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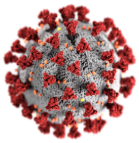
vACCine covid-19  monitoring readinESS

EVENT DEFINITION FORM

Event: Single Organ Cutaneous Vasculitis
Outcome/covariate: Outcome
Version: 1
Status: Final

Contributing authors

authors	**Role**	**Date**
Ruth Engelen	Medical/draft v0.1	24-6-2020
Miriam Sturkenboom	Epi review	13-07-2020
Leila Belbachir	Medical review	12-08-2020
Miriam & Leila	Discussion & update	25-08-2020
Corinne Willame	Algorithm proposal	02-09-2020
Miriam Sturkenboom	Revision of codes	14-2-2021
Carlos Durán	Rev. narrow/possible assignment	26-03-2021
Miriam Sturkenboom	Inclusion of codes for final report	23-8-2021

1. Event definition

From Brighton Collaboration case definition (Zanoni et al. 2016)
Single Organ Cutaneous Vasculitis is a syndrome characterized by clinical and histological features of small vessel vasculitis of the skin without involvement of other organ systems. It can be the first sign of systemic vasculitis. The definition is divided in different levels of diagnostic certainty.

Case definition for single organ cutaneous vasculitis from Brighton Collaboration (references 1-7):

For all levels of diagnostic certainty
Clinical features:
Hemorrhagic papules
OR
Urticaria-like lesions
OR
Purpuric rash involving the face, ears, and extremities AND edema AND low grade fever (only for acute haemorrhagic edema of infancy (AHEI))

Level 1 of diagnostic certainty
Histology:

Perivascular inflammatory cells infiltrates dominated by neutrophils with fragmented nuclei (leukocytoclasia)
AND
Erytrocyte extravasation or haemorrhage into the dermis
AND
Fibrinoid necrosis or degeneration of the dermal postcapillary venules.

AND
Exclusion of other vasculitic organ system involvement

- Normochromic normocytic anemia, thrombocytopenia,
- Renal involvement (proteinuria, haematuria**,** hypertension, increased serum creatinine),
- Pulmonary involvement (dyspnea, cough, hemoptysis, patchy or diffuse alveolar infiltrates in chest X-ray),
- Gastrointestinal involvement (abdominal pain, vomiting, gastrointestinal bleeding)
- Liver involvement (elevated liver enzymes and bilirubin),
- Serosal involvement (pericardial and or pleural effusion) with ultrasound and/or X-ray examination in case of clinical suspicion,
- Arthritis (synovitis) with synovial aspirate in case of clinical suspicion,
- Central or peripheral nervous system involvement by neurologic physical examination,
- Presence of antinuclear antibodies, ANCA, rheumatoid factor, anti-citrullinated peptides antibodies (CCP), cryoglobulins,
- Reduced serum complement factors (C3, C4, C1q),

- Serologic evidence of hepatitis C, hepatitis B, EBV, Parvovirus B19 serology, antistreptolysin-O titre.

Level 2 of diagnostic certainty
Histology:

Perivascular inflammatory cells infiltrates dominated by neutrophils with fragmented nuclei (leukocytoclasia)
AND
Erytrocyte extravasation or haemorrhage into the dermis

AND
Exclusion of other organ or systemic involvement (see Level 1).

Level 3 of diagnostic certainty
Histology - not available
AND
Exclusion of other organ or systemic involvement (see Level 1).

2. Synonyms / lay terms for the event

Synonyms of single organ cutaneous vasculitis are:

- SOCV
- Leukocytoclastic vasculitis
- Hypersensitivity vasculitis
- Cutaneous leukocytoclastic angiitis
- Cutaneous leukocytoclastic vasculitis
- Cutaneous necrotizing venulitis
- Cutaneous small vessel vasculitis or CSVV

3. Laboratory tests that are specific for event

Laboratory testing can still be relevant to exclude some diagnosis, even if there are no systemic symptoms present, which is the case in SOCV. Tests that would be relevant are:

- C-reactive protein as inflammatory marker
- Complete blood count (CBC) which may indicate an underlying cause
- Basic metabolic panel:
  - Glucose, calcium
  - Sodium, potassium, bicarbonate and chloride
  - Blood urea nitrogen and creatinine to test the function of the kidney
- Liver function tests to see if there's hepatic involvement
- Urinalysis to look for haematuria or proteinuria, which would indicate renal involvement

4. Diagnostic tests that are specific for event

Skin biopsy is the gold standard with direct immunofluorescence.

The histology can show us the following: perivascular inflammatory cells infiltrates dominated by neutrophils with fragmented nuclei (leukocytoclasia), erythrocyte extravasation or haemorrhage into the dermis and fibrinoid necrosis or degeneration of the dermal postcapillary venules.
The direct immunofluorescence shows a predominance of IgM, fibrinogen and C3 in recent lesions, IgG in completely developed lesions, and fibrinogen and C3 in old lesions. IgA deposits may be more evident in patients at risk for renal failure. [9]

After vasculitis has been diagnosed from the skin biopsy it is important that all patients undergo the same workup. This includes the laboratory tests mentioned above, but also a chest radiograph to exclude a systemic disease. [9]

5. Drugs that are used to treat event

Treatment depends on the severity. In 90% of patients SOCV will be resolved in weeks to months of onset and only simple measures are recommended like bed rest with elevation of the lower limbs and treatment with nonsteroidal anti-inflammatory drugs or antihistamines. Topical therapies, such as corticosteroid and/or antibiotic creams, are often used, although no data support this practice.
Colchicine can be used for the more chronic, extensive or tender lesions and arthralgias. Colchicine is typically used at a dose of 0.6 mg twice daily, and response is noted in 1 to 2 weeks. Some studies believe that colchicine combined with dapsone is beneficial.
In case of severe cutaneous disease systemic corticosteroid therapy can be given, only for short periods of time. If patients don't respond to colchicine or dapsone therapy, or have a recurrence when corticosteroids are tapered, alternate therapy is indicated. The four agents usually considered in this setting are azathioprine (2 mg/kg per day), low-dose methotrexate (MTX) (<25 mg/wk), cyclosporine and cyclophosphamide. [9]

6. Procedures used specific for event treatment

There are no procedures needed for treatment of SOCV.

7. Setting (outpatient specialist, in-hospital, GP, emergency room) where condition will be most frequently /reliably diagnosed

The setting patients present themselves in are at the GP or emergency room. It depends on the severity.

8. Diagnosis codes or algorithms used in different papers to extract the events in Europe/USA: seek literature for papers that have studied this event, and see how they extracted/measured the event.

ICD-9-CM 709.1 vascular disorders of skin, 446.2 (hypersensitivity angiitis) and 287.0 (allergic purpura, including SHP).
ICD-10-CM

- L95: vasculitis limited to skin, not elsewhere classified
- L95.8: other vasculitis limited to the skin
- L95.9 vasculitis limited to the skin, unspecified

9. Experience of participating data sources in extracting the events prior to ACCESS

NA

10. Codes used in ACCESS

Coding system	Code	Code name	Concept	Concept name	Algorithm
ICD10/CM	D69.0	Allergic purpura	C0034152	Henoch-Schoenlein Purpura	Narrow
ICD10/CM	D69.0	Allergic vasculitis	C0151436	Vasculitis, Leukocytoclastic, Cutaneous	Narrow
ICD10/CM	L95	Vasculitis limited to skin, not elsewhere classified	C0494887	Vasculitis limited to skin, not elsewhere classified	Narrow
ICD10/CM	L95.0	Atrophie blanche (en plaque)	C2888634	Atrophie blanche (en plaque)	Narrow
ICD10/CM	L95.8	Other vasculitis limited to skin	C0477527	Other vasculitis limited to the skin	Narrow
ICD10/CM	L95.9	Vasculitis limited to skin, unspecified	C0262988	Vasculitis of the skin	Narrow
ICD10/CM	L98.8	Other specified disorders of skin and subcutaneous tissue	C0477529	Other specified disorders of skin and subcutaneous tissue	Possible
ICD10/CM	M31.0	Hypersensitivity angiitis	C0151436	Vasculitis, Leukocytoclastic, Cutaneous	Narrow
ICD9CM	287.0	Allergic purpura	C0034152	Henoch-Schoenlein Purpura	Narrow
ICD9CM	446.2	Hypersensitivity angiitis	C0151436	Vasculitis, Leukocytoclastic, Cutaneous	Narrow
ICD9CM	446.20	Hypersensitivity angiitis, unspecified	C0151436	Vasculitis, Leukocytoclastic, Cutaneous	Narrow
ICD9CM	709.1	Vascular disorders of skin	C0162819	Skin Diseases, Vascular	Narrow
ICPC2P	B83019	Purpura;Henoch-Schonlein	C0034152	Henoch-Schoenlein Purpura	Narrow
ICPC2P	K99016	Vasculitis	C0042384	Vasculitis	Possible
RCD2	D310.	Allergic purpura	C0034152	Henoch-Schoenlein Purpura	Narrow
RCD2	D3100	Henoch-Schonlein purpura	C0034152	Henoch-Schoenlein Purpura	Narrow
RCD2	D310z	Allergic purpura NOS	C0034152	Henoch-Schoenlein Purpura	Narrow
RCD2	G752.	Hypersensitivity angiitis	C0151436	Vasculitis, Leukocytoclastic, Cutaneous	Narrow
RCD2	G752z	Hypersensitivity angiitis NOS	C0151436	Vasculitis, Leukocytoclastic, Cutaneous	Narrow

RCD2	G76B.	Vasculitis	C0042384	Vasculitis	Possible
RCD2	M2y0.	Vascular disorders of skin	C0162819	Skin Diseases, Vascular	Narrow
RCD2	M2y0z	Vascular skin disorders NOS	C0162819	Skin Diseases, Vascular	Narrow
RCD2	Myu7A	[X]Oth vasculitis limited/skin	C0477527	Other vasculitis limited to the skin	Narrow
RCD2	Myu7C	[X]O spcf diso/skn+subcut tiss	C0477529	Other specified disorders of skin and subcutaneous tissue	Possible
RCD2	Myu7G	[X]Vasculit limited skin, unsp	C0262988	Vasculitis of the skin	Narrow
SCTSPA	11263005	enfermedad vascular de la piel	C0162819	Skin Diseases, Vascular	Narrow
SCTSPA	21148002	púrpura alérgica	C0034152	Henoch-Schoenlein Purpura	Narrow
SCTSPA	31912009	púrpura anafilactoide	C0034152	Henoch-Schoenlein Purpura	Narrow
SCTSPA	31996006	vasculitis	C0042384	Vasculitis	Possible
SCTSPA	53312001	vasculitis de la piel	C0262988	Vasculitis of the skin	Narrow
SCTSPA	60555002	vasculitis leucocitoclástica	C0151436	Vasculitis, Leukocytoclastic, Cutaneous	Narrow
SCTSPA	191306005	púrpura de Henoch-Schönlein	C0034152	Henoch-Schoenlein Purpura	Narrow
SCTSPA	191308006	púrpura alérgica, SAI	C0034152	Henoch-Schoenlein Purpura	Narrow
SCTSPA	195352009	angeítis por hipersensibilidad, SAI	C0151436	Vasculitis, Leukocytoclastic, Cutaneous	Narrow
SCTSPA	201424009	[X]otra vasculitis circunscripta a la piel	C0477527	Other vasculitis limited to the skin	Narrow
SCTSPA	201426006	[X]otros trastornos especificados de la piel y del tejido celular subcutáneo	C0477529	Other specified disorders of skin and subcutaneous tissue	Possible
SCTSPA	201430009	[X]vasculitis circunscripta a la piel, no especificada	C0262988	Vasculitis of the skin	Narrow
SCTSPA	246074004	púrpura de Schonlein-Henoch	C0034152	Henoch-Schoenlein Purpura	Narrow
SCTSPA	267565009	Púrpura: [alérgica] o [alergia de Henoch-Schonlein]	C0034152	Henoch-Schoenlein Purpura	Narrow
SCTSPA	267820009	trastornos vasculares de la piel, SAI	C0162819	Skin Diseases, Vascular	Narrow
SCTSPA	367437009	púrpura autoinmunitaria	C0034152	Henoch-Schoenlein Purpura	Narrow
SCTSPA	718217000	vasculitis leucocitoclástica cutánea	C0151436	Vasculitis, Leukocytoclastic, Cutaneous	Narrow
SCTSPA	239945009	Hypocomplementemic urticarial vasculitis (disorder)			narrow
SCTSPA	46286007	Lymphocytic vasculitis of skin (disorder)			narrow
SCTSPA	55275006	Nodular vasculitis (disorder)			narrow

SCTSPA	64832003	Neutrophilic vasculitis of skin (disorder)			narrow
SNOMEDCT_US	11263005	Vascular disease of the skin	C0162819	Skin Diseases, Vascular	Narrow
SNOMEDCT_US	11263005	Vascular disorders of skin			Narrow
SNOMEDCT_US	11263005	Vascular disorder of skin			Narrow
SNOMEDCT_US	11263005	Vascular disorders of skin			Narrow
SNOMEDCT_US	11263005	Vascular disorders of skin NOS			Narrow
SNOMEDCT_US	11263005	[X]Other vasculitis limited to the skin			Narrow
SNOMEDCT_US	21148002	Allergic purpura	C0034152	Henoch-Schoenlein Purpura	Narrow
SNOMEDCT_US	31912009	Anaphylactoid purpura	C0034152	Henoch-Schoenlein Purpura	Narrow
SNOMEDCT_US	31996006	Vasculitis	C0042384	Vasculitis	Possible
SNOMEDCT_US	49465005	Angioma serpiginosum			possible
SNOMEDCT_US	49465005	Angioma serpiginosum of skin			possible
SNOMEDCT_US	49465005	Angioma serpiginosum			possible
SNOMEDCT_US	53312001	Vasculitis of the skin	C0262988	Vasculitis of the skin	Narrow
SNOMEDCT_US	53312001	Vasculitis limited to skin, unspecified			narrow
SNOMEDCT_US	53312001	[X]Vasculitis limited to skin, unspecified			narrow
SNOMEDCT_US	56231002	Purpura annularis telangiectodes			narrow
SNOMEDCT_US	56231002	Purpura annularis telangiectodes			narrow
SNOMEDCT_US	56231002	Majocchi capillaritis			narrow
SNOMEDCT_US	56231002	Purpura annularis telangiectodes of Majocchi			narrow
SNOMEDCT_US	56231002	Majocchi's purpura			narrow
SNOMEDCT_US	56231002	Purpura annularis telangiectodes			narrow
SNOMEDCT_US	58872001	Erythema elevatum diutinum			narrow
SNOMEDCT_US	58872001	Erythema elevatum diutinum			narrow
SNOMEDCT_US	60555002	Hypersensitivity angiitis	C0151436	Vasculitis, Leukocytoclastic, Cutaneous	Narrow
SNOMEDCT_US	154823001	Allergic purpura	C0034152	Henoch-Schoenlein Purpura	Narrow
SNOMEDCT_US	191305009	Allergic purpura	C0034152	Henoch-Schoenlein Purpura	Narrow
SNOMEDCT_US	191306005	Henoch-Schönlein purpura	C0034152	Henoch-Schoenlein Purpura	Narrow
SNOMEDCT_US	191308006	Allergic purpura NOS	C0034152	Henoch-Schoenlein Purpura	Narrow
SNOMEDCT_US	195350001	Hypersensitivity angiitis	C0151436	Vasculitis, Leukocytoclastic, Cutaneous	Narrow

SNOMEDCT_US	195352009	Hypersensitivity angiitis NOS	C0151436	Vasculitis, Leukocytoclastic, Cutaneous	Narrow
SNOMEDCT_US	195375002	Vasculitis	C0042384	Vasculitis	Possible
SNOMEDCT_US	201305007	[X]Vasculitis limited to skin, unspecified	C0262988	Vasculitis of the skin	Narrow
SNOMEDCT_US	201306008	Vascular disorders of skin NOS	C0162819	Skin Diseases, Vascular	Narrow
SNOMEDCT_US	201424009	[X]Other vasculitis limited to the skin	C0477527	Other vasculitis limited to the skin	Narrow
SNOMEDCT_US	201426006	[X]Other specified disorders of the skin and subcutaneous tissue	C0477529	Other specified disorders of skin and subcutaneous tissue	Possible
SNOMEDCT_US	201430009	[X]Vasculitis limited to skin, unspecified	C0262988	Vasculitis of the skin	Narrow
SNOMEDCT_US	238762002	Livedoid vasculitis			possible
SNOMEDCT_US	238762002	White atrophy			possible
SNOMEDCT_US	238762002	Livedoid vasculitis			possible
SNOMEDCT_US	238762002	Atrophie blanche			possible
SNOMEDCT_US	238772004	Livedo reticularis			possible
SNOMEDCT_US	238772004	Livedo reticularis			possible
SNOMEDCT_US	238776001	Idiopathic livedo reticularis with systemic involvement			possible
SNOMEDCT_US	238776001	Sneddon's syndrome			possible
SNOMEDCT_US	246074004	Henoch-Sch?nlein purpura	C0034152	Henoch-Schoenlein Purpura	Narrow
SNOMEDCT_US	266325003	Angiitis	C0042384	Vasculitis	Possible
SNOMEDCT_US	267565009	Allergic purpura	C0034152	Henoch-Schoenlein Purpura	Narrow
SNOMEDCT_US	267820009	Vascular disorders of skin NOS	C0162819	Skin Diseases, Vascular	Narrow
SNOMEDCT_US	367437009	Autoimmune purpura (disorder)	C0034152	Henoch-Schoenlein Purpura	Narrow
SNOMEDCT_US	393589007	Vasculitis	C0042384	Vasculitis	Possible
SNOMEDCT_US	718217000	Cutaneous leukocytoclastic angiitis	C0151436	Vasculitis, Leukocytoclastic, Cutaneous	Narrow

11. Algorithm proposal

Broad algorithm:

- All Concept sets = (Vasculitis, Vascular_skin_diseases) in any provenance, no prior codes
- Index date: first occurrence of any of this concept set

Narrow algorithm:

- Concept set = (Vasculitis cutaneous) in any provenance, no prior codes
- Index date: first occurrence of any of this concept set

12. Background rates from literature

We used the following search string: ***"Single Organ Cutaneous Vasculitis" [tw] OR "SoCV" [tw] OR "cutaneous vasculitis" [tw] OR "hypersensitivity vasculitis" [tw] OR "cutaneous leukocytoclastic angiitis" [tw] OR "cutaneous small vessel vasculitis" [tw] AND ("incidence" [tw]) NOT (Comment[ptyp] OR Editorial[ptyp] OR News[ptyp] OR Newspaper Article[ptyp]) NOT ("animals"[Mesh] NOT "humans" [Mesh]) AND English [lang].*** **Filter: abstract, English and from 2010 – 2020.**

13. References

1. G.G. Hunder, W.P. Arend, D.A. Bloch, L.H. Calabrese, A.S. Fauci, J.F. Fries, *et al.* The American College of Rheumatology 1990 criteria for the classification of vasculitis. Introd Arthritis Rheumat, 33 (1990), pp. 1065-1067. DOI: 10.1002/art.1780330802.

2. J.C. Jennette, R.J. Falk, P.A. Bacon, N. Basu, M.C. Cid, F. Ferrario, *et al.* 2012 Revised International Chapel Hill consensus conference nomenclature of vasculitides. Arthritis Rheum, 65 (2013), pp. 1-11. DOI: 10.1002/art.37715.

3. R.G. Micheletti, V.P. Werth. Small vessel vasculitis of the skin. Rheum Dis Clin North Am, 41 (2015), pp. 21-32 vii. DOI: 10.1016/j.rdc.2014.09.006.

4. A. Peroni, C. Colato, D. Schena, G. GirolomoniUrticarial lesions: if not urticaria, what else? The differential diagnosis of urticaria: Part I. Cutaneous diseases. J Am Acad Dermatol, 62 (2010), pp. 541-555 quiz 55-6. DOI: 10.1016/j.jaad.2009.11.686.

5. A. Peroni, C. Colato, G. Zanoni, G. Girolomoni. Urticarial lesions: if not urticaria, what else? The differential diagnosis of urticaria: part II. Systemic diseases. J Am Acad Dermatol, 62 (2010), pp. 557-570 quiz 71-2. DOI: 10.1016/j.jaad.2009.11.687.

6. T. Zuberbier, M. Maurer. Urticarial vasculitis and Schnitzler syndrome Immunol Allergy Clin North Am, 34 (2014), pp. 141-147. DOI: 10.1016/j.iac.2013.09.007.

7. Zanoni G, Girolomoni G, Bonetto C, Trotta F, Häusermann P, Opri R, Bonhoeffer J; Brighton Collaboration Single Organ Cutaneous Vasculitis Working Group. Single organ cutaneous vasculitis: Case definition & guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine. 2016 Dec 12;34(51):6561-6571. doi: 10.1016/j.vaccine.2016.09.032. Epub 2016 Oct 28. PMID: 28029543.

8. Baigrie D, Bansal P, Goyal A, Crane JS. Leukocytoclastic Vasculitis (Hypersensitivity Vasculitis). In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 [Accessed on 8th of june 2020]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK482159/

9. Pulido-Pérez A, Avilés-Izquierdo JA, Suárez-Fernández R. Cutaneous Vasculitis. Actas Dermo-Sifiliográficas (English Edition). 1 april 2012;103(3):179–91. DOI: 10.1016/j.adengl.2011.06.001