Vasculitis and administration of COVID-19 vaccines

Introduction

To date, the European Medicines Agency (EMA) authorised four COVID-19 vaccines for active immunisation against SARS-CoV-2: BioNTech/Pfizer (Comirnaty®), Moderna (SpikeVax®), AstraZeneca (Vaxzevria®) and Janssen [1]. BioNTech/Pfizer and Moderna are both mRNA vaccines, encoding the viral spike (S) protein while AstraZeneca and Janssen are using an Adenovirus vector. All COVID-19 vaccines are subject to additional monitoring [2-5].

The most widely given vaccine in the Netherlands is the Pfizer/BioNTech vaccine (Comirnaty®) [6]. It is indicated for *active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus, in individuals 16 years of age and older* [2]. The nucleoside-modified messenger RNA in Comirnaty® is formulated in lipid nanoparticles, which enable delivery of the nonreplicating RNA into host cells to direct transient expression of the SARS-CoV-2 S antigen. The mRNA codes for membrane-anchored, full-length Spike glycoprotein with two point mutations within the central heli. Comirnaty® has been registered in Europe since December 21st, 2020 [2].

Vasculitis is a term for a group of rare autoimmune disease that have in common inflammation of blood vessels, both arteries and veins. The disease can be limited to the skin (cutaneous vasculitis), but can also affect any organ system of the body (systemic vasculitis). Vasculitis can range from mild to life-threatening. Early detection and treatment can prevent permanent damage [7].

Vasculitis is usually classified according to the size of vessel involved: small-vessel, medium-vessel, large-vessel and variable-vessel vasculitis. The 2012 International Chapel Hill Consensus Conference on the Nomenclature of Systemic Vasculitides (CHCC 2012) also developed names and definitions for the most common forms of vasculitis [7]. The most common form in Western countries is Giant Cell Arteritis [8]. Immunoglobulin A vasculitis (Henoch-Schönlein purpura) and Kawasaki disease are the most common vasculitides of childhood [9]. Table 1 shows the vessel size classification and the several types, incidence and age at time of onset of the vasculitides.

The most common causes of vasculitis include infections, immunologic conditions, drug reactions and malignancies. The cause of many vasculitides remains unresolved [10]. The pathophysiology of vasculitis is poorly understood. Clinical and laboratory-based evidence has supported the hypothesis that immunologic mechanisms appear to play an active role in mediating the necrotizing inflammation of blood vessels [11].

This signal provides an overview of all reports of vasculitis following COVID-19 vaccinations reported to the Netherlands Pharmacovigilance Centre Lareb, up to August 7th.

Table 1. Classification of vasculitis according to the 2012 CHCC classification including incidence and age of onset

Type	Incidence	Age of onset
Small-vessel vasculitis		
Antineutrophil cytoplasmic antibody (ACNA) associated vasculitis (AAV) - Granulomatosis with polyangiitis (Wegener's) (GPA) - Microscopic polyangiitis (MPA) - Eosinophilic granulomatosis with polyangiitis (Churg-Strauss) (EGPA)	The incidence in Europe is 20-25 cases of AAV per million per year [12].	AAV can present at any age, but incidence rises progressively with age until the mid-late 80s [12].
IgA vasculitis (Henoch-Schönlein purpura) (HSP)	The incidence in children is 6-22 per 100,000 personyears. The incidence in adults is 3.4-14.3 per 100,000 personyears [13].	HSP usually occurs in children aged between 2-10 years and mostly between 4-6 years. The disease occurs more frequently in male [9].
Cryoglobulinemic vasculitis	The incidence is unknown, but the prevalence is about 1 in 100,000 [14].	The disease appears more commonly in patients aged 45-65 years. The disease is more common in women [14].
Hypocomplementemic urticarial vasculitis (anti-C1q vasculitis) (HUV)	HUV is a rare disease. The incidence in Europe is unknown, but the incidence in Sweden is 0.7 cases per million [15].	In Sweden, the median age at diagnosis was 51 years. HUV is more common in women [15].

Type	Incidence	Age of onset
Anti-glomerular basement membrane disease (anti-GBM)	The estimated frequency is 1 to 2 cases per million population per year in European populations [16].	Anti-GBM disease seems to have a bimodal distribution, with younger patients (20–30 years old) being more frequently male and older patients (60–70 years old) being more frequently female [16].
Medium-vessel vasculitis		
Polyarteritis nodosa (PAN)	The annual incidence in three regions of Europe is about 4.4 to 9.7 per million [17].	PAN commonly occurs in middle-aged or older adults and incidence rises with age with a peak in the 6th decade of life. The disease occurs more frequently in male [17].
Kawasaki disease (KD)	The disease is more common in Asian countries than those in Europe. The annual incidence in Europe is 5-10 cases per 100,000 children < 5 years [18].	KD usually occurs in children < 5 years [18] The disease occurs more frequently in boys [19].
Large-vessel vasculitis		
Giant cell arteritis (GCA)	The highest reported incidence is 20 per 100,000 people ≥ 50 years (found in Scandinavian countries and Minnesota) [20].	GCA commonly occurs in older people (≥ 50 years) with a peak incidence in the age group 71-80 years. The incidence increases with age. GCA is more common in women [20].
Takayasu arteritis (TA)	The disease is more common in Asian countries than in Europe. The incidence in Europe is 0.4 to 1.5 cases per million [21].	TA commonly occurs in young people with a peak age of onset between 20 and 30 years. TA is more common in women [21].
Variable-vessel vasculitis		
Cogan's syndrome	Cogan's syndrome is a rare disease. The incidence is unknown [22].	The disease primarily affects young adults. The average age of disease onset is 29 years [22].
Behçet's disease (BD)	BD is very rare in Europe. The incidence in Europe is unknown, but the incidence in the UK is 0.64 cases per 100,000 [23].	BD typically affects young adults 20 to 40 years of age [23].

Reports

In the period from January 6th, 2021 until August 7th, 2021 the Netherlands Pharmacovigilance Centre Lareb received 65 spontaneous reports of vasculitides associated with administration of COVID-19 vaccines. In addition to the spontaneous monitoring system, Lareb also follows a cohort of vaccinated persons through an Intensive Monitoring Study (LIM). In this cohort, three persons reported vasculitis following COVID-19 vaccination (table 2). In total, 68 cases were included in this analysis.

Reports with the following MedDRA High Level Term (HLT) and Preferred Term (PT) were selected: HLT vasculitides NEC, HLT vasculitides, HLT skin vasculitides and PT erythema elevatum diutinum). Table 3 provides an list of the reported vasculitic events (PT level) and table 4 provides a more detailed overview of the 68 cases.

Table 2. Number of persons developing vasculitis in LIM (version date dataset: 30-09-2021)

	N male	N female	Cohort size in LIM	
			1st dose	2nd dose
Comirnaty®	1	1	12.887	10.927
Vaxzevria®	-	1	8.781	5.556
SpikeVax®	-	-	3.424	2.602
Janssen vaccine	-	-	2.458	-

Table 3. List of reported vasculitic events (spontaneous and LIM)[1]

Preferred Term	Number of times reported
Vasculitis	25
Cutaneous vasculitis	13
Giant cell arteritis	11
Vasculitic rash	8
Microscopic polyangiitis	2
Anti neutrophil cytoplasmic antibody (ANCA) positive vasculitis	2
Capillaritis	2
Erythema elevatum diutinum	1
Hypersensitivity vasculitis	1
Injection site vasculitis	1
Susac's syndrome	1
Palpable purpura	1
Urticarial vasculitis	1

Table 4. Overview of reported cases of vasculitic events in the Netherlands for COVID-19 vaccines (spontaneous and LIM)

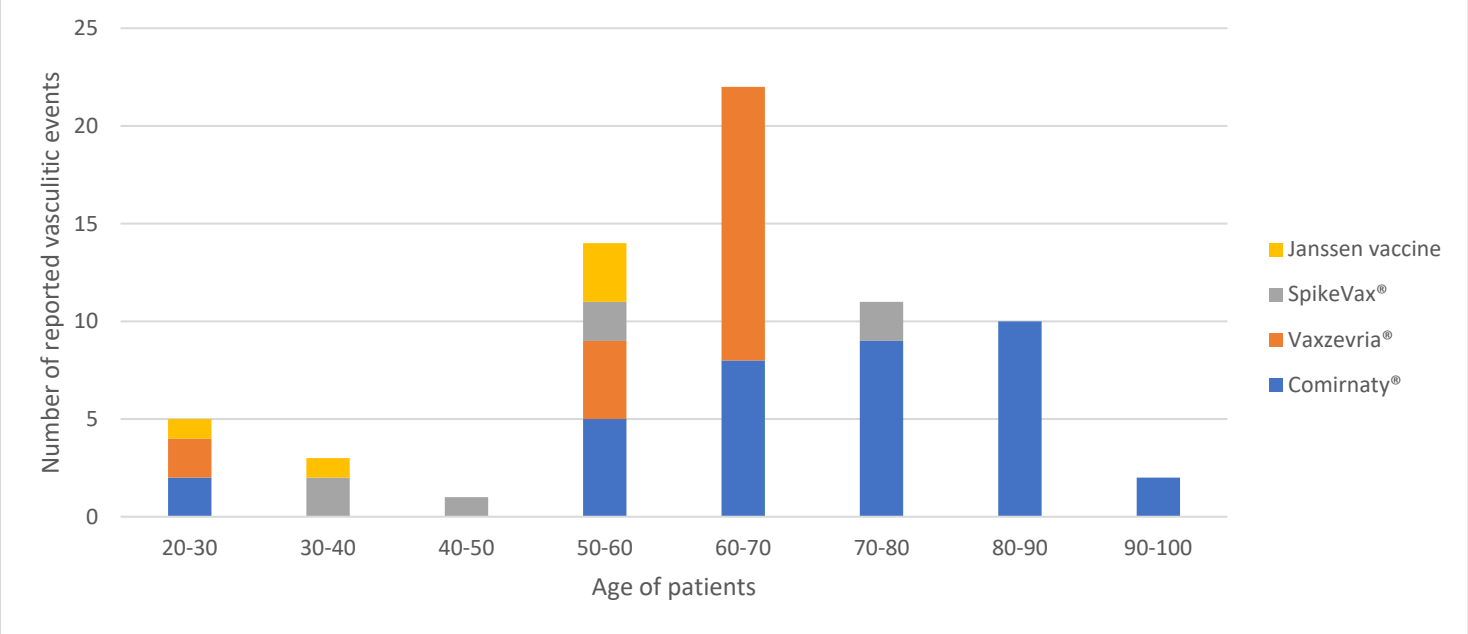
Brand	**Comirnaty®**	**Vaxzevria®**	**SpikeVax®**	**Janssen vaccine**
N Total	36	20	7	5
N Men (percentage)	12 (33.3%)	5 (25%)	2 (28.6%)	3 (60%)
N women (percentage)	24 (66.7%)	15 (75%)	5 (71.4%)	2 (40%)
After Dose 1 (percentage)	22 (61.1%)	19 (95%)**	4 (57.1%)	5 (100%)
After Dose 2 (percentage)	14 (38.9%)	2 (10%)**	3 (42.9%)	N/A
Median age (range)	73.5 (24 – 98)	62 (22 – 69)	54 (32 – 73)	52 (27 – 53)
Mean TTO# (range) in days	8.6 (0.2 – 24)	9.3 (0.25 – 26)	5.9 (1 – 16)	4.6 (2 – 9)
Median TTO (IQR$) in days	7 (2 – 15.75)	8 (3.75 – 12.75)	3 (3 – 10)	4 (2.5 – 7)
Percentage patient recovered or recovering (*at time of reporting*)	80.6%	80%	71.4%	80%
PT	10x vasculitis 9x cutaneous vasculitis 9x giant cell arteritis 4x vasculitic rash 2x apillaritis 1x ANCA	14x vasculitis 2x vasculitic rash 2x microscopic polyangiitis 1x ANCA 1x giant cell arterits 1x palpable purpura	2x vasculitic rash 1x vasculitis 1x susac's syndrome 1x injection site vasculitis 1x giant cell arteritis 1x erythema elevatum diutinum	4x vasculitis 1x urticarial vasculitis

[1] *The list contains a total of 69 adverse events. One of the reports (NL-LRB-00651263) contains two adverse events that fall within the selected PTs.*

	1x hypersensitivity vasculitis			

*** One patient developed vasculitis following the first and second vaccination*
 # TTO = Time to onset
$ ICR = Inter Quartile Range

Figure 1. Age differentiation of reported vascultic events with COVID-19 vaccines



Detailed description of selected cases
To illustrate, a description of 10 well documented cases is given below.

NL-LRB-00506820 (reported by student pharmacy)
A 80-90 years-old male developed injection site reactions, arthralgia, fatigue, malaise, lip oedema and erythematous induced confluent papules. The reactions occurred 12 days after his first Pfizer COVID-19 vaccine. Skin biopsy showed dermatitis and vasculitis. Lab tests showed elevated neutrophilic granulocytes and monocytes. The patient recovered.

Treatment: prednisone
Concomitant medication: not reported
Medical history: not reported

NL-LRB-00510090 (reported by physician)
A 80-90 years old man developed skin abnormalities on legs, arms and trunk 9 days following his first vaccination with the Pfizer COVID-19 vaccine. He also experienced leg oedema with decreased mobility. A skin biopsy was performed and leukocytoclastic vasculitis was diagnosed. The patient was seen at the ER but was not admitted. The patient did not experience any infection in the weeks before vaccination and neither in the time between vaccination and onset of the leucocytoclastic vasculitis. The patient recovered after 12 days.

The patient is known with renal failure with eGFR of 13 ml/min, which decreased to 11 ml/min and was 12 ml/min 19 days after recovery of the patient. Hemoglobin was 7,3, decreased to 5,8 and increased to 6,5 mmol/L 19 days after recovery.

Treatment: clobetasol (topical)
Concomitant medication: temazepam, omeprazole, amlodipine (usage for more than 2 years)
Medical history: prostatitis, small kidney, hemianopsia, chronic renal impairment, hypertension, cataract operation, tinnitus, deep venous thrombosis, chronic kidney disease stage 4 (based on nephrosclerosis)

NL-LRB-00525454 (reported by physician)
A 80-90 years old male developed exaggerated rash with numerous non-blanchable petechia on his arms and legs 2 days following vaccination with the Pfizer COVID-19 vaccine. The patient had no pruritis, pain, malaise, fever or

decreased appetite. Blood test showed no elevated infection levels. The photos sent matched the diagnosis vasculitis. The patient is recovering 26 days after onset.

Treatment: none
Concomitant medication: rivaroxaban, ferrous fumarate, paracetamol tamsulosin, cholecalciferol
Medical history: COVID-19 infection (three months before vaccination)

NL-LRB-00534391 (reported by consumer)
A 50-60 years old female experienced arthralgia, headache, pain in legs, leg oedema, fatigue and vasculitic rash 7 days after vaccination with the AstraZeneca COVID-19 vaccine. Blood test showed a normal thrombocyte count. Biopsy was not performed. The photos sent matched the diagnosis vasculitis. The patient had not recovered at the time of reporting.

Treatment: none
Concomitant medication: none
Medical history: none

NL-LRB-COVID-00479425 (reported via LIM)
A 80-90 years old male experienced fatigue and red bumpy rash respectively 1 and 8 days after second vaccination with the Pfizer COVID-19 vaccine. The rash started on his left leg and spread to his knee, calf, back, buttocks and chest. A skin biopsy was performed which showed capillaritis.

Treatment: not reported
Concomitant medication: loperamide, calcium carbonate/cholecalciferol
Medical history: not reported

NL-LRB-00552137 (reported by consumer)
A 60-70 years old female developed petechiae (especially on her lower legs) 9 days after her first vaccination with the AstraZeneca COVID-19 vaccine. Blood test showed an increased CRP and skin biopsy showed vasculitis. The photos sent matched the diagnosis vasculitis. The patient recovered after 2 weeks. After her 2nd COVID-19 vaccination, the reaction reoccurred after 9 days. This time, the reaction lasted 1 week.

Treatment: none
Concomitant medication: none
Medical history: COVID-19 infection

NL-LRB-00558817 (reported by physician)
A 60-70 years old female developed petechiae on her lower legs 2 days following vaccination with the first Pfizer COVID-19 vaccine. Skin biopsy was performed and diagnosis leukocytoclastic vasculitis was made. Blood tests showed a slightly increased RDW and increased liver enzymes (AP, GGT, ASAT). The patient did not experience any infection prior to vaccination and never experienced leukocytoclastic vasculitis before. The photos sent matched the diagnosis vasculitis. The patient was recovering 16 days after onset.

Treatment: clobetasol ointment
Concomitant medication: atorvastatin, levothyroxine
Medical history: fibroadenoma of breast, deep vein thrombosis, pulmonary embolism, hypercholesterolaemia, saphenectomy, colon carcinoma (treated with chemotherapy, 4 years in remission), polyneuropathy following chemotherapy

NL-LRB-00574763 (reported by A(N)IOS dermatology)
A 60-70 years old female developed blisters and painful spots on feet, legs, arms and hands 1 day after her fist AstraZeneca COVID-19 vaccination. Blood test was performed and platelet count was normal. There was no indication for systemic vasculitis. Skin biopsy was performed (HE and IF) and leukocytoclastic vasculitis was diagnosed. The patient did not experience any infection prior to vaccination. The patient never has experienced vasculitis before. The patient was recovering 4 weeks after onset.

Treatment: prednisone
Concomitant medication: none
Medical history: osteopenia, tension headache

NL-LRB-00603012 (reported by consumer)
A 50-60 years old female experienced stiffness, pain and oedema in calves, purpura and haematomas in the knee cavity and dorsal side of the lower legs. A skin biopsy was performed, but the results were not known at the time of reporting. Urine tests, ultrasound and blood tests showed no abnormalities, no inflammation and no thrombosis. The

patient has not had a recent infection. The patient did not experience vasculitis like symptoms in the past. The photos sent matched the diagnosis vasculitis. The patient had not recovered at the time of reporting.

Treatment: none
Concomitant medication: metoprolol, telmisartan, ophthalmic timolol, ophthalmic brinzolamide/brimonidine, ophthalmic bromfenac and ophthalmic hydrocortisone
Medical history: glaucoma, uveitis

NL-LRB-00603012 (reported by physician)
A 40-50 years old female experienced erythema elevatum diutinum 10 days after first vaccination with the Moderna vaccine. Erythema elevatum diutinum was confirmed by skin biopy. No further tests were performed. The GP consulted the dermatologist who suspected a casual relation with the vaccination. Therefore the second administration was postponed. The patient was recovering 12 days after onset.

Treatment: none
Concomitant medication: none
Medical history: none

Other sources of information

SmPC
Vasculitis is not listed in the SmPC of the Covid-19 vaccines [2-5].

Other databases
In VigiBase, the WHO global database of individual case safety reports (ICSRs), 2,124 reports with above mentioned HLTs and PTs were found (version date dataset: 26-09-2021). This number includes the reports from the Netherlands. The most reports were related to the Pfizer/BioNTech vaccine (Comirnaty®). The top 3 reported adverse events were vasculitis, giant cell arteritis and cutaneous vasculitis [24].

Data on usage
The table below provides an overview of number of dose administered per vaccine in the Netherlands.

Table 5. Overview of number of dose administered per vaccine in the Netherlands [6]

	Startdate vaccination	**Number of vaccinations until August 8th, 2021**
Comirnaty®	January 6th, 2021	16,193,199
Vaxzevria®	January 25th, 2021	2,778,829
SpikeVax®	February 12th, 2021	1,843,423
Janssen vaccine	April, 21st, 2021	777,377

Literature
Several case reports described vasculitis as possible adverse event of COVID-19 vaccination [25-42]. Table 6 provides an overview of the case reports.

Table 6. Overview of the case reports found on PubMed

Author	**Patient**	**Vaccine**	**Type vasculitis**	**Latency**	**Treatment**	**Recovery**	**Medical history**
Cohen et al. (2021)	Female, 46 years	BNT162b2 mRNA vaccine *(1st and 2nd dose)*	Leukocytoclastic vasculitis flare	2 days	Topical steroids and a prednisone taper	Unknown	Psoriasis, psoriatic arthritis, irritable bowel syndrome and leukocytoclastic vasculitis
Mücke et al. (2021)	Male, 76 years	BNT162b2 mRNA vaccine (2nd dose)	Cutaneous and gastrointestinal immune complex vasculitis	12 days	Prednisolone	Recovering	Compensated alcoholic liver cirrhosis, NYHA II heart failure, gastrectomy after gastroesophageal junction cancer, prostatectomy after prostate cancer and indwelling suprapubic catheter
Hines et al. (2021)	Female, 40 years	Pfizer vaccine (2nd dose)	Henoch-Schonlein purpura	Unknown, but within 20 days	None	Recovered	Occasional headache, Hashimoto's thyroiditis and intrauterine insemination

Author	Patient	Vaccine	Type vasculitis	Latency	Treatment	Recovery	Medical history
							(unknown days after vaccination) preceded by choriogonadotropin alfa injection and letrozole (a regimen she had received previously without complications)
Okuda et al. (2021)	Female, 37 years	Pfizer vaccine (1st dose)	ANCA-associated vasculitis	12 days	Topical steroids, garenoxacin mesylate hydrate	Recovering	Graves' disease for which propylthiouracil was taken
Shakoor et al. (2021)	Female, 78 years	Pfizer vaccine (2nd dose)	ANCA-associated vasculitis	28 days	Methylprednisolone, prednisone, rituximab	Recovering	Type 2 diabetes mellitus, hypertension, and paroxysmal atrial fibrillation
Vassallo et al. (2021)	Female, 51 years	Pfizer vaccine (1st dose)	Cutaneous lymphocytic vasculitis	6 hours	Systemic antihistamine and local steroid	Recovered	Previous COVID-19 infection
Larson et al. (2021)	Female, 83 years	Pfizer vaccine (2nd dose)	Leukocytoclastic vasculitis	Circa 5 days	Antibiotics and topical corticosteroids	Recovering	No prior dermatologic or autoimmune history or recent medication changes
	Female, 35 years	Moderna vaccine (1st dose)	Urticarial vasculitis	Within 24 hours	Antihistamines, methylprednisolone and dapsone	Recovering	Acne vulgaris and allergic rhinitis
Obeid et al. (2021)	Female, 78 years	Moderna vaccine (1st dose)	IgA vasculitis reactivation	7 days	Methylprednisolone	Recovered	IgA vasculitis with leukocytoclastic vasculitis, and renal and gastrointestinal involvement
Berry et al. (2021)	Male, 65 years	Jansen vaccine *(1st dose)*	Cutaneous small vessel vasculitis	7 days	Prednisone, triamcinolone cream and analgesics	Recovered	Hypertension, hyperlipidaemia and mechanical aortic valve replacement
Naitlho et al. (2021)	Male, 62 years	AstraZeneca vaccine (1st dose)	Henoch-Schönlein purpura	8 days	Prednisone	Recovered	Osteosarcoma of left tibia (treated with surgery and chemotherapy), intercostal shingles, tonsillectomy, prior COVID-19 infection
Villa et al. (2021)	Male, 63 years	AstraZeneca vaccine (1st dose)	ANCA-associated vasculitis	7 days	Glucocorticoids, prednisone and cyclophosphamide	Recovered	Nonrelevant medical background, previously normal kidney function, and no previous adverse reactions to vaccination
Gillion et al. (2021)	Male, 77 years	AstraZeneca vaccine *(1st dose)*	Acute granulomatous vasculitis	4 weeks	Methylprednisolone	Recovering	No significant medical history
Guzmán-Perez et al. (2021)	Female, 57 years	AstraZeneca vaccine *(1st dose)*	Cutanous small-vessel vasculitis	5 days	None	Recovering with sequelae (post-inflammatory pigmentation)	Hypertension and hypothyroidism
Sandhu et al. (2021)	Female, 55 years	ChAdOx1 nCoV-19 corona virus vaccine (recombinant) (1st dose)	Leukocytoclastic vasculitis	5 days	Prednisolone	Recovered	No comorbidities
		ChAdOx1 nCoV-19 corona virus vaccine (recombinant) (2nd dose)	Leukocytoclastic vasculitis	2 days	Topical corticosteroids	Recovered	Hypertension
Dash et al. (2021)	Male, 27 years	Whole virion inactivated coronavirus vaccine *(2nd dose)*	Urticarial vasculitis	1 day	Indomethacin, calamine lotion and levocetirizine	Recovered with sequelae (hyper-pigmentation)	No prior history of a similar disease

Author	Patient	Vaccine	Type vasculitis	Latency	Treatment	Recovery	Medical history
Bostan et al. (2021)	Male, 33 years	Inactivated COVID-19 vaccine *(1st dose)*	Leukocytoclastic vasculitis with IgA deposition	3 days	Topical mometasone furoate	Recovering	Previous COVID-19 infection
Kar et al. (2021)	Female, 46 years	Inactivated viral vaccine (COVAXIN®) (1st dose)	Cutaneous small-vessel vasculitis	5 days	Antihistamines	Recovered	Unremarkable medical history and no history of any drug intake
Kharkar et al. (2021)	Female, 31 years	Inactivated viral vaccine (COVAXIN®) (2nd dose)	Cutaneous small vessel vasculitis	4 days	Anithistaminics	Recovered with sequelae (hyper-pigmentation)	No comorbidities, no systemic problems and no prior medications

Mechanism
It is well known that vasculitis can be triggered by some drugs [10]. Vasculitic events have been described in the literature following vaccinations with various vaccines, such as influenza, human papillomavirus, hepatitis A/B, and rotavirus vaccinations [43]. Unfortunately, no mechanism has been found yet.

Vasculitis is also associated with COVID-19 disease as was described by Becker in his review [44]. The immunological mechanism leading to vasculitis in COVID-19 infection may also play a role in vaccine-induced vasculitis. This means that the reaction is not necessarily allergic, but more reactive in nature. In that case, it is expected that a second vaccination should not cause the same complaints. Lareb received one case report (NL-LRB-00552137) of a patient who experienced vasculitis after both the first and second COVID-19 vaccination. The second time the patient got vasculitis, the complaints lasted less long. In the other cases, it is not known whether the second vaccine was given or whether vasculitic events reoccurred.

Discussion and conclusion
In the period from January 6th, 2021 until August 7th, 2021 the Netherlands Pharmacovigilance Centre Lareb received 68 reports of vasculitides associated with administration of COVID-19 vaccines. More than half of the reports were well documented and contained tests, photos and/or follow up information. Slightly more than half of the reports were reported by health care professionals (56%).

Most patients (87%) in the Lareb reports were 50 years of older with a median age of 64 years. They developed the vasculitic events between 0 and 26 days with a median time of onset of 7 days. Most patients were female (68%). The data of the reports received by Lareb corresponds reasonably well with the data from the case reports in the literature. In the literature, 19 patients with vasculitic events were described. The median age of these patients was 55 years and they developed the symptoms between 0 and 28 days with a median time of onset of 5 days.12 of the 19 patients were female.

The most reported vasculitic events were vasculitis (25x), cutaneous vasculitis (13x), giant cell arteritis (11x) and vasculitic rash (8x). In all cases the disease was limited to the skin without known systemic involvement, which is beneficial for the patients. In most cases, the type of vasculitis was not specified. For example, multiple types of vasculitis can cause vasculitis, cutaneous vasculitis or vasculitic rash and therefore we cannot say for sure that one type of vasculitis stands out. However, the high number of reports of GCA is striking. GCA is also the most common type of vasculitis in the Western countries. GCA is more frequent in women. Lareb received ten reports about women with GCA associated with COVID-vaccination and one report about a man.

A possible mechanism for vaccine-induced vasculitis has not yet been found. Since vasculitis is also associated with COVID-19 infection, it can be hypothesized that the immunological mechanism leading to vasculitis in COVID-19 infection may also play a role in vaccine-induced vasculitis. This means that the reaction is not necessarily allergic in nature and it is expected that a second vaccination should not cause a reoccurrence. Unfortunately, Lareb has received very little data on the outcomes of the second vaccination in patients who developed vasculitis after their first vaccination.

Most reports to Lareb and to the WHO global database were related to the Pfizer/BioNTech vaccine (Comirnaty®). However, this vaccine has been given to most people by far. Most case reports in the literature were also associated with the Pfizer/BioNTech vaccine.

Based on the reports of vasculitis and the lack of other potential causes, a causal relationship for vasculitis and COVID-19 vaccination is suggested and should be further investigated.

References

1. European Medicines Agency. COVID-19 vaccines: authorised. (access date 14-6-2021) https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/covid-19-vaccines-authorised
2. European SPC of COVID-19 vaccine BioNTech/Pfizer (Comirnaty®). (version date 2-6-2021) https://www.ema.europa.eu/en/documents/product-information/comirnaty-epar-product-information_en.pdf
3. European SPC of COVID-19 vaccine Moderna. (version date 11-6-2021) https://www.ema.europa.eu/en/documents/product-information/covid-19-vaccine-moderna-epar-product-information_en.pdf
4. European SPC of COVID-19 vaccine AstraZeneca (Vaxzevria®). (version date 26-5-2021) https://www.ema.europa.eu/en/documents/product-information/vaxzevria-previously-covid-19-vaccine-astrazeneca-epar-product-information_en.pdf
5. European SPC of COVID-19 vaccine Janssen. (version date7-5-2021) https://www.ema.europa.eu/en/medicines/human/EPAR/covid-19-vaccine-janssen#product-information-section
6. Ministerie van VWS. Coronavirus dashboard. Version date dataset 19-09-2021 (accessed 28-09-2021)
7. Watts RA, Robson J. Introduction, epidemiology and classification of vasculitis. Best Pract Res Clin Rheumatol. 2018;32(1):3-20.
8. Sharma A, Mohammad AJ, Turesson C. Incidence and prevalence of giant cell arteritis and polymyalgia rheumatica: A systematic literature review. Semin Arthritis Rheum. 2020;50(5):1040-8.
9. Gardner-Medwin JM, Dolezalova P, Cummins C, Southwood TR. Incidence of Henoch-Schönlein purpura, Kawasaki disease, and rare vasculitides in children of different ethnic origins. Lancet. 2002;360(9341):1197-202.
10. Shavit E, Alavi A, Sibbald RG. Vasculitis-What Do We Have to Know? A Review of Literature. Int J Low Extrem Wounds. 2018;17(4):218-26.
11. Langford CA. Vasculitis. J Allergy Clin Immunol. 2010;125(2 Suppl 2):S216-25.
12. Hunter RW, Welsh N, Farrah TE, Gallacher PJ, Dhaun N. ANCA associated vasculitis. Bmj. 2020;369:m1070.
13. Lei WT, Tsai PL, Chu SH, Kao YH, Lin CY, Fang LC, et al. Incidence and risk factors for recurrent Henoch-Schönlein purpura in children from a 16-year nationwide database. Pediatr Rheumatol Online J. 2018;16(1):25.
14. Silva F, Pinto C, Barbosa A, Borges T, Dias C, Almeida J. New insights in cryoglobulinemic vasculitis. J Autoimmun. 2019;105:102313.
15. Sjöwall C, Mandl T, Skattum L, Olsson M, Mohammad AJ. Epidemiology of hypocomplementaemic urticarial vasculitis (anti-C1q vasculitis). Rheumatology (Oxford). 2018;57(8):1400-7.
16. Gulati K, McAdoo SP. Anti-Glomerular Basement Membrane Disease. Rheum Dis Clin North Am. 2018;44(4):651-73.
17. Hasanzadeh S, Alavi SM, Masnavi E, Jokar S, Rohani M. Case Report: Polyarteritis nodosa or complicated Henoch-Schonlein purpura (IgAV), a rare case. F1000Res. 2018;12(7):49.
18. Lin MT, Wu MH. The global epidemiology of Kawasaki disease: Review and future perspectives. Glob Cardiol Sci Pract. 2017;2017(3):e201720.
19. Singh S, Vignesh P, Burgner D. The epidemiology of Kawasaki disease: a global update. Arch Dis Child. 2015;100(11):1084-8.
20. Sharma A, Mohammad AJ, Turesson C. Incidence and prevalence of giant cell arteritis and polymyalgia rheumatica: A systematic literature review. Semin Arthritis Rheum. 2020;50(5):1040-8.
21. Onen F, Akkoc N. Epidemiology of Takayasu arteritis. Presse Med. 2017;46(7-8 Pt 2):e197-e203.
22. Iliescu DA, Timaru CM, Batras M, De Simone A, Stefan C. COGAN'S SYNDROME. Rom J Ophthalmol. 2015;59(1):6-13.
23. Davatchi F, Chams-Davatchi C, Shams H, Shahram F, Nadji A, Akhlaghi M, et al. Behcet's disease: epidemiology, clinical manifestations, and diagnosis. Expert Rev Clin Immunol. 2017;13(1):57-65.
24. Uppsala Monitoring Centre (UMC). VigiBase. Version date dataset 26-09-2021 (accessed 28-09-2021)
25. Berry CT, Eliliwi M, Gallagher S, Panaccione S, Klein WM, Healy AL, et al. Cutaneous small vessel vasculitis following single-dose Janssen Ad26.COV2.S vaccination. JAAD Case Rep. 2021;15:11-4.
26. Bostan E, Gulseren D, Gokoz O. New-onset leukocytoclastic vasculitis after COVID-19 vaccine. Int J Dermatol. 2021;60(10):1305-6.
27. Cohen SR, Prussick L, Kahn JS, Gao DX, Radfar A, Rosmarin D. Leukocytoclastic vasculitis flare following the COVID-19 vaccine. Int J Dermatol. 2021;60(8):1032-3.
28. Dash S, Behera B, Sethy M, Mishra J, Garg S. COVID-19 vaccine-induced urticarial vasculitis. Dermatol Ther. 2021:e15093.Berry CT, Eliliwi M, Gallagher S, Panaccione S, Klein WM, Healy AL, Stoecker B, Kallas R. Cutaneous small vessel vasculitis following single-dose Janssen Ad26.COV2.S vaccination. JAAD Case Rep. 2021 Sep;15:11-14. doi: 10.1016/j.jdcr.2021.07.002. Epub 2021 Jul 14. PMID: 34337124; PMCID: PMC8302840.
29. Gillion V, Jadoul M, Demoulin N, Aydin S, Devresse A. Granulomatous vasculitis after the AstraZeneca anti-SARS-CoV-2 vaccine. Kidney Int. 2021;100(3):706-7.
30. Guzmán-Pérez L, Puerta-Peña M, Falkenhain-López D, Montero-Menárguez J, Gutiérrez-Collar C, Rodríguez-Peralto JL, et al. Small-vessel vasculitis following Oxford-AstraZeneca vaccination against SARS-CoV-2. J Eur Acad Dermatol Venereol. 2021.
31. Hines AM, Murphy N, Mullin C, Barillas J, Barrientos JC. Henoch-Schönlein purpura presenting post COVID-19 vaccination. Vaccine. 2021;39(33):4571-2.
32. Kar BR, Singh BS, Mohapatra L, Agrawal I. Cutaneous small-vessel vasculitis following COVID-19 vaccine. J Cosmet Dermatol. 2021.
33. Kharkar V, Vishwanath T, Mahajan S, Joshi R, Gole P. Asymmetrical cutaneous vasculitis following COVID-19 vaccination with unusual eosinophil preponderance. Clin Exp Dermatol. 2021.
34. Larson V, Seidenberg R, Caplan A, Brinster NK, Meehan SA, Kim RH. Clinical and histopathological spectrum of delayed adverse cutaneous reactions following COVID-19 vaccination. J Cutan Pathol. 2021.
35. Mücke VT, Knop V, Mücke MM, Ochsendorf F, Zeuzem S. First description of immune complex vasculitis after COVID-19 vaccination with BNT162b2: a case report. BMC Infect Dis. 2021;21(1):958.
36. Naitlho A, Lahlou W, Bourial A, Rais H, Ismaili N, Abousahfa I, et al. A Rare Case of Henoch-Schönlein Purpura Following a COVID-19 Vaccine-Case Report. SN Compr Clin Med. 2021:1-4.
37. Obeid M, Fenwick C, Pantaleo G. Reactivation of IgA vasculitis after COVID-19 vaccination. Lancet Rheumatol. 2021;3(9):e617.
38. Okuda S, Hirooka Y, Sugiyama M. Propylthiouracil-Induced Antineutrophil Cytoplasmic Antibody-Associated Vasculitis after COVID-19 Vaccination. Vaccines (Basel). 2021;9(8).
39. Sandhu S, Bhatnagar A, Kumar H, Dixit PK, Paliwal G, Suhag DK, et al. Leukocytoclastic vasculitis as a cutaneous manifestation of ChAdOx1 nCoV-19 Corona Virus Vaccine (Recombinant). Dermatol Ther. 2021:e15141.
40. Shakoor MT, Birkenbach MP, Lynch M. ANCA-Associated Vasculitis Following Pfizer-BioNTech COVID-19 Vaccine. Am J Kidney Dis. 2021;78(4):611-3.
41. Vassallo C, Boveri E, Brazzelli V, Rampino T, Bruno R, Bonometti A, et al. Cutaneous lymphocytic vasculitis after administration of COVID-19 mRNA vaccine. Dermatol Ther. 2021:e15076.
42. Villa M, Díaz-Crespo F, Pérez de José A, Verdalles Ú, Verde E, Almeida Ruiz F, et al. A case of ANCA-associated vasculitis after AZD1222 (Oxford-AstraZeneca) SARS-CoV-2 vaccination: casualty or causality? Kidney Int. 2021;100(4):937-8.
43. Felicetti P, Trotta F, Bonetto C, Santuccio C, Brauchli Pernus Y, Burgner D, et al. Spontaneous reports of vasculitis as an adverse event following immunization: A descriptive analysis across three international databases. Vaccine. 2016;34(51):6634-40.
44. Becker RC. COVID-19-associated vasculitis and vasculopathy. J Thromb Thrombolysis. 2020;50(3):499-511.