. Arthritis Rheum 1992;35(11):1343–9.

[86] Dabbagh MF, Aurora L, D'Souza P, Weinmann AJ, Bhargava P, Basir MB. Cardiac tamponade secondary to COVID-19. JACC Case Rep 2020 Jul 15;2(9):1326–30. https://doi.org/10.1016/j.jaccas.2020.04.009. Epub 2020 Apr 23. PMID: 32328588; PMCID: PMC7177077.

[87] Hua A, O'Gallagher K, Sado D, Byrn J. Life-threatening cardiac tamponade complicating myo-pericarditis in COVID-19. Eur Heart J 7 June 2020;41(22):2130. https://doi.org/10.1093/eurheartj/ehaa253.

[88] Sawalha K, Abozenah M, Kadado AJ, Battisha A, Al-Akchar M, Salerno C, et al. Systematic review of COVID-19 related myocarditis: Insights on management and outcome. Cardiovasc Revasc Med 2020 Aug 18;23:107–13. https://doi.org/10.1016/j.carrev.2020.08.028. Epub ahead of print. PMID: 32847728; PMCID: PMC7434380.

[89] Zhou Y, Han T, Chen J, et al. Clinical and autoimmune characteristics of severe and critical cases of COVID-19. Clin Transl Sci 2020;13(6):1077–86. https://doi.org/10.1111/cts.12805.

[90] Viner RM, Whittaker E. Kawasaki-like disease: Emerging complication during the COVID-19 pandemic. Lancet May 2020;395:1741–3.

[91] Menter T, Haslbauer JD, Nienhold R, Savic S, Hopfer H, Deigendesch N, et al. Postmortem examination of COVID-19 patients reveals diffuse alveolar damage with severe capillary congestion and variegated findings in lungs and other organs suggesting vascular dysfunction. Histopathology 2020 Aug;77(2):198–209. https://doi.org/10.1111/his.14134. Epub 2020 Jul 5. PMID: 32364264; PMCID: PMC7496150.

[92] Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 2020;8:420–2.

[93] Yao XH, Li TY, He ZC, et al. A pathological report of three COVID-19 cases by minimally invasive autopsies [in Chinese]. Zhonghua Bing Li Xue Za Zhi 2020;49:411–7.

[94] Manenti A, Farinetti A, Manco G, Mattioli A. Vasculitis and aortitis: COVID-19 challenging complications. J Vasc Surg 2021;73(1):347–8.

[95] Roncati L, Ligabue G, Fabbiani L, Malagoli C, Gallo G, Lusenti B, et al. Type 3 hypersensitivity in COVID-19 vasculitis. Clin Immunol 2020;217.

[96] Li XM, Ma YT, Yang YN, Liu F, Chen BD, Han W, et al. Downregulation of survival signalling pathways and increased apoptosis in the transition of pressure overload-induced cardiac hypertrophy to heart failure. Clin Exp Pharmacol Physiol 2009;36:1054–61.

[97] Siddiqi HK, Libby P, Ridker PM. COVID-19 – a vascular disease. Trends Cardiovasc Med 2021 Jan;31(1):1–5. https://doi.org/10.1016/j.tcm.2020.10.005.

[98] Casas CG, Catala A, Hernandez GC, et al. Classification of the cutaneous manifestations of COVID-19: a rapid prospective nationwide consensus study in Spain with 375 cases. Br J Dermatol 2020 Jul;183(1):71–7. https://doi.org/10.1111/bjd.19163. Epub 2020 Jun 10. PMID: 32348545; PMCID: PMC7267236.

[99] Colmenero I, Santonja C, Alonso-Riaño M, Noguera-Morel L, Hernández-Martín A, Andina D, et al. SARS-CoV-2 endothelial infection causes COVID-19 chilblains: histopathological, immunohistochemical and ultrastructural study of seven paediatric cases. Br J Dermatol 2020 Oct;183(4):729–37. https://doi.org/10.1111/bjd.19327. Epub 2020 Aug 5. PMID: 32562567; PMCID: PMC7323219.

[100] Kanitakis J, Lesort C, Danset M, Jullien D. Chilblain-like acral lesions during the COVID-19 pandemic ("COVID toes"): histologic, immunofluorescence, and immunohistochemical study of 17 cases. J Am Acad Dermatol 2020;83(3):870–5. https://doi.org/10.1016/j.jaad.2020.05.145.

[101] El Hachem M, Diociaiuti A, Concato C, Carsetti R, Carnevale C, Ciofi Degli Atti M, et al. A clinical, histopathological and laboratory study of 19 consecutive italian paediatric patients with chilblain-like lesions: lights and shadows on the relationship With COVID-19 infection. J Eur Acad Dermatol Venereol 2020;34(11):2620–9. https://doi.org/10.1111/jdv.16682.

[102] de Masson A, Bouaziz JD, Sulimovic L, et al. SNDV (French National Union of Dermatologists-Venereologists). Chilblains is a common cutaneous finding during the COVID-19 pandemic: a retrospective nationwide study from France. J Am Acad Dermatol 2020 Aug;83(2):667–70. https://doi.org/10.1016/j.jaad.2020.04.161. Epub 2020 May 4. PMID: 32380219; PMCID: PMC7198162.

[103] Castelnovo L, Capelli F, Tamburello A, Faggioli PM, Mazzone A. Symetric cutaneous vasculitis in COVID-19 pneumonia. J Eur Acad Dermatol Venerol August 2020;34:e362–3.

[104] Kösters K, Schwarzer S, Labuhn A, et al. Cutaneous vasculitis in a patient with COVID-19. Open Forum Infect Dis 2020;7(10). https://doi.org/10.1093/ofid/ofaa474. ofaa474. Published 2020 Oct 5.

[105] Mayor-Ibarguren A, Feito-Rodriguez M, Quintana Castanedo L, Ruiz-Bravo E, Montero Vega D, Herranz-Pinto P. Cutaneous small vessel vasculitis secondary to COVID-19 infection: a case report. J Eur Acad Dermatol Venereol October 2020;34(10):e541–2.

[106] Adekiigbe R, Ugbode F, Seoparson S, Katriyar N, Fetterman A. A 47-year-old hispanic man who developed cutaneous vasculitic lesions and gangrene of the toes following admission to hospital with covid-19 pneumonia. Am J Case Rep 2020;21:1–5.

[107] de Perosanz-Lobo D, Fernandez-Nieto D, Burgos-Blasco P, Selda-Enriquez G, Carretero I, Moreno C, et al. Urticarial vasculitis in COVID-19 infection: a vasculopathy-related symptom? J Eur Acad Dermatol Venereol 2020 Oct;34(10):e566–8. https://doi.org/10.1111/jdv.16713. Epub 2020 Jun 26. PMID: 32510648; PMCID: PMC7300972.

[108] Camprodon Gómez M, González-Cruz C, Ferrer B, Barberá MJ. Leucocytoclastic vasculitis in a patient with COVID-19 with positive SARS-CoV-2 PCR in skin biopsy. BMJ Case Rep October 29, 2020;13(10). p. e238039.

[109] Oxley TJ, Mocco J, Majiidi S, et al. Large vessel stroke as a presenting feature of COVID-19 in the young. N Engl J Med 2020;382(20):e60.

[110] Varatharaj A, Thomas N, Ellul MA, Davies NWS, Pollak TA, et al. Neurological and neuropsychiatric complications of COVID-19 in 153 patients: a UK-wide surveillance study. Lancet Psychiatry 2020;10:875–82.

[111] Hanafi R, Roger PA, Perin B, Öuchcinski G, Deleval N, Dallery F, et al. COVID-19 neurologic complication with CNS vasculitis-like pattern. Am J Neuroradiol 2020;41(8):1384–7.

[112] de Sousa GC, de Sousa TC, Sakiyama MAK, da Silva JSNL, de Sousa EDJS. Vasculitis-related stroke in young as a presenting feature of novel coronavirus disease (COVID19) – case report. J Clin Neurosci 2020;79:169–71.

[113] Oliveira RMC, Santos DH, Olivetti BC, Takahashi JT. Bilateral trochlear nerve palsy due to cerebral vasculitis related to COVID-19 infection. Arq Neuropsiquiatr 2020;78:385–6.

[114] Dixon L, Coughlan C, Karunaratne K, et al. Immunosuppression for intracranial vasculitis associated with SARS-CoV-2: therapeutic implications for COVID-19 cerebrovascular pathology. J Neurol Neurosurg Psychiatry 2021;92:103–4.

[115] Natoli S, Oliveira V, Calabresi P, Maia LF, Pisani A. Does SARS-Cov-2 invade the brain? Translational lessons from animal models. Eur J Neurol 2020 Sep;27(9):1764–73. https://doi.org/10.1111/ene.14277. Epub 2020 May 22. PMID: 32333487; PMCID: PMC7267377.

[116] Salvat Davila C, Suarez Fernandez JP, Dominguez Grande ML, Vigil Diaz C, Fernandez Llana B, Martin Fernandez N, et al. SARS-CoV-2 (COVID-19) pneumonia: incidental finding on (18)F-FDG PET/CT study for vasculitis diagnosis. Rev Esp Med Nucl Imagen Mol 2020. https://doi.org/10.1016/j.remn.2020.06.013 [Epub ahead of print].

[117] Oda R, Inagaki T, Ishikane M, Hotta M, Shimomura A, Sato M, et al. Case of adult large vessel vasculitis after SARS-CoV-2 infection. Ann Rheum Dis 2020. https://doi.org/10.1136/annrheumdis-2020-218440 [Epub ahead of print].

[118] Sollini M, Ciccarelli M, Cecconi M, et al. Vasculitis changes in COVID-19 survivors with persistent symptoms: an [18F]FDG-PET/CT study. Eur J Nucl Med Mol Imaging 2020. https://doi.org/10.1007/s00259-020-05084-3.

[119] Hussein A, Al Khalil K, Bawazir YM. Anti-neutrophilic cytoplasmic antibody (ANCA) vasculitis presented as pulmonary hemorrhage in a positive COVID-19 patient: a case report. Cureus 2020;12(8):e9643.

[120] Uppal NN, Kello N, Shah HH, et al. De novo ANCA-associated vasculitis with glomerulonephritis in COVID-19. Kidney Int Rep 2020 Nov;5(11):2079–83. https://doi.org/10.1016/j.ekir.2020.08.012. Epub 2020 Aug 20. PMID: 32839744; PMCID: PMC7439090.

[121] Moeinzadeh F, Dezfouli M, Naimi A, et al. Newly diagnosed glomerulonephritis during COVID-19 infection undergoing immunosuppression therapy, a case report. Iran J Kidney Dis 2020;14:239–42.

[122] Bressler MY, Pathak N, Cervellione K, Bagheri F, Epstein E, Mir A, et al. New onset granulomatosis with Polyangiitis associated with COVID-19. Case Rep Dermatol Med 2021;2021 Jan 13:8877292. https://doi.org/10.1155/2021/8877292.

[123] Weston T, Powell Julie A, Campbell Francesca Ross, Jiménez Patricia Peña, Rudzinski Erin R, Dickerson Jane A. Acute ANCA vasculitis and asymptomatic COVID-19. Pediatrics April 2021;147(4):e2020033092. https://doi.org/10.1542/peds.2020-033092.

[124] Persiano T, Grulli F, Cornara P, et al. Necrotising vasculitis in Covid-19: watch out for bowel perforation. 17 September 2020. https://doi.org/10.21203/rs.3.rs-79258/v1. PREPRINT (Version 1) available at Research Square.

[125] Vacchi C, Meschiari M, Milic J, Marietta M, Tonelli R, Alfano G, et al. COVID-19-associated vasculitis and thrombotic complications: from pathological findings to multidisciplinary discussion. Rheumatology (Oxford) 2020;59:e147–50. https://doi.org/10.1093/rheumatology/keaa581.

[126] Carnevale S, Beretta P, Morbini P. Direct endothelial damage and vasculitis due to SARS-CoV-2 in small bowel submucosa of COVID-19 patient with diarrhea. J Med Virol 2021;93:61–3. https://doi.org/10.1002/jmv.26119.

[127] Barnes BJ, Adrover JM, Baxter-Stoltzfus A, et al. Targeting potential drivers of COVID-19: neutrophil extracellular traps. J Exp Med 2020;217(6).

[128] Guilpain P, Le Bihan C, Foulongne V, et al. Rituximab for granulomatosis with polyangiitis in the pandemic of covid-19: lessons from a case with severe pneumonia. Ann Rheum Dis 2021 Jan;80(1):e10. https://doi.org/10.1136/annrheumdis-2020-217549. Epub 2020 Apr 20, 32312768.

[129] Fallet B, Kyburz D, Walker UA. Mild course of COVID-19 and spontaneous virus clearance in a patient with depleted peripheral blood B cells due to rituximab treatment. Arthritis Rheumatol 2020;72:1581–2. https://doi.org/10.1002/art.41380.

[130] Rutherford MA, Scott J, Karabayas M, Antonelou M, Gopaluni S, Gray D, et al. Risk factors for severe outcomes in patients with systemic vasculitis & COVID-19: a bi-national registry-based cohort study. Arthritis Rheumatol 2021 Mar 22. https://doi.org/10.1002/art.41728 [Epub ahead of print].

[131] Allez M, Denis B, Bouaziz JD, Battistella M, Zagdanski AM, Bayart J, et al. COVID-19-related IgA vasculitis. Arthritis Rheumatol 2020;72(11):1952–3.

[132] Sandhu S, Chand S, Bhatnagar A, Dabas R, Bhat S, Kumar H, et al. Possible association between IgA vasculitis and COVID-19. Dermatol Ther 2021 Jan;34(1):e14551. https://doi.org/10.1111/dth.14551. Epub 2020 Nov 25. PMID: 33200863; PMCID: PMC7744895.

[133] Suso AS, Mon C, Alonso IO, et al. IgA vasculitis with nephritis (Henoch-Schonlein Purpura) in a COVID-19 patient. Kidney Int 2020;5:2074–8.
[134] Li NL, Papini AB, Shao T, Girard L. Immunoglobulin-a vasculitis with renal involvement in a patient with COVID-19: a case report and review of acute kidney injury related to SARS-CoV-2. Can J Kidney Health Dis 2021 Feb 5;8. https://doi.org/10.1177/2054358121991684. 2054358121991684.
[135] Yu H, Sun B, Fang Z, et al. Distinct features of SARS-CoV-2-specific IgA response in COVID-19 patients. Eur Respir J 2020. https://doi.org/10.1183/13993003.01526-2020.
[136] Becker RC. COVID-19 associated vasculitis and vasculopathy. J Thromb Thrombolysis 2020;50(3):499–511.
[137] Noval Rivas M, Wakita D, Franklin MK, Carvalho TT, Abolhesn A, Gomez AC, et al. Intestinal permeability and IgA provoke immune vasculitis linked to cardiovascular inflammation. Immunity 2019;51:508–21.
[138] Heineke MH, Ballering AV, Jamin A, Ben Mkaddem S, Monteiro RC, Van Egmond M. New insights in the pathogenesis of immunoglobulin a vasculitis (Henoch-Schönlein purpura). Autoimmun Rev 2017 Dec;16(12):1246–53. https://doi.org/10.1016/j.autrev.2017.10.009. Epub 2017 Oct 14, 29037908.
[139] Castagnoli R, Votto M, Licari A, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review. JAMA Pediatr 2020;174(9):882–9. https://doi.org/10.1001/jamapediatrics.2020.1467.
[140] Jones VG, Mills M, Suarez D, et al. COVID-19 and Kawasaki disease: novel virus and novel case. Hosp Pediatr 2020;10:537–40.
[141] Cheung EW, Zachariah P, Gorelik M, Boneparth A, Kernie SG, Orange JS, et al. Multisystem inflammatory syndrome related to COVID-19 in previously healthy children and adolescents in new York City (Epub ahead of print) JAMA 2020;324(3):294–6. https://doi.org/10.1001/jama.2020.10374.
[142] Jiang L, Tang K, Levin M, et al. COVID-19 and multisystem inflammatory syndrome in children and adolescents. Lancet Infect Dis 2020;20:e276–88. https://doi.org/10.1016/S1473-3099(20)30651-4. PMID:32818434.
[143] Ozen S, Ruperto N, Dillon MJ, et al. EULAR/PReS endorsed consensus criteria for the classification of childhood vasculitides. Ann Rheum Dis 2006;65:936–41.
[144] Verdoni L, Gervasoni A, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. Lancet 2020;(10239):1771–8.
[145] Belhadjer Z, Meot M, Bajolle F, Khraiche D, Legendre A, Abakka S, et al. Acute heart failure in multisystem inflammatory syndrome in children (MIS-C) in the context of global SARS-CoV-2 pandemic (Epub ahead of print) Circulation 2020;142:429–36.
[146] Whittaker E, Bamford A, Kenny J, Kaforou M, Jones CE, Shah P, et al. Clinical characteristics of 58 children with a pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. JAMA 2020;324:259–69.
[147] Lio K, Uda K, Hataya H, Yasui F, Honda T, Sanada T, et al. Kawasaki disease or Kawasaki-like disease: influence of SARS-CoV-2 infections in Japan. Acta Paediatr 2020;16:16.
[148] Feldstein LR, Rose EB, Horwitz SM, et al. Multisystem inflammatory syndrome in U.S. children and adolescents. N Engl J Med 2020;383(4):334–46.
[149] Toubiana J, Poirault C, Corsia A, Bajolle F, Fourgeaud J, Angoulvant F, et al. Kawasaki-like multisystem inflammatory syndrome in children during the COVID-19 pandemic in Paris, France: prospective observational study. BMJ 2020:369.
[150] Rowley AH. Understanding SARS-CoV-2-related multisystem inflammatory syndrome in children. Nat Rev Immunol 2020;20:453–4. https://doi.org/10.1038/s41577-020-0367-5.
[151] Kone-Paut I. Cimaz R is it Kawasaki shock syndrome, Kawasaki-like disease or pediatric inflammatory multisystem disease? The importance of semantic in the era of COVID-19 pandemic. RMD Open 2020;6(2):06.
[152] Zazoulina J, Cheung CC, Hurlburt A, Chahal D, Wong S. A case of adult-onset kawasaki disease Shock syndrome complicated by coronary aneurysms. CJC Open 2019;1:206–8.
[153] Sokolovsky S, Soni P, Hoffman T, Kahn P, Scheers-Masters J. COVID-19 associated Kawasaki-like multisystem inflammatory disease in an adult. Am J Emerg Med 2021;39. pp. 253.e1-e2.
[154] Shaigany S, Gnirke M, Guttmann A, Chong H, Meehan S, Raabe V, et al. An adult with Kawasaki-like multisystem inflammatory syndrome associated with COVID-19. Lancet 2020;396(10246):e8–10.
[155] Burns JC, Herzog L, Fabri O, et al. Seasonality of Kawasaki disease: a global perspective. PLoS One 2013;8:e74529.
[156] Turnier JL, Anderson MS, Heizer HR, et al. Concurrent respiratory viruses and Kawasaki disease. Pediatrics 2015;136:e609–14.
[157] Kim GB, Park S, Kwon BS, et al. Evaluation of the temporal association between Kawasaki disease and viral infections in South Korea. Korean Circ J 2014;44:250–4.
[158] Cheng MH, Zhang S, Porritt RA, Rivas MN, Paschold L, Willscher E, Binder M, Arditi M, Bahar I. Superantigenic character of an insert unique to SARS-CoV-2 spike supported by skewed TCR repertoire in patients with hyperinflammation. Proceedings of the National Academy of Sciences Oct 2020;117(41):25254–62. https://doi.org/10.1073/pnas.2010722117.
[159] Kotb M, Norrby-Teglund A, McGeer A, El-Sherbini H, Dorak MT, Khurshid A, et al. An immunogenetic and molecular basis for differences in outcomes of invasive group a streptococcal infections. Nat Med 2002;8:1398–404.
[160] Tirado SM, Yoon KJ. Antibody-dependent enhancement of virus infection and disease. Viral Immunol 2003;16:69–86.