

Complication observed	Patient characteristics	Co-morbidities	Type of vaccine	Duration to symptom onset following vaccination	COVID status and additional investigations	Clinical features and outcome
Digital ischaemia	1. 78-year-old female	Hypertension for 5 years. Controlled on losartan.	BBIBP-CorV	48-72 hours after second dose. Milder self-limiting symptoms 3 days after the first dose. Had tingling and paraesthesia of finger tips which resolved over 1 week.	RAT and PCR both negative, ANA positive 1:80 cytoplasmic granular pattern, anti-SCL-70 antibody negative, cryoglobulins and antiphospholipid antibody screen negative, blood picture- no evidence of haemagglutination, DAT negative, myeloma screen negative, CECT chest/abdomen/pelvis negative for malignancy, CA-125, CA-19,9 and CEA negative.	Transferred from local hospital for vascular surgical opinion for acute limb ischaemia. Both hands showed ischaemia of finger tips with intact peripheral pulse. Angiogram showed patent large and medium arteries with non-visualization of digital small vessels. Dry gangrene of 8 of the finger tips (entire distal phalanges) despite prostacyclin. Pain resolved after 1 month. 2-3 months later, bilateral ankle oedema. Moderate to severe pulmonary hypertension on 2D-echocardiography with distal small multiple segment thromboembolism on CTPA. This happened while she was on apixaban and therefore switched to warfarin. Patient died 8 months later from complication of heart failure.
	2. 65 year old female	Diabetes mellitus for 15 years (on sitagliptin and insulin), hypertension, coronary artery disease	mRNA-1273	7 days after the second dose	RAT negative, ANA/anti-Scl 70 negative, cryoglobulins and APLS screen negative, blood picture- no haemagglutination, bilateral upper	Severe pain in bilateral hands and feet with bluish discoloration. Referred by the vascular surgeon querying Raynaud's phenomenon. Nifedipine and sildenafil not tried due to recent myocardial infarction and use of nitrates. Rapid response of symptoms with bosentan 62.5mg bd and

		with recent NSTEMI			and lower limb arterial duplex showed no significant large or medium vessel narrowing.	prednisolone 20mg mane, latter tapered over 4 weeks. Complete resolution without tissue loss.
	3. 68-year-old female	Diabetes mellitus, hypertension and dyslipidaemia for 3 years. Well controlled on sitagliptin 50mg mane, losartan 50mg daily and rosuvastatin 20mg nocte.	AZD1222 (ChAdOx1)	48-72 hours after the second dose	ANA and ANCA negative, cryoglobulin negative, APLS screen negative, CT angiogram and skin biopsy declined by patient, upper and lower limb arterial duplex- normal upper limb arteries, right lower limb arteries showing arteriosclerosis and atherosclerotic plaques with 40% occlusion of the proximal part of posterior tibial artery. Left lower limb normal. Malignancy screening (CECT chest/abdomen/pelvis, CA-125, CEA, CA-19,9) negative, CMV	First presentation to surgical casualty with fresh bleeding per rectum. Sigmoidoscopy- severe ulcerative proctitis. Biopsy not attempted due to friable mucosa. Noted to have severe oral ulceration at the same time. 24 hours later, severe pain in both hands and feet with cyanosis of digital tips. Gangrene of a pre-existing small wound and a capillary blood sugar monitoring site on two digits of right hand. Concomitant extensive vasculitic rash of gravity dependent areas (buttocks, both lower limbs with more around ankles, around elbows). Acral cyanosis resolved with bosentan 62.5mg bd rapidly titrated to 125mg bd over 1 week. On-going pain needed pain-team intervention. Vasculitic rash and oral/rectal ulceration responded to prednisolone 60mg daily tapered off over 4 months to nil. Patient off all medication except regular medication 12 months from symptom onset. Lost two distal phalanges of right hand and two toes of right foot.

					IgM and IgG negative.	
	4. 60-year-old female	Diabetes for 5 years and hypothyroidism for 3 years.	mRNA-1273 2 doses and the 3 rd dose BNT162b 2	Within 1 week of Pfizer vaccine	COVID RAT and PCR both negative on admission on day 1 of symptoms	Rapidly progressive discolouration (bluish black) of multiple fingers bilaterally. Proximal and distal pulse normal with no bruits. ANA positive at 1:320 (cytoplasmic patterns) but no other features of an autoimmune connective tissue disease. Progression of gangrene stopped on bosentan combined with prednisolone 20mg mane on a tapering regimen. Bosentan stopped after 6 months. Cryoglobulins, serum protein electrophoresis, blood picture, clotting studies normal and APLS screening negative. Full functional recovery with only tissue loss at the tip of right thumb.
De novo inflammatory arthritis	5. 58-year-old female	Hypertension for 3 years. Controlled on losartan. Urolithiasis	Gam-COVID-Vac	14 days after the second dose	COVID RAT negative when tested 2 days after symptom onset	Overnight explosive development of polyarthritis. Presented 2 weeks after onset of joint symptoms. Swollen joints-10, tender joints-6, visual analogue scale 9/10 for pain. Partial pain response to NSAIDs from the GP but joint swelling worsening. Same with oral prednisolone. Rheumatoid factor negative, cannot afford HLA B27 and ANA. Started on methotrexate alongside tapering steroids. Attained remission at 3 months. Later lost to follow-up.
	6. 28-year-	Previously well	BNT162b 2	10-14 days after second dose	Unknown. Initial presentation 3 months after	Developed bilateral ankle joint pain and swelling associated with bilateral plantar fasciitis. Good

	old male				symptom onset once treatment from GP had failed.	response to NSAID's but cannot tolerate due to side effects. Good response to steroids but relapsing on tapering to less than 10mg daily, 3 months after the onset. Started on sulphasalazine and achieved remission at 3 months. Negative rheumatoid factor. Cannot afford HLA B27 and ANA.
	7. 32-year-old male	Previously healthy	mRNA-1273	10 days after the 2 nd dose	Unknown. Presented 2 months from symptom onset.	Right ankle followed by right knee and later bilateral shoulder inflammatory pain with swelling. Persisting more than 2 months despite NSAID's by GP. Started on prednisolone and methotrexate and achieved remission within 3 months. Negative rheumatoid factor. Cannot afford HLA B27 and ANA.
	8. 56-year-old female	Previously healthy	mRNA-1273	1 week after the second dose	COVID RAT negative on day 1 of symptoms	Severe inflammatory polyarthralgia. Treated by GP with NSAID's but no response. Later treated with oral methylprednisolone successfully. Presented 1 week after stopping steroids in a severe flare, unable to walk due to severe synovitis of left knee. Moderate synovitis noted in 7 other joints. Rheumatoid factor 156 U/L (normal <14 U/L). Achieved remission within 2 months on methotrexate.
	9. 27-year-	Previously healthy	BNT162b 2	7 days after the second dose	COVID RAT not done at the time of onset of	Bilateral ankle and knee inflammatory pain with morning stiffness over 2 hours. Associated

	old male				symptoms. No respiratory symptoms at the time. Presented 2 months after symptom onset.	right plantar fasciitis. Initially managed with NSAIDs as reactive arthritis but recurred on stopping treatment twice, and symptoms persisted beyond 3 months. Later managed as peripheral spondyloarthritis. Attained remission which he maintains on methotrexate alone currently. Rheumatoid factor negative. ANA- not done since cannot afford.
	10. 62-year-old female	Bronchial asthma for 40 years	Gam-COVID-Vac	2-3 weeks after the second dose	COVID RAT negative on day 2 of symptoms	Bilateral ankle and metatarsophalangeal joint (all) asymmetrical Inflammatory arthritis with symptom onset 2-3 weeks after the vaccine. Rheumatoid factor negative. Several courses of NSAIDs given by GP and symptoms recurred on stopping each time. Remission induced with steroids and now maintaining remission on sulphasalazine.
	11. 52-year-old female	Thalassaemia trait	mRNA-1273	5-7 days after first dose with step-wise progression with booster doses	COVID testing not done	Widespread enthesitis and bilateral knee and ankle inflammatory arthritis progressively worsening with each booster dose. Presented 7 months from symptom onset with several relapses on tapering steroids by GP. Currently in remission with methotrexate 20mg/week.
	12. 64-year-	Diabetes mellitus, hypertension and	Gam-COVID-Vac 2 doses and	Step-up worsening of inflammatory arthralgia 2-3	COVID RAT not done. But no respiratory symptoms.	2-3 days after each dose, inflammatory polyarthralgia. 10-14 days after the third dose, symptoms significantly worsened with

	old female	dyslipidaemia for 6 years with good control	BNT162b 2 as the 3 rd dose	days after each dose		inflammatory arthritis. Now in remission with methotrexate, having failed steroid monotherapy. Rheumatoid factor- 16 IU/L (lab normal range <8 IU/L)
Severe autoimmune haemolytic anaemia with positive ANA	13. 53-year-old female	Previously well.	mRNA-1273	2-3 days after the second dose	COVID RAT and PCR both negative	Progressive shortness of breath, fatigue and palpitations starting 2-3 days after the second dose of the vaccine. Cold antibody autoimmune haemolytic anaemia diagnosed later with Hb 6g/dL. C3d DAT positive. Complement C4 low (5.6 mg/dL), C3 normal. ANA positive 1:160 nuclear homogeneous pattern. Initial good response to IV methylprednisolone but relapse following switch to oral prednisolone 1mg/kg/day. After 2 months of failure of achieving response despite high dose steroids, started on rituximab. Currently maintaining remission off steroids and on hydroxychloroquine 200mg daily.
Cutaneous vasculitis with inflammatory oligoarthritis	14. 41-year-old male	Previously healthy	mRNA-1273	7 days after the second dose	COVID RAT negative on day 2 of symptoms	Bilateral ankle and foot joint swelling with inflammatory pain and vasculitic rash up to bilateral knee level. ANCA negative. ANA positive nuclear cytoplasm pattern 1:320. ESR 50 mm/1 st hour. Good response to 30mg of prednisolone with tapering but inflammatory arthritis recurred 2 weeks after stopping steroids. Patient could not tolerate methotrexate. Currently maintaining remission on leflunomide 20mg

						daily, 8 months after starting treatment.
Isolated cutaneous vasculitis	15. 45-year-old female	Previously healthy	BNT162b 2	5-7 days after the second dose	COVID RAT and PCR both negative	Cutaneous vasculitis over both lower limbs up to mid-thigh level without any systemic involvement. ANCA and ANA negative. Skin biopsy refused by patient. Rapidly responded to 0.5mg/kg/day of prednisolone and maintained remission on stopping steroids.
Worsening pre-existing autoimmune rheumatological conditions	16. 32-year-old female	Peripheral spondyloarthritis treated by a rheumatologist for 2 years with sulphasalazine and later stopped successfully. Asymptomatic for 5 years off treatment.	BBIBP-CorV	10-14 days after second dose	Seen 12 weeks after onset of symptoms when self-treatment with NSAIDs failed. Therefore COVID testing not available.	14 tender joints and 8 swollen joints on presentation. Responded to prednisolone but relapsed on stopping. No response to sulphasalazine after 3 months. Later achieved remission on methotrexate.
	17. 56-year-old male	Seropositive rheumatoid arthritis for 15 years. In remission for 7 years on hydroxychloroquine 200mg bd and methotrexate 15mg/week	mRNA-1273	10-14 days after the second dose	COVID testing not done	No response to two courses of tapering prednisolone with relapse at doses less than 7.5mg per day and walking with crutches by 2 months after onset of flare. DAS28: 7.39. Later maximized DMARDs and currently maintaining remission on methotrexate 22.5mg per week and hydroxychloroquine 200mg bd.
	18. 24 year old female with	SLE with class VI lupus nephritis and end-stage	BBIBP-CorV	7 days after the 1 st dose	COVID RAT and PCR both negative	Quiescent extra-renal disease for 7 months preceding. Presented with suicidal ideation, very low mood and self-inflicted injury. ESR >100

		chronic kidney disease. Active extra-renal disease needing varying doses of azathioprine, prednisolone, hydroxychloroquine and intermittent doses of rituximab since referral to our centre 8 years before.				mm/1 st hour with complement C3 and C4 both dropping. Hb 6g/dl on admission with evidence of active autoimmune haemolysis. She had haemolysis as part of SLE only at the time of diagnosis >11 years ago and never had recurrence after that. Treated with IV methylprednisolone and IV rituximab with remission achieved.
	19. 32-year-old female	Seropositive rheumatoid arthritis for 10 years and in remission for 2 years on methotrexate 20mg/week	Gam-COVID-Vac 2 doses and BNT162b2 as the 3 rd dose	No symptoms following the first 2 doses. Symptom onset 5-7 days after the 3 rd dose	COVID RAT negative	Admitted to ward with a severe polyarticular flare 5-7 days after 3 rd dose. Poor response to oral prednisolone 20mg mane for several days. Responded to IV methylprednisolone 500mg single dose and later combined methotrexate with leflunomide to maintain remission.
	20. 32-year-old female	SLE for over 5 years with good control on azathioprine and hydroxychloroquine for 2 years.	mRNA-1273 2 doses and BNT162b2 1 dose	Onset 2-3 weeks after the first dose and step-wise worsening 10-14 days following each booster dose	COVID RAT and PCR both negative	2-3 weeks after the 1 st dose, constitutional symptoms with increasing hair loss and rising ESR. Step-up worsening with subsequent doses and not controlled on high dose oral prednisolone. 10 days after the 3 rd dose, admitted with moderately severe acute cutaneous and subacute cutaneous lupus. BILAG A severity in mucocutaneous and constitutional domains. Low complement C3 and C4. Remission achieved with IV cyclophosphamide

RS3PE-like picture	21. 78-year-old male	Hypertension for 12 years and diabetes mellitus for 8 years. Well-controlled	mRNA-1273	5-7 days after the second dose	COVID testing not available.	Severe dorsal palm oedema with pain and stiffness in all fingers. Distribution like RS3PE. Partial response to NSAIDs. Presented 2-3 weeks after onset. Excellent response to prednisolone 20mg daily but relapsed on slow taper. Currently in remission with methotrexate 20mg weekly, leflunomide 20mg daily and prednisolone 5mg every other day. Rheumatoid factor and ANA negative, malignancy screening negative.
Unusual cognitive symptoms with positive ANA	22. 19-year-old girl	Previously healthy	BNT162b2	4 days after the first dose,	COVID RAT and PCR both negative	Admitted to a national grade hospital with severe shortness of breath and inability to walk. Described as legs not obeying her commands with head feeling muddled and dissociated. Widespread paraesthesia. Pulmonary embolism excluded, neurological examination objectively normal. ESR 26mm/1 st hours, MRI brain normal and all other investigations normal initially. ANA positive 1:80 cytoplasmic pattern. Managed as a functional neurological disease referred to a psychiatrist. Referred to rheumatologist 6 weeks later due to on-going dissociated feeling, headache and inability to concentrate with the positive ANA. Side effects with anti-depressants and anxiety medication. Started on

						prednisolone 15mg daily with a slow taper over 3 weeks. Within 24 hours of the first dose, marked improvement in all the symptoms. Currently off steroids and back to baseline.
Primary cerebral vasculitis	23. 56-year-old female	Previously healthy	mRNA-1273	Within 2-3 weeks of the second dose,	COVID RAT and PCR both negative	Admitted to orthopaedic ward with an unwitnessed fall from a height and a compound fracture of the left lower limb. Fall appeared to be accidental. Family members reported preceding subtle personality changes with the patient being more moody and withdrawn over preceding one week. MRI with venogram and arteriogram of brain: cerebral vasculitis with fresh lesions and absent old lesions. ANA positive 1:320, NUMA pattern. Complements normal and no other peripheral features of SLE. Open wound at fracture site with infection. Therefore treated with IVIg. Dramatic response of behavioural changes and raised ESR. Currently in remission on azathioprine.
	24. 56-year-old female	Previously healthy	mRNA-1273	5-7 days of first dose and step-wise progression with the second booster dose.	COVID RAT negative on first presentation 3 weeks from the 2 nd booster dose	Described about 7 years of subjective feeling of imbalance. But could manage very well. Investigated but never found a cause. Within a few days of the 1 st dose, worsening imbalance. By the time of the 2 nd dose 3 months later, could not even stand in the line independently due to imbalance. Within 2 weeks of the

						<p>second dose, needed support to get up from seated due to imbalance. Visible tendency to fall. Neurological examination normal with no cerebellar signs except positive tandem gait. Romberg's negative. MRI brain- cerebral vasculitis with fresh lesions only. ANA positive 1:1000 cytoplasmic granular pattern. Initial excellent response to IV methylprednisolone but recurrence on switching to high dose oral prednisolone. Cyclophosphamide 500mg/m² 2 weekly for 6 doses with good response. Maintenance on tapering steroids and mycophenolate mofetil. MRI 1 year later-no new lesions. Currently tapering MMF.</p>
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Supplemental file table 1- details of the clinical cases of patients with immunologic and thrombotic complications following COVID 19 vaccination. (*RAT- Rapid Antigen Test, PCR- Polymerase Chain Reaction, DAT- Direct Antiglobulin Test, CTPA- Computerized Tomography Pulmonary Angiogram, ANA- Anti-Nuclear Antibody, APLS- Anti-Phospholipid Syndrome, CECT- Contrast Enhanced Computerized Tomography, CEA- Carinoembryonic Antigen, NSTEMI- Non ST-Elevation Myocardial Infarction, ANCA- Anti-Neutrophil Cytoplasmic Antibody, NSAID- Non-Steroidal Anti-Inflammatory Drug, HLA B27- Human Leukocyte Antigen B27, ESR- Erythrocyte Sedimentation Rate, DAS 28- Disease Activity Score 28, DMARD- Disease Modifying Anti-Rheumatoid Drug, BILAG- British Isles Lupus Assessment Group, RS3PE- Remitting Symmetrical Seronegative Synovitis and Pitting Edema, MRI- Magnetic Resonance Imaging, SLE- Systemic Lupus Erythematosus, IVIg- Intravenous Immunoglobulin, MMF- Mycophenolate mofetil*)