Intracranial aneurysms and systemic sclerosis: A causal association or sheer coincidence?

Dear Editor,

Systemic sclerosis is a chronic inflammatory autoimmune disease characterised by microvascular damage and fibrosis of the skin and systemic organs. The main targets of the disease are the skin and viscera like the lung, heart, kidney and gastrointestinal system. Contrary to other collagen disorders, involvement of the nervous system has rarely been reported and has largely been attributed to the paucity of connective tissue in the brain with the sparse media and adventitia in the intracerebral arteries.[1] We report a case of systemic sclerosis associated with an intracranial aneurysm.

A 57-year-old woman, a homemaker, presented with a sudden onset severe headache associated with vomiting and transient loss of consciousness 12 hours before. A general physical examination revealed a Glasgow Coma Score of 14 (E4M4V6) and bilateral reactive pupils. The rest of the vitals and sensory and motor examination were within normal limits. Cutaneous examination revealed binding down of the skin on the upper limbs extending proximal to the elbows, face and lower limbs (modified Rodnan skin score: 11). Multiple, irregularly distributed, depigmented macules on the face and upper trunk with perifollicular pigment retention at places resembling salt-and-pepper appearance and positive Ingram sign were also noted [Figure 1]. Haemogram showed anaemia (Hb; 8.5g/dl), renal function tests, liver function tests, coagulation profile and serum electrolytes were within normal limits and urinalysis showed proteinuria. Antinuclear antibody was positive (3+, nucleolar and coarse speckled). The clinical and immunological profiles were suggestive of diffuse cutaneous systemic sclerosis.

Computed tomography angiography of the head showed multiple aneurysms at the origin of the posterior inferior cerebellar artery [Figure 2], diffuse subarachnoid haemorrhage and hydrocephalus. Magnetic resonance imaging and digital subtraction angiography confirmed the rupture of the right posterior inferior cerebellar artery aneurysm (5.1 mm × 4.4 mm) and the patient underwent craniotomy and clipping of the same. However, on postoperative day 4, she developed

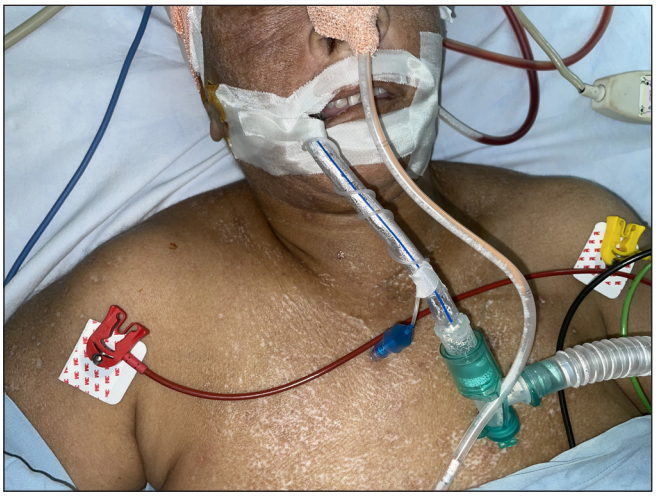

Figure 1: Depigmented macules on the face and chest resembling salt-and-pepper pigmentation.

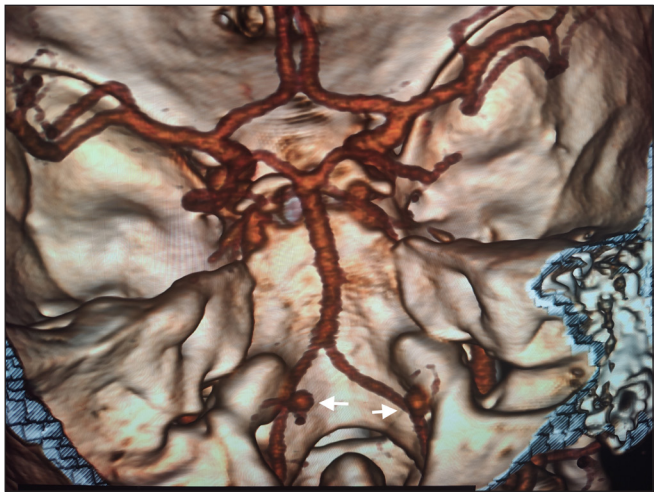

Figure 2: Computed tomography angiography image of the brain showing bilateral aneurysms at the origin of the posterior inferior cerebellar artery (white arrows).

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pulmonary oedema and myocardial dysfunction secondary to severe vasospasm and expired.

The mechanism of aneurysm formation in systemic sclerosis is poorly understood. The proposed hypotheses are: (a) weakening of the vessel wall due to narrowing of the lumen of vasa vasorum due to fibrosis; (b) renal dysfunction leading to hypertension which is a risk factor for aneurysms; (c) increased risk of atherosclerosis which in turn is a risk factor for aneurysms and (d) anti-cell antibodies, reactive oxygen species and inflammatory cytokines leading to endothelial damage.[1]

The occurrence of intracranial aneurysms in systemic sclerosis patients raises the question of the relationship between these two. We believe that systemic sclerosis has a causal relationship with the development of aneurysms because of clinical and pathological differences from idiopathic/vasculopathic intracranial aneurysms. Systemic sclerosis-associated aneurysms are usually large (>1 cm), multiple, fusiform in shape and present later in life in the sixth decade [Table 1].[2–7] The higher incidence of large aneurysms in systemic sclerosis can be explained by excessive production of the extracellular matrix which prevents rupture of aneurysms. Even though the excessive extracellular matrix in systemic sclerosis prevents the rupture of aneurysms for a while, they eventually rupture, leading to subarachnoid haemorrhage.[1,3,7] The multiple aneurysms in systemic sclerosis are probably due to the diffuse nature of the autoimmune process.[7] In contrast, idiopathic aneurysms and vasculitis-associated aneurysms present early (30–40 years), are smaller, involve distal arteries and rupture easily.

This case highlights the increased risk of aneurysms in systemic sclerosis and screening for intracranial aneurysms may be considered in individuals who present with clinical features of intracranial aneurysm (headache, dizziness and cranial nerve palsy) and prophylactic clipping of aneurysms may help in patients who are at risk of rupture (before subarachnoid haemorrhage and documented enlargement of aneurysm). Further prospective studies with large sample sizes are required to know the true incidence of intracranial aneurysms in systemic sclerosis.

Table 1: Summary of cases of systemic sclerosis associated with intracranial aneurysm

Authors	Year	Age/ sex	Diagnosis	Clinical presentation	Location of aneurysm	Shape	Size (range)	Treatment	Outcome
Ortiz *et al*.[2]	1991	66/F	CREST	Gradual bilateral vision loss	Right ICA (two) Left ICA (three) Right MCA (one)	Saccular	1.6 to 12 mm	Surgical clipping and reinforced with muslin	NA
Blaustein *et al*.[3]	1999	57/F	CREST	SAH	Basilar artery	Saccular	NA	Surgical clipping	NA
Kaku *et al*.[1]	2004	73/F	DcSSc	SAH	Left MCA and right ACA	Saccular	Small	Surgical clipping	Neurologically normal
		65/F	DcSSc	SAH	Basilar artery	Saccular	Small	Surgical clipping	Neurologically normal
		52/M	DcSSc	SAH	Let PCA	Fusiform	NA	No surgical treatment	Neurologically intact with no further episodes of SAH
		62F	DcSSc	Ataxia	Basilar artery (two) Left vertebral artery	Fusiform Saccular	Small Giant	Endovascular (coiling)	Neurologically normal
Zoumalan *et al*.[4]	2004	50/F	CREST	Migraine	Right ICA	Saccular		Surgical clipping	The patient's recovery was uneventful
Nakae *et al*.[5]	2009	53/F	CREST	TIA	Right MCA Left MCA Left ICA Left ACA	Saccular	2–12 mm	Surgical clipping	No neurological deficit
		64/F	CREST	Incidental	Left MCA	Fusiform	NA	Surgery (wrapping with autologous fascia and coating with fibrin glue)	No neurological deficit
Masuoka *et al*.[6]	2010	61/F	CREST	Incidental (Evaluation of tinnitus)	Right ICA (three) Left ICA	Saccular	2.7–9 mm	Surgical clipping	No neurological deficit
Jabre *et al*.[7]	2020	67M	DcSSc	SAH	Right MCA ACoA	Saccular	5–25 mm	Surgical clipping	NA
Our case	2023	57/F	DcSSc	SAH	Right ACA Vertebral artery (two)	Saccular	3.1–5.1 mm	Surgical clipping	Death on postoperative day 4

CREST, calcinosis, Raynaud phenomenon, oesophageal dysmotility, sclerodactyly and telangiectasia; DcSSc, diffuse cutaneous systemic sclerosis; SAH, subarachnoid haemorrhage; NA, not available; ACA, anterior cerebral artery; ACoA, anterior communicating artery; ICA, internal carotid artery; MCA, middle cerebral artery; PCA, posterior cerebral artery; TIA, transient ischemic attack; small, diameter < 5 mm; giant, diameter > 25 mm

Declaration of patient consent

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Use of artificial intelligence (AI)-assisted technology for manuscript preparation

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