Benha Journal of Applied Sciences (BJAS) **print: ISSN 2356–9751**
Vol. (7) Issue (11) (2022), (83-92) **online: ISSN 2356–976x**
http://bjas.journals.ekb.eg

Post-Covid-19 Arthritis

S.M.Khalil[1], N.I.Hashaad[2], and R.EL-Tantawy[2]
[1]Rheumatology, Rehabilitation and Physical Medicine., Dept., Faculty of Medicine, Tanta Univ., Tanta, Egypt
[2]Rheumatology, Rehabilitation and Physical Medicine ., Dept., Faculty of Medicine, Benha Univ., Benha, Egypt
Email: Samar.Khalil21@fmed.bu.edu.eg

Abstract

The majority of documented cases of arthritis occurred between 2 and 4 weeks following the discovery of COVID positive. These cases mostly involved the minor joints of the hands. Rheumatoid arthritis, psoriatic arthritis, vasculitis, systemic sclerosis, septic arthritis, and post-covid flares of preexisting inflammatory arthritis are all examples of post-Covid-19 arthritis. Patients with COVID-19 vaccination-related new-onset arthritis, arthralgias, joint disease flare-up, and bursitis often experience joint swelling, discomfort, stiffness, and possibly restricted range of motion. Molecular mimicry, the generation of specific autoantibodies, and the involvement of certain vaccine adjuvants are the primary processes by which the COVID-19 vaccine causes autoimmune. The purpose of this paper was to provide a summary and clarify recent developments in our understanding of arthritis after COVID-19.

Keywords: Covid-19, Post-Covid-19, Arthritis, Vaccination.

1. Introduction

COVID-19 is caused by Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2; formerly 2019 nCoV), an enveloped, positive-sense single -stranded genomic RNA virus. A first-ever report of SARS-CoV-2 in China has emerged from Wuhan. It is highly infectious among humans and has spread fast over the globe as a result of close human contact or the dissemination of infected individuals' respiratory secretions (coughs, sneezes) [1].

Studies of individuals with mild and severe SARS infections show that the illness places a heavy load on the musculoskeletal system, including skeletal muscle, the nervous system, bones, and joints [2].

Although the respiratory system is the primary target of the virus's destructive power, other systems, such as the musculoskeletal system, feel the impacts as a secondary consequence. Musculoskeletal dysfunction is often accompanied by the COVID-19 symptoms of fatigue, arthralgia, and myalgia [3].

The high prevalence of autoimmune and rheumatic illnesses among COVID-19 survivors is a major concern. The prompt detection of people displaying auto-immune and rheumatic symptoms is of paramount importance. COVID-19 is associated with a wide range of musculoskeletal disorders, including arthritis and other inflammatory conditions [4].

Multiple autoimmune/autoinflammatory phenomena, as stated, have emerged. among them is reactive arthritis (inflammatory arthritis) [5].

A wide variety of inflammatory manifestations linked to COVIDs have been documented in light of the current epidemic. Reactive arthritis after chronic opportunistic virus infection has been recorded in adults, but is seldom described in children. It has been hypothesised that molecular mimicry is the immune mechanism at play here. Most cases of arthritis were reported between 2 and 4 weeks after COVID positive was identified [6]. These cases mostly involved the knees and ankles, but might also manifest in the tiny joints of the hands.

The purpose of this study is to provide a comprehensive evaluation of arthritis after COVID-19.

COVID-19 virus

Anatomy of the Problem and Epidemiology

SARS-CoV-2, a new coronavirus, causes COVID-19, a highly contagious and infectious illness. It is commonly known that the first COVID-19 related infections were reported in December 2019 in Wuhan, Hubei Province, China, and were associated with the Huanan Seafood Market. Since then, it has expanded to more than 216 nations and territories [7].

An early easing of government-enforced lockdown measures may be to blame for the second wave of COVID-19 infections that have been reported in numerous nations. Multiple nations have reported a second wave of rising cases, with daily totals surpassing those of the initial outbreak in March 2020 [8].

Pathophysiology

Genome and structure of SARS coronavirus type 2

SARS-CoV-2, as measured by transmission electron microscopy, has a diameter of 60 to 140 nm and exhibits a shape typical of coronaviruses. Genetically, SARS-CoV-2 is 96% similar to bat coronavirus (RaTG13), 80% similar to SARS-CoV-1, and 50% similar to Middle East respiratory syndrome coronavirus (MERS-CoV) [9].

Single-stranded positive-sense RNA encodes around 27 proteins for SARS-CoV-2, some of which are comparable to proteins with recognised activities while others have uncertain or unknown roles. Nucleocapsid (N) protein, hemagglutinin-esterase (HE) protein, spike (S) glycoprotein, and tiny envelope (E) protein are all structural proteins. Viruses rely on the E and M proteins for assembly, budding, and morphogenesis. SARS-primary CoV-2's surface glycoprotein, S, is involved in receptor binding and membrane fusion [10].

How it's transmitted

The World Health Organization (WHO) claims that the currently available information indicates that SARS-CoV-2 is spread by respiratory droplets and contact. Direct contact with infective respiratory droplets, such as those expelled during coughing and sneezing, is necessary for droplet transmission. This happens when a susceptible individual is in close proximity (less than 1 metre) to an infected person exhibiting such symptoms. Fomites on surfaces in the sick person's immediate vicinity may potentially serve as a vector for transmission. Endotracheal intubation, cardiac resuscitation, the administration of nebulized therapies, and other procedures that generate aerosols provide a risk of airborne transmission [11].

Pathogenesis

SARS-CoV-2, when breathed, most likely attaches to epithelial cells lining the nasal canal and begins multiplying there. The SARS-CoV2 virus primarily interacts with ACE2. Ciliated cells are primary cells in the conducting airways, as shown by in vitro studies with SARS-CoV [12].

The virus replicates and spreads down the conducting airways of the respiratory tract, activating a stronger innate immune response as it travels down the respiratory system. The SARS coronavirus type 2 (SARS-CoV-2) and early indicators of the innate immune response may be extracted from nasal swabs or sputum. COVID-19 is a clinically significant illness now [13].

Some possible post-viral arthritis processes include joint infection, immunologic complex formation, and immunological dysregulation. Molecular mimicry between SARS-CoV-2 epitopes and the synovial membrane is widely held to be the root cause of local inflammation, however some theories point to the presence of circulating immune complexes or the virus's direct location on joint tissue. Furthermore, SARS-CoV-2 triggers cytokine storm and macrophage activation syndrome by augmenting IL-6-related pathways. Interferon-dependent and antigen-presenting pathways are equally susceptible to disruption. These alterations to the inflammatory response may trigger autoimmunity in susceptible people [14].

Management

Medical diagnosis

Fever, cough, myalgia, and dyspnea are the most often reported symptoms, whereas gastrointestinal issues such nausea, vomiting, diarrhoea, ageusia, and conjunctival congestion are reported less frequently. From a clinical standpoint, the COVID-19 was divided into three groups: mild to moderate (non-pneumonia and pneumonia), severe (dyspnoea, respiratory frequency over 30/min, oxygen saturation less than 93%, PaO2/FiO2 ratio less than 300, and/or lung infiltrates more than 50% of the lung field within 24-48 hours) and critical.

In addition, changes in taste and olfactory problems have been reported, especially in the first stages of the illness. Patients who have contracted the infection have also shown skin signs, including urticaria and eryhtematous rashes. The cardiovascular system has also been linked to COVID-19. Patients have also shown neurological symptoms such as headache, altered conscious state, dizziness, and acute cerebrovascular illness. In COVID-19, liver injury may occur for a number of different causes, including drug-related hepatotoxicity and immune-mediated damage caused by cytokines [16].

Chronic diseases such as cardiovascular disease, lung disease, renal disease, and malignant tumours were evident in many of the older individuals with severe sickness. The elderly (those aged 65 and above) have a greater chance of having a severe SARS-CoV-2 infection due to the increased prevalence of preexisting conditions. However, while far less common, younger individuals are still being admitted to hospitals with life-threatening illnesses. Less severe illness and symptomatic infection occur less often in children [7].

Investigations

Lymphocytopenia, an increased C reactive protein, and an elevated erythrocyte sedimentation rate were the most indicative of COVID-19 in the lab. Damage to lymphocytes, either by necrosis or apoptosis, causes lymphocytopenia. COVID-19 is reflected in the degree of lymphocytopenia. Most documented paediatric instances [17] also had coinfection, and the presence of an increased procalcitonin level was a frequent feature of these patients.

Viral identification by RT-PCR from nasal and oral swabs, as well as sputum and faeces, a chest x-ray, and dynamic monitoring of inflammatory mediators (e.g. cytokines) [18] are the mainstays of COVID-19 diagnosis.

For SARS-CoV-2 nucleic acid amplification testing, the World Health Organization and the Centers for Disease Control and Prevention both advise using respiratory specimens. Patients who are asymptomatic may be screened by taking an upper respiratory specimen, such as a nasopharyngeal swab, an oropharyngeal swab, a nasopharyngeal wash/aspirate, or a nasal aspirate. When it comes to diagnosing SARS-CoV-2 infection, viral culture and RT-PCR are among the most effective and trustworthy procedures [19].

Due to a paucity of testing kits, radiological diagnostics, namely Computed tomography (CT) scan, has been employed as an early diagnosis technique for COVID-19 in several countries. The COVID-19 diagnostic criteria included abnormal findings on the chest CT scan. The chest CT scans of COVID-19 patients often showed ground-glass opacities in the early stage of the illness, both bilaterally and peripherally, and irregular-shaped pavement patterns in the later stage. ICU patients with COVID-19 at several stages of illness are shown on chest CT scans in Figure 1 [20].

Treatment

Early identification, prompt patient isolation, and protective circumstances were key to the therapy of COVID-19 patients. Traditional treatments for COVID-19 illness included dietary and respiratory assistance. COVID-19 therapeutic concepts derive mostly from studies of MERS and SARS [21].

Rest and other symptomatic therapies are standard general therapy. The World Health Organization (WHO) recommends providing patients with moderate COVID-19 with symptomatic care, including antipyretics for fever and discomfort, appropriate nourishment, and dehydration. Extracorporeal membrane oxygenation (ECMO) is recommended by the World Health Organization for individuals with refractory hypoxemia [22].

Glucocorticoids, an anti-inflammatory drug, may prevent or slow the development of respiratory failure and mortality by modulating inflammation-mediated lung damage [23]. The World Health Organization (WHO) recommends avoiding regular corticosteroid medication unless necessary for other reasons, such as the presence of chronic obstructive pulmonary disease (COPD), septic shock, or acute respiratory distress syndrome (ARDS) [24].

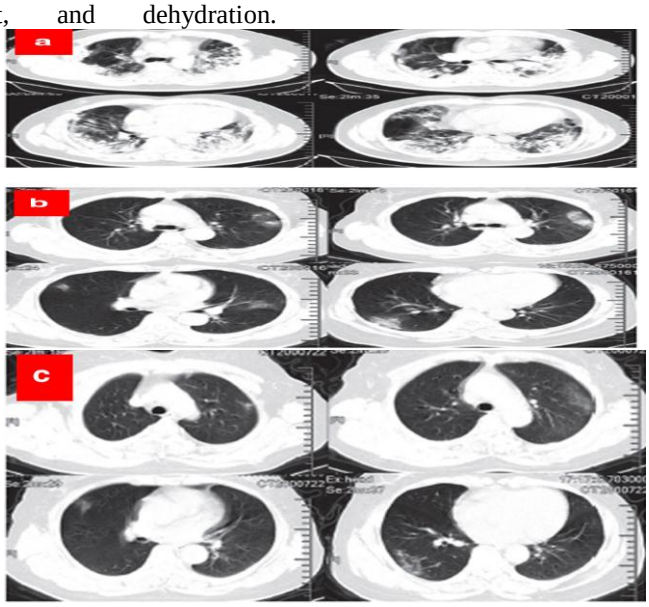

Fig. (1) (a) shows typical appearance of bilateral multiple lobular and subsegmental areas in the chest CT images. (b) shows both bilateral ground-glass opacity and subsegmental areas in the chest CT images of non-ICU patients with COVID-19, and (c) shows only the bilateral ground-glass opacity in the chest CT images at later stage of the disease **[20]**

Tocilizumab is prescribed for severe cases of rheumatoid arthritis, systemic juvenile idiopathic arthritis, giant cell arthritis, and potentially fatal cytokine release syndrome. Because tocilizumab is anti-IL-6, it is hypothesised that it may be useful in therapeutic settings. [25]

It has been observed that azithromycin improves the effectiveness of hydroxychloroquine in the treatment of severe COVID-19 patients. However, the WHO no longer recommends hydroxychloroquine in conjunction with azithromycin as therapy or prevention for COVID-19 since its effectiveness has been called into doubt by multiple major clinical investigations conducted in recent years [26].

The antiviral medication remdesivir has been demonstrated to be effective against SARS-CoV-2 in both in vitro and in vivo studies. There are a few direct anti-viral drugs for SARS-CoV-2, and this one has been authorised by regulatory agencies across the world [27].

Lung damage and ARDS may be ameliorated by mesenchymal stem cells due to their potent anti-inflammatory and immuno-modulatory capabilities, which reduce the influx of immune cells into lung tissues and the emission of pro-inflammatory cytokines. Additionally, it improves tissue healing and lessens lung fibrosis. In critically sick patients, MSCs may treat cytokine storm syndromes in addition to standard antiviral therapy, therefore halting the course of COVID-19 and decreasing death [28].

The antiviral antibodies seen in convalescent plasma (CP) taken from individuals who have made a full recovery are plentiful. Infectious illnesses like Ebola have benefited greatly from CP's usage as a curative. Neutralizing antibodies are used in the passive immunotherapy known as CP treatment. Antibodies made by CP may help the phagocytosis and complement activation processes, which together can stop the virus from replicating [29].

Rheumatoid Arthritis After Covid Injury

Joint inflammation in response to an external trigger

Formerly known as Reiter's syndrome, reactive arthritis (ReA) is now recognised as a distinct kind of spondylarthritis. It is a systemic sickness brought on

by an infection and manifested by sterile synovitis in a susceptible individual's joints [30].

Many times, a gastrointestinal or STD infection will come first. There seems to be a link between this and respiratory illnesses caused by bacteria and viruses. In young individuals, between the ages of 18 and 40, ReA is diagnosed at a higher incidence than in older populations [31].

To make a "definite" diagnosis of ReA, both main criteria and a relevant minor criterion must be met, whereas meeting either one major criterion and one or more of the minor criteria constitutes a "probable" diagnosis. It's also important to pinpoint the specific pathogen that set off the outbreak. In Table 1 [32], we have outlined the clinical criteria that must be met.

Rheumatological symptoms that develop after a confirmed diagnosis of COVID-19 and nasopharyngeal real-time polymerase chain reaction (RT-PCR) negativity at the time of articular signs beginning may be used to establish a post-COVID-19 ReA diagnosis. Relapse may occur even after a patient has been in remission [33], thus it's crucial to note that RT-PCR positive might linger even after a patient has been declared cured.

reported that the knee, talocrural (ankle), and metatarsophalangeal joints were the most often affected by ReA, which is in line with the present findings. ReA cases after COVID-19 are consistent with the clinical state of other viral-associated arthritis, which occur with a polyarticular pattern similar to rheumatoid arthritis [31], including the involvement of the hand joints.

Table (1) Clinical criteria of reactive arthritis [32]

Major criteria	1. Arthritis with 2 of 3 of the following findings: • Asymmetric • Monoarthritis or oligoarthritis • Lower limb involvement 2. Preceding symptomatic infection with 1 or 2 of the following findings: • Enteritis (defined as diarrhea for at least 1 day, and 3 days to 6 weeks before the onset of arthritis) • Urethritis (dysuria or discharge for at least 1 day, 3 days to 6 weeks before the onset of arthritis)
Minor criteria	At least one of the following: 1. Evidence of triggering infection: • Positive urine ligase reaction or urethral/cervical swab for Chlamydia trachomatis • Positive stool culture for enteric pathogens associated with reactive arthritis 2. Evidence of persistent synovial infection (positive immunohistology or PCR for Chlamydia)

- **Post covid rheumatoid arthritis**

Evidence suggests that parainfluenza and coronavirus infections, in particular, may contribute to an increased risk of developing RA. To generate an immune response and prevent future RA, it is hypothesised that early respiratory virus infections occur in the oral mucosa and lungs [34].

Joint diseases like RA have been linked to viral infections. New evidence suggested that COVID-19 infection could trigger autoimmunity. Several autoimmune disorders, including Guillain-Barré syndrome, SLE, dermatomyositis, myelitis, autoimmune hemolytic anaemia, and vasculitis, have been linked to this virus [35].

Furthermore, in severe instances of COVID-19 infection, inflammatory cells are recruited and pro-inflammatory cytokines (IL-1, IL-6, IL-10, and TNF-) are secreted. Patients with COVID-19 have also been documented to have hyperinflammatory syndrome due to an immunological over-reaction, which has been referred to as a "cytokine storm." Additionally, lymphopenia resulting in temporary immunosuppression and loss of self-tolerance [36] might account for the occurrence of autoimmunity after COVID-19.

Once COVID-19 was eradicated, there was no noticeable change in the treatment of RA [37].

Psoriatic arthritis after corticosteroid treatment

An significant extracutaneous form of psoriasis is psoriatic arthritis (PsA), a chronic, diverse, inflammatory disease affecting the musculoskeletal system. So far, only three instances of Post covid psoriatic arthritis have been documented in the medical literature. Psoriasis runs in the family in one of the reported instances. Therefore, SARS-CoV-2 infection in a susceptible individual causes psoriatic spondylarthritis [38].

Histologically verified cases of cutaneous vasculitis and a Kawasaki-like vasculitis have been associated with COVID-19 post covid vasculitis. Immune dysregulation, such as an antiphospholipid syndrome-like state or activation of complement, viral dissemination with direct systemic endothelial infection, viral RNAaemia with immune thrombosis, clotting pathway activation mediated by hypoxaemia, and immobility have all been proposed as potential underlying mechanisms for these severe manifestations [39].

Both AAV and COVID-19 often manifest with pulmonary symptoms. Multifocal bilateral ground glass opacities (GGOs) are considered the primary

radiological manifestation of the illness in COVID-19, and they may be accompanied by pleural effusion and cavitation. Due to alveolar bleeding, initial lung involvement in AAV might seem like non-specific interstitial pneumonia or a patchy ground-glass appearance, which can be misleading. Because of this, it is advised to employ serological testing and clinical data to differentiate SARSCoV-2 infection from the underlying autoimmune lung illness [40].

An infection with SARS-CoV-2 may serve as a "trigger factor" for the development of vasculitis. If a patient develops acute kidney damage after being exposed to COVID19, they should be evaluated for ANCA-associated vasculitis [39].

IgA vasculitis is linked to the 2019 coronavirus (COVID-19) infection in both children and adults. IgA vasculitis caused by COVID-19 mostly affects adults and is limited to men. Adults were shown to have a higher prevalence of arthralgia in their COVID-19-associated IgA vasculitis than children. All kidney biopsies showed IgA in the patient's system [41].

Systemic sclerosis after exposure to CoV

Interferon activation may hasten the onset of autoimmune dysregulation and the development of autoimmune disorders in those who are genetically prone to them. Intriguing parallels may be seen between COVID-19 and SSc. High amounts of IL-6, IL-10, and MCP-1 in the bloodstream are seen in both disorders, suggesting that they have a common pathophysiology. Damage to the endothelium and systemic sclerosis (SSc) are both possible outcomes of a COVID-19 infection, and both are accompanied with interstitial lung fibrosis. Radiological ground glass opacity may be seen in the early stages of both COVID-19 infection and SSc-related nonspecific interstitial pneumonia (NSIP) [42].

Arthritis post-colitis

The effect of COVID-19 on host immunological responses and functioning has generated a substantial body of study. Researchers have recently discovered that COVID-19 inhibits host innate and adaptive immune responses by interacting with various immune cells and having an influence on those cells. Suppression of host immunological responses caused by severe acute respiratory syndrome-coronavirus2 (SARS-CoV2) infection is referred to as "immunologic collapse." Patients with COVID-19 are at a higher risk of contracting opportunistic infectious germs like S. aureus because of this disease [43].

Rheumatoid arthritis with a flare-up after covid exposure

Acute exacerbation of psoriatic arthritis

Infection with SARS-CoV-2 has been linked to PsA Flares. During the period of February 2020 and April 2020, 18 psoriatic arthritis (PsA) patients with a nasopharyngeal PCR-confirmed diagnosis of COVID-19 were assessed for a PsA clinical flare. Three measurements of disease activity in psoriatic arthritis (DAPSA) were taken. DAPSA score rose after COVID-19 infection in patients with PsA [44].

Exacerbation of systemic lupus erythematosus

There have been reports of SLE flares caused by infections with parvovirus B19, herpes-zoster virus, and cytomegalovirus [45].

gout and pseudogout

Pseudogout and gout attacks after receiving the COVID-19 vaccine are very rare. Other vaccinations, such as the recombinant zoster vaccine, have also been linked to gout attacks. Most standard adult immunizations include aluminium adjuvants, and this response is thought to be mediated by the NLR family pyrin domain containing 3 (NLRP3) inflammasome. Due to the absence of aluminium adjuvants in the COVID-19 vaccine (Pfizer-BioNTech), a mechanism distinct from the activation of a wide variety of stimuli may be at play. Most hospital hospitalizations are due to a gout or pseudogout flare, and acute diseases such infections are a key risk factor for these attacks [46].

Flare of Sjögren disease (increased eye and mouth dryness) owing to covid infection was documented in a paper titled "The Impact of the COVID 19 Pandemic on Romanian Patients with Primary Sjögren Syndrome." [47].

Acute onset of vasculitis

Two examples of IgA vasculitis reactivation after COVID-19 infection have been documented in the medical literature. We provide two examples of patients in persistent remission from ophthalmic, renal, cutaneous, and articular IgA vasculitis who had a recurrence of their vasculitis soon after contracting SARS-CoV-2. Two cases were found; one had minor COVID-19 symptoms, while the other showed no signs of the virus at all. Case two came with cutaneous and renal illness suggestive with ANCA linked vasculitis, whereas case one had a recurrence characterised by hematuria, arthralgia, and cutaneous fare. Both had significant vasculitis symptoms. It is possible that COVID19 serves as an immunological trigger for vasculitis, which may have contributed to the progression of preexisting illness [48].

Disruption in the progression of systemic sclerosis

Skin inflammation, which progresses to affect the lungs and heart, is a hallmark of the documented flare. In this case, the intensity of the flare did not correspond to the moderate clinical history of COVID-19 [49], which is significant given that the patient had long-standing, stable, restricted cutaneous SSc illness.

Vaccines for COVID-19

When it comes to preventing severe illness and mortality from SARS-CoV-2 infection, vaccination is one of the most effective therapies. There is a worldwide push to vaccinate children, yet most vaccines on the market haven't been subjected to rigorous testing for safety and effectiveness [50].

Different COVID-19 Vaccines

Total viral inoculation (Sinopharm, Sinovac)

Two intramuscular injections are necessary. Protection against COVID-19 is induced by vaccination with a weakened or inactivated version of the virus. Both Sinopharm and Sinovac utilise inactivated pathogens in their vaccines, rendering them unable to infect cells or multiply while yet eliciting an immune response. Inactivated whole virus vaccines have many benefits, including being safe for those with impaired immune systems, being easy to produce, and having a long track record of success, all of which are cited by Gavi, the Vaccine Alliance (GAVI). It's possible you'll need a booster shot [51].

Vaccine mRNA or RNA (Pfizer-BioNTech, Moderna)

There should be 2 intramuscular injections. The mRNA form may seem unfamiliar and hence be misunderstood in the medical field. Cytomegalovirus (CMV), influenza, rabies, and the Zika virus are only a few of the diseases and disorders for which mRNA vaccines have been investigated in the past [52].

Laboratory-produced mRNA molecules, in this case encoding for the SARS-CoV-2 spike protein, make up the COVID-19 RNA vaccine. When injected into a living organism, mRNA guides cells to generate antigens, such as the spike protein discussed above, which are recognised by other immune cells and cause a reaction from the body's lymphocytes. The B-cells and helper T-cells promote antibody synthesis, while the killer T-cells destroy the infected cells. Future humans exposed to the coronavirus COVID-19 would be protected because their immune systems would be primed to identify it [53].

There are a number of drawbacks to using RNA as a vaccine, including the potential for unwanted immunological reactions, the difficulty of storing the vaccine in a stable form, and the fact that no such vaccine has ever been approved for use in people [54].

Sputnik V (Gamaleya Research Institute) is a non-replicating viral vector developed by Oxford-AstraZeneca.

Two intramuscular injections are necessary. Besides Fluzone, the following vaccinations have been approved for use with this method: Ebola This vaccine employs a harmless, modified strain of the virus (the "vector") to transport the antigen's genetic coding. The spike proteins on the surface of COVID-19 coronavirus are the "vector" in this vaccination. Cells that have been "infected" by a pathogen are then "trained" to create a plethora of antigens, which in turn provoke an immune response [55].

Component protein (Novavax)

Two intramuscular injections are necessary. Instead of using the whole pathogen, as with whole-pathogen vaccines, the protein subunit vaccine uses purified "pieces" of the pathogen to produce an immune response. It is assumed that unwanted effects may be reduced by limiting the immune response to the whole virus. Immunocompromised people may also benefit from the well-established method of protein subunit immunisation. It may be difficult to mass-produce this vaccine because of the potential need for adjuvants and booster injections [56].

Delta variant vaccine efficacy

British Research: Hospitalization may be avoided with only 2 doses of the vaccination. Pfizer's vaccine has an efficacy range of 79%-96%. (preventing hospitalization). According to AstraZeneca, its efficacy in avoiding hospitalisation is 92% [57].

Disease Prevention and Control Centers

Vaccination during pregnancy or breastfeeding is safe and may be given any of the approved COVID-19 vaccinations. (There is a lack of information on the safety of COVID-19 vaccinations during pregnancy, although pregnant women who get the virus are at a higher risk of serious illness or death). Any COVID-19 vaccine that has been approved by the FDA may be given to people with autoimmune disorders. To clarify, not all vaccinations include live organisms. Any COVID-19 vaccine approved by the FDA may be given to immunocompromised individuals. The Pfizer-BioNTech COVID-19 vaccination is suitable for adolescents older than 12 years. (various immunizations for those older than eighteen) [58].

Guidelines for the therapeutic use of the ACR COVID-19 vaccination in patients with rheumatic and musculoskeletal illnesses

Updated vaccination clinical guideline for patients with rheumatic and musculoskeletal illnesses has been prepared by the American College of Rheumatology (ACR) (RMD). Disease treatment in the setting of SARS-CoV-2 immunisation is always going to be case-by-case, but the ACR's COVID-19 Vaccine Clinical Guidance Task Force has prepared recommendations that may serve as a framework [59].

Factors that might increase the likelihood of contracting COVID-19

Patients with AIIRD (such as RA, PsA, axSpA, gout, lupus, vasculitis) are at a greater risk for hospitalisation because to COVID-19 and have worse results as a result. When compared to the general population of a comparable age and sex, those with AIIRD should be given access to the COVID-19 vaccination first because of the increased risk they face from the disease. [60].

Vaccine-related things to think about

Based on the current body of evidence, no one particular mRNA COVID-19 vaccination stands out as superior than the others. No data exist about the effectiveness or safety of the mRNA COVID-19 vaccine for RMD patients. Patients with RMD stand to gain a lot from vaccinations, but there is no reason to anticipate that the risks will exceed the benefits [61].

Proper dosing

Changing the dosing schedule of the following drugs may aid while adhering to a COVID-19 immunisation regimen; contact with your rheumatologist for further information. Patients with RMD who have been vaccinated against COVID-19 should nevertheless practise good hygiene and avoid close contact with others [62].

JAK inhibitors: baricitinib (Olumiant), tofacitinib (Xeljanz), upadacitinib (Rinvoq), abatacept (Orencia), and rituximab; methotrexate; mycophenolate; cyclophosphamide; (Rituxan, Ruxience, Truxima)

Recommendations

Currently, there are a variety of COVID-19 vaccines to choose from.

Patients who have autoimmune and inflammatory disorders should be immunised more often.

The American College of Rheumatology has spoken out in favour of the COVID-19 vaccination for those who suffer from rheumatic and musculoskeletal conditions.

Arthritis after covid immunisation

The protective effects of the adaptive immune response may be triggered by vaccination, which in turn may cause an inflammatory reaction. After vaccination, healthy people show potent anti-SARS-CoV-2-neutralizing antibody production along with acute elevations in type I IFN expression, oxidative stress, and DNA damage accumulation in blood mononuclear cells [50].

Serum CRP and ESR values were found to be increased in majority of the reported cases, suggesting their use in making a diagnosis. In certain circumstances, doctors choose to do an arthrocentesis on the afflicted joint to better understand the extent of the damage and rule out more serious conditions including septic arthritis, gout, or osteoarthritis. For certain individuals, imaging was considered to rule out structural anomalies or trauma and to provide a more precise pathological diagnosis. The majority of arthritis patients were treated with oral and intra-articular corticosteroids, which led to clinical remission at all follow-up sessions [63].

arthritic reaction

Vaccine-induced Reactions to Antigen (ReA) have been described; like other AIIDs, their causes are complex, including a number of different elements that might lead to an overactive immune response (e.g., genetics, hormones, the environment, etc.). The occurrence of ReA after immunisation against COVID-19 is uncommon. Immunization should be provided in accordance with current guidelines [64] since the benefits of vaccination significantly exceed the hazards.

Rheumatoid arthritis after immunisation

COVID-19 (BioNTech-Pfizer), an mRNA-based vaccination, has been linked to a case of rheumatoid arthritis (RA) in a previously healthy individual. Interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF-alpha) were not the only arthrogenic cytokines with increased serum concentrations during the active phase; type I interferon (IFN) was also upregulated. Serum levels of type I IFN, IL-6, and TNF- decreased significantly when remission was induced with methotrexate and tocilizumab. These data imply that production of type I IFN, IL-6, and TNF-α caused by COVID-19 immunisation could be implicated in this instance with new-onset RA [65].

after immunisation SLR outburst

Flares of clinical SLE after immunisation were defined as occurring within 42 days after the second dose (if second dose not received) or 4 weeks within the first dose (if second dose not received) of COVID-19 vaccination [66].

It is possible that the COVID-19 vaccines cause SLE flares following immunisation by activating these pathways through Toll-like receptor signalling. SARSCoV-2 vaccination does not seem to raise the risk of SLE flares. Flare-ups after immunisation are more common in patients with active SLE serology or a history of arthritis/discoid lesion [67].

Henoch-Schönlein purpura (HSP) is a vasculitis that may occur after vaccination; cases have been recorded mostly during the first 12 weeks after vaccination.

It was reported that a case of HSP developed after a COVID mRNA vaccination was given, suggesting that this vaccine was the probable culprit. In light of the temporal relationship, this vaccine has the risk of inducing post-vaccination vasculitis, a rather uncommon side event [68].

Timely associations between COVID-19 vaccinations from different manufacturers and cutaneous leukocytoclastic vasculitic responses have been reported [69].

References

[1] M. Hasöksüz, S. Kilic, F. Saraç. Coronaviruses and SARS-COV-2. Turk J Med Sci;50:549-56. 2020

[2] N.P. Disser, A.J. De Micheli, M.M. Schonk, M.A. Konnaris, A.N. Piacentini, D.L. Edon, et al. Musculoskeletal consequences of COVID-19. J Bone Joint Surg Am;102:1197-204. 2020

[3] M.S. Mukarram, M. Ishaq Ghauri, S. Sethar, N. Afsar, A. Riaz, K. Ishaq. COVID-19: an emerging culprit of inflammatory arthritis. Case Rep Rheumatol;2021:1102-15. 2021

[4] S. Ahmed, O. Zimba, A.Y. Gasparyan. COVID-19 and the clinical course of rheumatic manifestations. Clin Rheumatol;40:2611-9. 2021

[5] H. Zacharias, S. Dubey, G. Koduri, D. D'Cruz. Rheumatological complications of Covid 19. Autoimmun Rev;20:102-7. 2021

[6] S. Dutta, S. Dey, A. Poddar, P. Pal. Post-COVID reactive arthritis. Indian J Pediatr;89:103-5. 2022

[7] 7. X. Huang, F. Wei, L. Hu, L. Wen, K. Chen. Epidemiology and clinical characteristics of COVID-19. Arch Iran Med;23:268-71. 2020

[8] S. Rahman, M.T.V. Montero, K. Rowe, R. Kirton, F. Kunik, Jr. Epidemiology, pathogenesis, clinical presentations, diagnosis and treatment of COVID-19: a review of current evidence. Expert Rev Clin Pharmacol;14:601-21. 2021

[9] A.C. Brant, W. Tian, V. Majerciak, W. Yang, Z.M. Zheng. SARS-CoV-2: from its discovery to genome structure, transcription, and replication. Cell Biosci;11:136-45. 2021

[10] A. Sharma, S. Tiwari, M.K. Deb, J.L. Marty. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2): a global pandemic and treatment strategies. Int J Antimicrob Agents;56:106-17. 2020

[11] R. Karia, I. Gupta, H. Khandait, A. Yadav, A. Yadav. COVID-19 and its modes of transmission. SN Compr Clin Med;2:1798-801. 2020

[12] 12. H. Sharma, S. Singh, S. Pathak. Pathogenesis of COVID-19, disease outbreak: A review. Curr Pharm Biotechnol;22:1591-601. 2021

[13] M.A. Al Dhamen, A.F. Alhashim, H.H. Alqattan, F.H. Pottoo. COVID-19: An update on pathogenesis and treatment. Curr Pharm Des;27:3454-61. 2021

[14] 14. S.I. Taha, S.F. Samaan, R.A. Ibrahim, E.M. El-Sehsah, M.K. Youssef. Post-COVID-19 arthritis: is it hyperinflammation or autoimmunity? Eur Cytokine Netw;32:83-8. 2021

[15] R. da Rosa Mesquita, L.C. Francelino Silva Junior, F.M. Santos Santana, T. Farias de Oliveira, R. Campos Alcântara, G. Monteiro Arnozo, et al. Clinical manifestations of COVID-19 in the general population: systematic review. Wien Klin Wochenschr;133:377-82. 2021

[16] X.W. Xu, X.X. Wu, X.G. Jiang, K.J. Xu, L.J. Ying, C.L. Ma, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. BMJ;368:606-15. 2020

[17] Z.L. Zhang, Y.L. Hou, D.T. Li, F.Z. Li. Laboratory findings of COVID-19: a systematic review and meta-analysis. Scand J Clin Lab Invest;80:441-7. 2020

[18] A. Pourbagheri-Sigaroodi, D. Bashash, F. Fateh, H. Abolghasemi. Laboratory findings in COVID-19 diagnosis and prognosis. Clin Chim Acta;510:475-82. 2020

[19] C.C. Yip, C.C. Ho, J.F. Chan, K.K. To, H.S. Chan, S.C. Wong, et al. Development of a novel, genome subtraction-derived, SARS-CoV-2-specific COVID-19-nsp2 Real-Time RT-PCR assay and its evaluation using clinical specimens. Int J Mol Sci;21:35-45. 2020

[20] A. Zarifian, M. Ghasemi Nour, A. Akhavan Rezayat, R. Rahimzadeh Oskooei, B. Abbasi, R. Sadeghi. Chest CT findings of coronavirus disease 2019 (COVID-19): A comprehensive meta-analysis of 9907 confirmed patients. Clin Imaging;70:101-10. 2021

[21] J. Majumder, T. Minko. Recent developments on therapeutic and diagnostic approaches for COVID-19. AAPS J;23:14-20. 2021

[22] H.F. Tsang, L.W.C. Chan, W.C.S. Cho, A.C.S. Yu, A.K.Y. Yim, A.K.C. Chan, et al. An update on COVID-19 pandemic: the epidemiology, pathogenesis, prevention and treatment strategies. Expert Rev Anti Infect Ther;19:877-88. 2021

[23] P. Horby, W.S. Lim, J.R. Emberson, M. Mafham, J.L. Bell, L. Linsell, et al. Dexamethasone in hospitalized patients with Covid-19. N Engl J Med;384:693-704. 2021

[24] A. Parasher. COVID-19: Current understanding of its pathophysiology, clinical presentation and treatment. Postgrad Med J;97:312-20. 2021

[25] T. Kewan, F. Covut, M.J. Al-Jaghbeer, L. Rose, K.V. Gopalakrishna, B. Akbik. Tocilizumab for treatment of patients with severe COVID-19: A retrospective cohort study. EClinicalMedicine;24:100-18. 2020

[26] P. Gautret, J.C. Lagier, S. Honoré, V.T. Hoang, P. Colson, D. Raoult. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open label non-randomized clinical trial revisited. Int J Antimicrob Agents;57:106-25. 2021

[27] H.R. Taha, N. Keewan, F. Slati, N.A. Al-Sawalha. Remdesivir: A closer look at its effect in COVID-19 pandemic. Pharmacology;106:462-8. 2021

[28] W. Yao, L. Shi, Y. Zhang, H. Dong, Y. Zhang. Mesenchymal stem/stromal cell therapy for COVID-19 pneumonia: potential mechanisms, current clinical evidence, and future perspectives. Stem Cell Res Ther;13:124-35. 2022

[29] B. Joob, V. Wiwanitkit. Convalescent plasma and covid-19 treatment. Minerva Med:236-40. 2020

[30] K. Habas, C. Nganwuchu, F. Shahzad, R. Gopalan, M. Haque, S. Rahman, et al. Resolution of coronavirus disease 2019 (COVID-19). Expert Rev Anti Infect Ther;18:1201-11. 2020

[31] B.F. Kocyigit, A. Akyol. Reactive arthritis after COVID-19: a case-based review. Rheumatol Int;41:2031-9. 2021

[32] K. Ono, M. Kishimoto, T. Shimasaki, H. Uchida, D. Kurai, G.A. Deshpande, et al.

Reactive arthritis after COVID-19 infection. RMD Open;6:37-45. 2020

[33] D. Wendling, C. Prati, M. Chouk, F. Verhoeven. Reactive arthritis: Treatment challenges and future perspectives. Curr Rheumatol Rep;22:29-35. 2020

[34] S. Bouzid, K. Ben Abdelghani, S. Miledi, A. Fazaa, A. Laatar. Can SARS-CoV-2 infection trigger rheumatoid arthritis? A case report. Clin Case Rep;10:57-68. 2022

[35] M. Deeb, P.B. Moloney, G. McCarthy, J. Stack, T. Lynch, Y. Llamas Osorio. Inflammatory arthritis post COVID-19 infection. Ir Med J;115:525-9. 2022

[36] M. Slouma, T. Mhemli, M. Abbes, W. Triki, R. Dhahri, L. Metoui, et al. Rheumatoid arthritis occurring after coronavirus disease 2019 (COVID-19) infection: Case based review. Egypt Rheumatol:125-35. 2022

[37] K.M. D'Silva, Z.S. Wallace. COVID-19 and rheumatoid arthritis. Curr Opin Rheumatol;33:255-61. 2021

[38] 38. F. Essien, L. Chastant, C. McNulty, M. Hubbard, L. Lynette, M. Carroll. COVID-19-induced psoriatic arthritis: a case report. Ther Adv Chronic Dis;13:204-12. 2022

[39] D. McGonagle, C. Bridgewood, A.V. Ramanan, J.F.M. Meaney, A. Watad. COVID-19 vasculitis and novel vasculitis mimics. Lancet Rheumatol;3:224-33. 2021

[40] J. Kabeerdoss, R.K. Pilania, R. Karkhele, T.S. Kumar, D. Danda, S. Singh. Severe COVID-19, multisystem inflammatory syndrome in children, and Kawasaki disease: immunological mechanisms, clinical manifestations and management. Rheumatol Int;41:19-32. 2021

[41] 41. P.M. Jedlowski, M.F. Jedlowski. Coronavirus disease 2019-associated immunoglobulin A vasculitis/Henoch-Schönlein purpura: A case report and review. J Dermatol;49:190-6. 2022

[42] S. Fineschi. Case report: Systemic sclerosis after COVID-19 infection. Front Immunol;12:68-85. 2021

[43] M. Khodashahi, R. Khodashahi, Z. Saremi. Simultaneous occurrence of knee septic arthritis and coronavirus disease 2019 (COVID-19): A case report. Egypt Rheumatol;44:343-5. 2022

[44] B. Zhou, S. Kojima, A. Kawamoto, M. Fukushima. COVID-19 pathogenesis, prognostic factors, and treatment strategy: Urgent recommendations. J Med Virol;93:2694-704. 2021

[45] S. Raghavan, S. Gonakoti, I.R. Asemota, B. Mba. A case of systemic lupus erythematosus flare triggered by severe coronavirus disease 2019. J Clin Rheumatol;26:234-5. 2020

[46] 46. F.W. Wireko, S. Khalafalla, T. Jamshidi, S. Mahgoub. Septic and crystal-induced arthritis (pseudogout) post-COVID-19 vaccination. Cureus;14:239-42. 2022

[47] A. Serban, A. Mihai, A. Dima, D.V. Balaban, M. Jinga, C. Jurcut. The impact of the COVID-19 pandemic on patients with primary Sjögren syndrome. Rheumatol Int;41:1933-40. 2021

[48] 48. C. Valero, J.P. Baldivieso-Achá, M. Uriarte, E.F. Vicente-Rabaneda, S. Castañeda, R. García-Vicuña. Vasculitis flare after COVID-19: report of two cases in patients with preexistent controlled IgA vasculitis and review of the literature. Rheumatol Int;42:1643-52. 2022

[49] C. Campochiaro, G. De Luca, N. Farina, D. Vignale, A. Palmisano, M. Matucci-Cerinic, et al. Severe acute respiratory syndrome coronavirus-2-induced flare of systemic sclerosis. Scand J Rheumatol;51:156-8. 2022

[50] 50. C.C. Chen, C.J. Chen. New-onset inflammatory arthritis after COVID-19 vaccination: A systematic review. Int J Rheum Dis:27-35. 2022

[51] S.S. Khandker, B. Godman, M.I. Jawad, B.A. Meghla, T.A. Tisha, M.U. Khondoker, et al. A systematic review on COVID-19 vaccine strategies, their effectiveness, and issues. Vaccines (Basel);9:204-8. 2021

[52] F.P. Polack, S.J. Thomas, N. Kitchin, J. Absalon, A. Gurtman, S. Lockhart, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med;383:2603-15. 2020

[53] R. Noor. Developmental status of the potential vaccines for the mitigation of the COVID-19 pandemic and a focus on the effectiveness of the pfizer-biontech and moderna mRNA vaccines. Curr Clin Microbiol Rep;8:178-85. 2021

[54] J.A. De Soto, F. DSSc. Evaluation of the Moderna, Pfizer/BioNtech, AstraZeneca. Adv Res J Med Clin Sci;7:408-14. 2020

[55] R. Vanaparthy, G. Mohan, D. Vasireddy, P. Atluri. Review of COVID-19 viral vector-based vaccines and COVID-19 variants. Le Infezioni in Medicina;29:328-33. 2021

[56] J.H. Tian, N. Patel, R. Haupt, H. Zhou, S. Weston, H. Hammond, et al. SARS-CoV-2 spike glycoprotein vaccine candidate NVX-CoV2373 immunogenicity in baboons and protection in mice. Nat Commun;12:372-8. 2021

[57] A. Pormohammad, M. Zarei, S. Ghorbani, M. Mohammadi, M.H. Razizadeh, D.L. Turner, et al. Efficacy and safety of covid-19 vaccines: A systematic review and meta-analysis of randomized clinical trials. Vaccines (Basel);9:150-4. 2021

[58] Centers for Disease Control Prevention. Interim clinical considerations for use of COVID-19 vaccines currently authorized in the United States 2022 [Available from: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html.

[59] J.R. Curtis, S.R. Johnson, D.D. Anthony, R.J. Arasaratnam, L.R. Baden, A.R. Bass, et al. American college of rheumatology guidance for COVID-19 vaccination in patients with rheumatic and musculoskeletal diseases: version 1. Arthritis Rheumatol;73:1093-107. 2021

[60] V. Furer, C. Rondaan, N. Agmon-Levin, S. van Assen, M. Bijl, M.C. Kapetanovic, et al. Point of view on the vaccination against COVID-19 in patients with autoimmune inflammatory rheumatic diseases. RMD Open;7:125-35. 2021

[61] A. Tavilani, E. Abbasi, F. Kian Ara, A. Darini, Z. Asefy. COVID-19 vaccines: Current evidence and considerations. Metabol Open;12:100-24. 2021

[62] M.R. Seo, J.W. Kim, E.J. Park, S.M. Jung, Y.K. Sung, H. Kim, et al. Recommendations for the management of patients with systemic rheumatic diseases during the coronavirus disease pandemic. Korean J Intern Med;35:1317-32. 2020

[63] R. Dawoud, D. Haddad, V. Shah, V. Patel, G. Abbas, S. Guduru, et al. COVID-19 vaccine-related arthritis: A descriptive study of case reports on a rare complication. Cureus;14:267-77. 2022

[64] 64. Q.J. An, D.A. Qin, J.X. Pei. Reactive arthritis after COVID-19 vaccination. Hum Vaccin Immunother;17:2954-6. 2021

[65] T. Watanabe, K. Minaga, A. Hara, T. Yoshikawa, K. Kamata, M. Kudo. Case report: New-onset rheumatoid arthritis following COVID-19 vaccination. Front Immunol;13:859-63. 2022

[66] G. Khatri, Priya, S. Shaikh, Aashish, A. Rai, H.A. Cheema, et al. Systematic lupus erythematous patients following COVID-19 vaccination: Its flares up and precautions. Ann Med Surg (Lond);80:104-25. 2022

[67] C.C. Mok, K.L. Chan, S.M. Tse. Hesitancy for SARS-CoV-2 vaccines and post-vaccination flares in patients with systemic lupus erythematosus. Vaccine;40:5959-64. 2022

[68] A.M. Hines, N. Murphy, C. Mullin, J. Barillas, J.C. Barrientos. Henoch-Schönlein purpura presenting post COVID-19 vaccination. Vaccine;39:4571-2. 2021

[69] L. Đorđević Betetto, B. Luzar, Ž. Pipan Tkalec, S. Ponorac. Cutaneous leukocytoclastic vasculitis following COVID-19 vaccination with Ad26.COV2.S vaccine: a case report and literature review. Acta Dermatovenerol Alp Pannonica Adriat;31:83-7. 2022