CASE REPORT

Cerebral Sinus Thrombosis in Scleroderma: A Case Report

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Abstract- Scleroderma or systemic sclerosis is a multisystem disease due to excessive collagen deposition in different organs and autoimmunity by production of autoantibodies. According to previous reports, brain is rarely affected in scleroderma, however recent studies show central nervous system can be affect not only as a complication of systemic involvement (hypertension, renal failure) but also as a primary manifestation.In scleroderma, thrombus formation in central nervous system and peripheral systems is uncommon may be due to endothelial cells damage which causes to release antithrombotic factors. We discuss a scleroderma patient with high titter of anticardiolipin antibody who developed to cerebral sinus thrombosis and cerebellum infarction. Then we review literature for both primary brain involvement and thrombotic event in systemic sclerosis.

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Introduction

Scleroderma or systemic sclerosis is a multisystem disease that can affect several organs due to excessive collagen deposition and autoimmunity by production of autoantibodies (1).The most common manifestation and hallmark of this conditionare cutaneous involvement with thickening (sclerosis) of skin (2). In the nervous system, peripheral structures are more affected, but central nervous system especially brain is also involved which may be due to microvasculardamage secondary to hypertension, kidney failure, vacuities or antiphospholipid antibodies. In recent reports, primary central consequences of scleroderma have been reported too (3-5),and distinction between primary and secondary involvement of the brain could not be easily established in these pathological reports (6). In this report, we discuss a young woman who firstly presented by central nervous system manifestation(cerebral sinus thrombosis and cerebellum infarction) and after further work-up diagnosis of scleroderma was made for him. It is a rare presentation of a rare disease, which encourages us to report this case.

Case Report

A 37-years-old woman was admitted in hospital with sudden onset slurred speech and right sided clumsiness. She had no history of seizure, fever or head trauma. In past medical history, she suffered from mild undiagnosed hypertension (diagnosed after admission) and secondary infertility. There is no complaint of previous fetal loss. Drug (including oral contraception pills) and personal histories were negative. She had a history of skin thickening and Reynaud's with bluish discoloration in her fingers from 3 years ago and arthralgia since 2 years ago.

In general physical examination, she had blood pressure150⁄90 mmHg and normal temperature. All distal pulses in extremities were present and symmetric. Fingers' skin was relatively thick without pitting ulcer. The remainder of the general examination including lung examination did not reveal any abnormalities. Neurological examination showed normal mental state with mild dysarthric speech. In cerebellum evaluation, right side finger-to-finger and rapid alternative movement were impaired. There was no sensory and motor complaint or cranial nerves abnormality. Both plantar reflexes were flexor.

Further investigations disclosed the followings: platelets count 263000⁄mm, white blood cell count 6100⁄mm, hemoglobin level 11.2 mg⁄dl, anticardiolipin antibody (ACLA) 23units(normal range<10)and antinuclear antibody (ANA) >100units(normal range<8), activated prothrombin time (aPTT) 28, and normal urinalysis.

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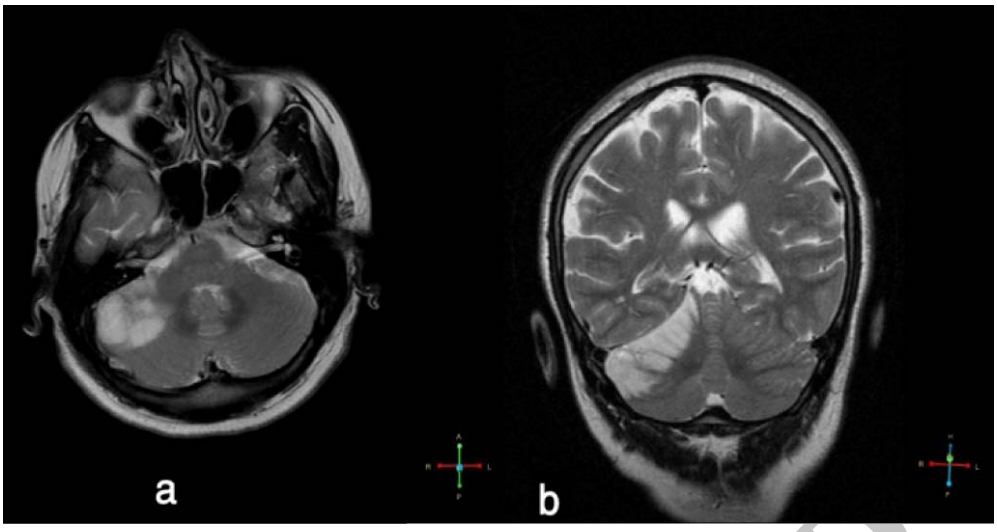

Figure 1. Axial (a) and coronal (b) views of T2 weighted Magnetic Resonance Imaging of the brain show right side cerebellar infarction.

Chest x-ray showed normal lungs, heart and mediastinum.

Brain CT scan and MRI showed cerebellum infarction in the right hemisphere (Figure 1a,b).

Magnetic resonance venography (MRV) of brain obviously showed complete obstruction of right transverse sinus (Figure 2 a,b). Other cerebral sinuses and Venuses were patient. Magnetic Resonance Angiography (MRA) of brain was normal too.

Thus, with diagnosis of cerebral sinus thrombosis, we evaluated her further for probable under-line cause and results were as the following: HBs-Ag, HCV-Ab, HIV-Ab, VDRL, C-ANCA, P-ANCA and Factor V Lieden were negative. Serum iron and TIBC, Protein C, Protein S, and antithrombin ш level were in normal ranges. Antiphospholipid antibody for IgG was 2.0 U/mL and for IgM was 5.4 U/mL (normal range<15). Repeated ANA level was greater than 100. dsDNA, β2Gp1, Lupus Anticoagulant, VDRL, C3 and C4 were normal.

All immunological tests for Extractable Nuclear Antigen (ENA) werewithinnormallimit (Absforn RNP, Sm, SS-A, Ro-52, SS-B, Jo-1, CENPB, Nucleosomes,

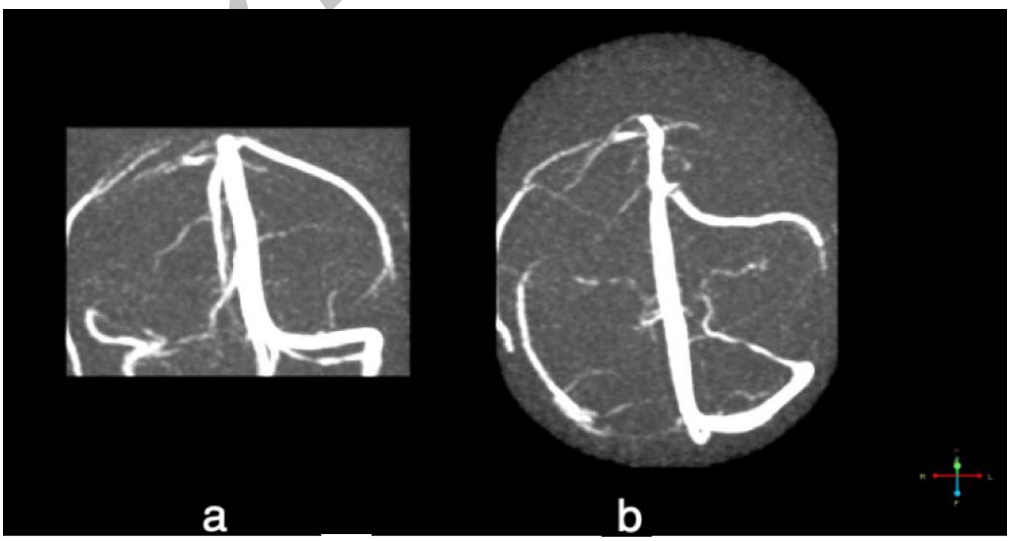

Figure 2. Magnetic Resonance Venography of the brain shows complete obstruction of right transverse sinus (a: coronal and b: axial view).

Histones, Ribosomal P-protein) except for Scl-70 that was 105 U/mL (normal range<7), thus she was referred her for capillaroscopy in periungal area. Eight nail folds were evaluated. There was mild decreased skin transparency, decreased number of normal hairpin shape capillaries with disorganization of capillary pattern, increased bushy capillaries and meandering of capillaries along with neoangiogenesis, rare giant loops, no hemorrhage, no dilated capillaries, and the conclusion was microangiopathy compatible with scleroderma pattern.

Discussion

Annual incidence of scleroderma is 6-12 patients per million populations and female male ratio are seven. This disorder can involve many organs, but hidebound skin is the hallmark (2). Despite the diffuse nature of the disease, neurological presentations are rarely seen. Patients who are positive for anti-U_1 RNP and anti Scl 70 antibodies have a higher risk of developing neurological complications (7).Different pathogenic mechanisms have been proposed for these complications in recent studies, for example, micro or macro angiopathy and vasculitis, a central role of oxidative stress, antiphospholipid immunity or protease-like circulating factors have been hypothesized in primary brain involvement (3,6).

In this patient, development of cerebral sinus thrombosis may be a link to an immunity process. She had significant increased in ANA and ACLA levels, which may prone her to hypercoagulable state and central thrombotic event but exact causes of this catastrophic event in scleroderma are unclear. Up to 25% of patients with scleroderma have anticardiolipine antibody. This antibody is a major cause of thrombus formation in Systemic Lupus Erythematous(SLE) and Antiphospholipid antibody syndrome, but it is very unusual cause of thrombus in scleroderma may be due to endothelial cells damage in scleroderma, which causes to release antithrombotic factors. However, some recent studies have showed ACLA rarely presented by thrombotic event in scleroderma patients (8).

In one cohort study in India (2002 to 2006) Gupta *et al.,* evaluated 72 scleroderma patients who are positive for ACLA and concluded that the presence of this antibody does not influence the severity of complications such as digital infarction, deep venous thrombosis or pulmonary hypertension and they did not report cerebral venous sinus thrombosis in their patients (9).

There are increasing evidences, which show specific arterial in volvement in scleroderma in the form of transient ischemic attack, seizure, cognitive impairment and encephalopathy independent of systemic problems (5,7).These show that isolated central arterial involvement in scleroderma is more prevalent that was thoughtpreviously.

Estey*et al.,* in 1979 reported a known case of scleroderma with encephalopathy and Pathakand Gabor in 1991 introduced a crest syndrome who presented with focal subarachnoid hemorrhage, which both were the results of primary cerebral arteritis independent of systemic vascular involvement. They believed that cerebral vessels can be involve in scleroderma as initial process before developing fibrosis (4,10).

In the other study Kaku *et al.,*discussed4 cases of scleroderma with cerebral aneurysm and supposed relationship between scleroderma and aneurysm formation by microangiopathy of vasavasorum and endothelial injury due to inflammatory responses (11).

Regarding to above hypotheses, we suppose immunity process (excessive titter of ACLA and ANA) is a major cause of cerebral sinus thrombosis. However, other causes of vessels dysfunctions may have a role in developing cerebral sinus thrombosis in this patient. It needs to further studies and follows for understanding the pathogenesis of scleroderma disease in the brain and its vessels.

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