A Review on Cutaneous Manifestations of Cerebrovascular Accident

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Introduction

A neurological condition known as a stroke or cerebrovascular accident (CVA) can be either hemorrhagic or ischemic due to blood vessel obstruction. Brain clots prevent blood flow and thus result in the abrupt death of brain cells due to a lack of oxygen. The second biggest cause of mortality worldwide is stroke. There are certain modifiable and nonmodifiable risk factors linked with CVA. Modifiable risk factors include hypertension, smoking, diabetes, alcohol, and dyslipidemia. Nonmodifiable risk factors are age, gender, race, and genetics.[1] As we all know 'eye is an index of the mind', while our largest organ 'skin' is an eye for detecting many systemic abnormalities. The pathomechanism includes predominantly vaso-occlusion either as a primary phenomenon (antiphospholipid antibody syndrome, sneddon syndrome, degos disease, cholesterol emboli) or secondary to vasculitis (neurosyphilis, systemic lupus erythematosus) or indirect association with metabolic syndromes. A detailed 'PubMed' and 'Google Scholar' search was done using the keyword 'skin' OR 'cutaneous manifestations' OR 'dermatological features' AND 'stroke' OR 'cerebrovascular infarct' OR 'neurological features' OR 'cerebrovascular accident' OR 'brain'. To date, there is little literature on summarizing these cutaneous manifestations linked to stroke. Hereby, our review is an attempt to concisely summarize the features.

1. Acquired Cutaneous Disorders with direct association with CVA

- **Anti Phospholipid Antibody Syndrome (APS):** The cutaneous presentation of APS includes livedo reticularis, retiform purpura, and peripheral gangrene. The most frequent systemic feature of APS is ischemic stroke. Thrombotic and embolic processes are thought to be the causes of ischemic stroke. It is mostly linked with valvular anomalies, hence transesophageal echocardiography is strongly advised.[2]
- **Sneddon syndrome (SS):** Generalized livedo racemose and repeated cerebrovascular episodes are hallmarks of the episodic or chronic, slowly progressing condition known as SS. Thrombotic vasculopathy of small- and medium-sized cerebral and dermal arteries.[3]
- **Vasculitis:** An association with stroke has been linked with Wegener's granulomatosis, microscopic polyangiitis, Churg strauss syndrome, Bechet's disease, cryoglobulinemic vasculitis, and Takayasu arteritis.[4-6]
- **Scleromyxedema:** Scleromyxedema is an uncommon condition with an unclear etiology that mostly affects the skin. It presents as generalized papular eruption on a background of sclerodermoid changes. Memory loss, vertigo, balance issues, stroke, seizures, psychosis, and dermatoneural syndrome are all central nervous system symptoms. The dermatoneural syndrome is considered the most dreaded complication.[5]
- **Neurosyphilis:** In meningovascular syphilis, obliterative endarteritis of small-sized (Nissl-Alzheimer) and medium-sized (Heubner's) intracranial arteries resulting in luminal constriction, cerebrovascular thrombosis, and ischemic infarction due to fibroblastic and collagenous growth inside the artery walls.[7]
- **Infective endocarditis (IE):** Patients with IE frequently present with cerebral microbleeds, which indicates subacute microvascular inflammation that precedes mycotic aneurysms. Osler

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nodes, Janeway lesions, splinter hemorrhage, and purpura are the cutaneous manifestations of IE.[8]

- **Cholesterol emboli (Blue toe syndrome/BTS):** BTS presents with petechiae, purpura, cyanosis, livedo reticularis, and gangrene. Since small-diameter arteries are affected by embolism, peripheral pulses are frequently palpable. Palpable pulses and distal gangrene/ulcers are strongly indicative of blue toe syndrome. Systemic manifestations include major vessel aneurysm, stroke, and myocardial infarcts.[9]
- **Systemic lupus erythematosus (SLE):** In patients with SLE 0.5–15% of the cases have an association with stroke and transient ischemic attacks. SLE is the main cause of ischemic stroke, especially in young patients. Inflammation-induced endothelial injury and subsequent thrombotic process are linked to the pathogenesis of SLE-related stroke.[10] In patients of SLE, cutaneous findings of livedo reticularis or palmar vasculitis antiplatelet low-dose aspirin will be added to prevent thrombotic episodes.
- **Degos disease:** Skin lesions precede systemic symptoms (gastrointestinal and cerebral infarct) for months to years. It presents as crops of asymptomatic, pink to red, dome-shaped papules that later turn umbilicated with central necrosis, which further progresses to central porcelain-white pallor and scaling, over the trunk and extremities; sparing palms, soles, and face.[4]

2. Acquired Cutaneous Disorders with indirect association with CVA

- **Psoriasis:** The prevalence of metabolic syndrome (truncal obesity, hyperlipidemia, hypertension, and insulin resistance) in psoriasis patients is rising, which indirectly increases the risk of myocardial infarction and stroke.[4]
- **Bullous pemphigoid:** It presents with a prodrome of urticaria, eczema, and later, tense bullae appear over the prebullous stages. This has been linked to a variety of neurological and psychiatric conditions (due to the presence of bullous pemphigoid antigen in neural tissue), such as cognitive decline, Parkinson's disease, stroke, epilepsy, multiple sclerosis, uni-and bipolar disorders, as well as cognitive impairment.[4]
- **Large plaque parapsoriasis or mycosis fungoides (MF):** According to data from a Danish cohort study, parapsoriasis and MF are linked to a higher risk of coronary artery disease and stroke. Th1-mediated inflammatory response, and dyslipidemia due to retinoids are the risk factors.[11] Cutaneous features of MF range from patch, plaque, noduloulcerative lesions with lymphadenopathy.

Lipid-lowering agents, lifestyle, and dietary modifications reduced the risk of stroke in patients with metabolic syndromes.

3. Geno dermatosis linked with CVA

Genodermatoses such as Hutchinson Gilford progeria, Cockayne syndrome, phosphomannomutase 2 deficiency, Majewski osteodysplastic primordial dwarfism type II, Sturge–Weber syndrome, Fabry's disease, incontinentia pigmenti, Ehlers–Danlos syndrome, hereditary hemorrhagic telangiectasia, autoinflammatory syndromes like deficiency of adenosine deaminase 2 (DADA2), and MELAS (Mitochondrial myopathy, Encephalopathy, Lactic Acidosis, and Stroke-like episodes syndrome) are associated with an increased risk of cerebrovascular infarction. Patho mechanisms suggested are chromosomal instability, defective DNA repair mechanisms, metabolic syndrome, and vascular syndrome.[11-14]

4. Patients with CVA presenting with cutaneous features

- **Trigeminal neuropathic pain syndrome:** In brainstem infarct, destruction of pain and temperature fibers of the trigeminal nerve leads to neurotrophic alterations where chronic stinging, burning, and pain in the trigeminal nerve region are accompanied by an overwhelming urge to pick at the affected skin.[4]
- **Focal anhidrosis/hyperhidrosis:** Disorders occurring anywhere from the level of the cerebral cortex to the eccrine sweat ducts lead to hypo to anhidrosis. Cerebrovascular infarction at any level from the cortex to the spinal cord leads to autonomic nerve failure leading to focal anhidrosis and compensatory hyperhidrosis.[4]
- **Plica Polonica:** Reactive depression in patients with cerebrovascular infarction leads to decreased hair care and results in hair twisting, and matting.[15]
- **Sparing effect:** Hemiplegia has been shown to have a protective effect in rheumatic illnesses, although systemic sclerosis spectrum disorder reports are infrequent. There are a few case reports where asymmetric progression of binding down of skin, Raynaud's phenomenon, and acral osteolysis in hemiplegia patients.[16]
- **Moya Moya angiopathy (MA):** MA is diagnosed based on clinical and radiological criteria that include bilateral internal carotid artery occlusions visualized on angiography. The cerebrovascular episodes, both ischemic and hemorrhagic, are the most frequent illness symptoms. Pediatric NF1 patients had an average MA prevalence of 0.6%. Café-au-lait macules, blashcko linear hypopigmentation, livedo racemosa, hemangiomas, canities, and chilblains are the cutaneous manifestations, and these can be coincidental findings as per the review done by Mitri *et al*.[17]
- **Trophic Ulcer:** A pressure ulcer is a localized area of tissue damage brought on by compression between a bony prominence and the surface. The most significant force on tissue is pressure, but additional forces like friction, shear, wetness, co-morbidities in the

patient, and mechanical properties of the bone, skin, fat, and muscle also play a role. The sacrum, heels, ischium, elbows, occiput, are the anatomical areas, where pressure ulcers most frequently occur.[4]

- **Asymmetric skin temperature:** A common effect of autonomic failure in stroke patients appears to be a decrease in temperature in the limbs opposite the site of infarction. Wallenberg's syndrome and pyramidal tract symptoms appear to be linked to the condition. The degree of uneven temperature in hemispheric infarction is linked with the seriousness of limb paresis.[18]

5. Cutaneous side effects due to Drugs used in CVA

- **Ichthyosis:** Symmetrical brown thick scales over legs, arms, trunk, and back with sparing of flexures due to statins and malnutrition.[4]
- **Petechia and ecchymosis:** Antiplatelets and anticoagulants used for ischemic stroke cause non-inflammatory petechia and ecchymosis, respectively.[4]
- **Heparin-induced thrombocytopenia (HIT):** Heparin is used to prevent DVT in chronically bedridden CVA patients. Simple hemorrhage with ecchymoses, erythema, and rarely urticaria or indurated plaques that are purpuric, painful, and have retiform expansions at their margins seen at the sites of subcutaneous injection. Early HIT develops between days 5–10 of heparin therapy, whereas delayed heparin necrosis is seen for up to 3 weeks.[4]
- **Hemorrhagic bullous dermatosis (HBD):** Days to weeks after initiation of heparin medication, mostly enoxaparin, patients experience asymptomatic bullae on the trunk and/or the extremities. Histopathology shows erythrocyte-filled subcorneal, intraepidermal, or subepidermal bullae that are non-inflammatory. Bullae disappear in a matter of days to weeks, whether heparin medication is continued or stopped. HBD's pathophysiology is unknown.[19]
- **Warfarin and coumarin congener skin necrosis:** Warfarin necrosis is characterized by sudden onset of pain in the affected area 3–5 days after initiation of warfarin; later it develops well-circumscribed erythema and progresses to hemorrhage, necrosis, and bullae or eschar. It is seen in areas of abundant fatty tissues such as breasts, buttocks, and thighs.[4] An early, nonnecrotic purpuric lesion underwent biopsy, and the results revealed signs of leukocytoclastic vasculitis—thrombi in capillaries, venules, and tiny veins together with infarction of the epidermis and subcutaneous tissue during the necrotic phase.[20] Table 1 summarizes the cutaneous spectrum of CVA.

Conclusion

There are few reviews on cutaneous manifestations of stroke, hence we extrapolated data from various sources and summarized it in our article.

Table 1: Summarizes the cutaneous manifestations linked with cerebrovascular accident (CVA)

Acquired Cutaneous Disorders where CVA is a part	
Inflammatory conditions	Psoriasis
	Bullous pemphigoid
	Vasculitis
	Systemic lupus erythematosus
Deposition disorder	Scleromyxdema
Vaso-occlusive conditions	Anti Phospholipid Antibody syndrome
	Livedo reticularis
	Sneddon syndrome
	Degos disease
Lymphoproliferative dermatosis	Large plaque parapsoriasis
	Mycosis fungoides
Infective	Neurosyphilis
	Infective endocarditis
Geno dermatosis linked with CVA	
Genodermatosis	Hereditary Hemorrhagic Telangiectasia
	Hutchinson Gilford Progeria syndrome
	Cockayne syndrome
	MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes) syndrome
	Phosphomannomutase 2 deficiency
	Sturge weber syndrome
	PHACE (posterior fossa malformation, hemangioma, anatomic abnormalities of cerebral or carotid arteries, cardiac anomalies, and eye abnormalities)
	Fabry disease
	Incontinentia pigmenti
	Ehler–Danlos syndrome Vascular type
	Majewski osteodysplastic primordial dwarfism type II
Patients with CVA presenting with cutaneous features	
	Trigeminal neuropathic pain syndrome
	Complex regional pain syndrome
	Focal anhidrosis
	Hyperhidrosis
	Disuse atrophy
	Plica polonica
	Dermatitis neglecta
	Diaper dermatitis
	Trophic ulcer
Cutaneous side effects due to Drugs used in CVA	
	Ichthyosis
	Petechia and ecchymosis
	Heparin-induced thrombocytopenia
	Hemorrhagic bullous dermatosis
	Warfarin necrosis

Contd...

Table 1: Contd...
Cutaneous manifestations of risk factors linked to CVA
Smoking
Obesity
Diabetes
Hypertension

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Conflicts of interest

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