Sneddon Syndrome - A Rare Cause of Stroke in Young

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Abstract

Sneddon’s syndrome (SS) is a rare entity with non-inflammatory thrombotic vasculopathy and is characterized by the combination of cerebrovascular manifestations in form of stroke with livedo racemosa (LR). It is diagnosed with typical histopathological findings on skin biopsy and focal neurological deficits. The etiology of SS is not established as yet. Larger studies of SS patients are required to establish the potential mechanism of this syndrome and its manifestations. Our patient was a young female of 35 years with recurrent stroke (2 episodes till now and this time 2nd episode), presented with few episodes of TIA followed by aphasia and right hemiparesis with skin lesions in form of livedo reticularis, digital infarction and 1 episode of left focal seizure. MRI was suggestive of infarcts in different stages both acute and chronic in different vascular distribution. Possibility of vasculitis and embolic event was there. Skin biopsy was suggestive of Sneddon syndrome that matched our clinical presentation as well.

Keywords: Sneddon Syndrome; Stroke; Young

Introduction

Sneddon’s syndrome (SS) is a rare entity with non-inflammatory thrombotic vasculopathy and is characterized by the combination of cerebrovascular manifestations in form of stroke with livedo racemosa (LR) [1]. In general population the incidence of SS is 4 per 1 million per annum and it is more common in women between the ages of 20 and 42 years [2]. It is diagnosed with typical histopathological findings on skin biopsy and focal neurological deficits. Hypercoagulable state and intrinsic small-vessel vasculopathy is the main pathogenesis behind the disease. Though long-term anticoagulation is touted as a way to treat cerebral ischemic events on the basis of presumed pathogenesis, a solution for optimal management of SS is not completely understood [1]. We report a case of young female patient suffering from SS with manifestations of livedo racemosa, hypertension, and stroke.

Case Study

35-year old female patient, resident of Jaipur, with no addictions, recently diagnosed to be hypertensive was admitted with chief complaints of pain in toes with bluish discolouration and ulceration of toes for 3 months, acute onset weakness of right Upper limb (UL) and lower limb (LL) (UL > LL) for 1 day and episodes of difficulty in speaking with slurring of speech for 1 day. Bluish discolouration of toes started simultaneously in toes of both lower limbs and it increased progressively in winters. On the day of admission in morning she had repeated attacks of slurring of speech which improved spontaneously after few minutes. An hour later while combing her hair she felt weakness of her right hand and she was unable to hold comb and comb her hair. At the same time she had difficulty in speaking with a laboured speech with ability to utter only few words but she was able to understand the spoken words to her.

She gave history of episodes of throbbing holocranial headache associated with nausea, photophobia, phonophobia for several years. She gave history of two abortions of first trimester in the past. She also gave history of one episode of left focal seizure followed by left hemiparesis in November 2014. She did not seek medical attention that time. She was evaluated later after 1 year. MRI brain done that time was suggestive of multiple chronic infarcts in right fronto-parietal lobes (Figure 1). EEG was normal. She took antiepileptics and antiplatelets for one year and then stopped. She was diagnosed to have Hypertension six months back and since then she was on regular treatment. Her mother reported that she had increased anger and agitation for last 4 years. There was no history of vomitings, loss of consciousness, no complaint of numbness, paresthesias, any visual symptoms, difficulty in swallowing. There was no history of valvular heart disease or Diabetes/Tuberculosis in past nor any history of exposure to Sexually transmitted disease. She did not give any history.
of fever, malaise, myalgias, arthritis and weight loss. There was no significant family history. On examination her BP was normal and all peripheral pulses including bilateral carotids were palpable. Cutaneous examination showed bluish black discoloration of the skin over toes of both lower limbs with multiple well defined deep ulcers of varying size on the bilateral feet an odema with surrounding erythema (Figure 2 and 3). She also had violaceous irregular net like pattern over her lower limbs suggestive of livedo racemose (Figure 4). On neurological examination she was aphasic (Broca's aphasia) with right hemiparesis and hemiparetic gait. So we had a patient with recurrent stroke (two episodes till now) with few episodes of TIA followed by aphasia and right hemiparesis with skin lesions and a prior history of abortions and one episode of left focal seizure. From investigations we found she had microcytic anemia. ANA, CRP, APLA profile, RA factor, Anti ds DNA, Anti CCP, Anti Ro, Anti La, ANCA, S. homocysteine, Serum electrophoresis was normal. ECG and 2 D echo was normal. NCV of both lower limbs done was normal. MRI brain was suggestive of acute left MCA infarct involving left parietal lobe cortical and subcortical region (Figure 5) and chronic infarct in right MCA territory involving left side parietal lobe (Figure 6 and 7). CT angio of brain, neck vessels and bilateral lower limb was normal. Skin consultation was done for skin lesions (Figure 8 and 9). In view of negative APLA profile and negative vasculitic profile, APLA syndrome and collagen vascular disease were ruled out. She did not fit in the criteria of PAN and cryoglobulinaemic vasculitis. Looking into the clinical and investigation profile and radiological findings of the patient and discussion with the radiologist and dermatologist we kept the possibility of SS. Our patient was advised skin biopsy. It was taken from the lesion of livedo racemosa. It was suggestive of features of vasculitis - endothelial inflammation with partial occlusion of arterioles.
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Figure 6

Figure 7

Figure 8

Keeping the diagnosis of SS she was started on antiplatelets, anticoagulants, steroids and vasodilators. She showed improvement in symptoms in form of improvement in aphasia, hemiparesis and skin lesions. Initially at the time of presentation she had global aphasia but after treatment she was able to speak, comprehend, read and write. Her power improved from grade 4/5 to 5/5 and skin lesions improved as shown in figures (Figure 10 and 11).

Discussion and Conclusion

The etiology of SS is not established as yet [3]. Livedo racemosa is observed as an important manifestation of SS - this is possibly due to thrombosis of subcutaneous arterioles and compensatory capillary dilation resulting in stagnation of the blood and subsequently mottled discoloration [4]. Histopathological analysis showed involvement of small and medium arteries of skin and brain [3,5]. It affects arms and legs as well as the trunk and buttocks. Cold and pregnancy worsens livedo reticularis [6]. Our 1st patient also had skin lesions in form of erythematous violaceous, irregular, net-like pattern in the skin called livedo racemosa which was worsened by cold. Ischemic stroke followed livedo reticularis in our patient. It is also observed as another hallmark of SS and may precede or follow livedo reticularis. Reduced blood flow to brain leads to stroke which further lead to neurological deficit in form of reduced intellectual ability, memory loss, personality changes, and/or other neurological symptoms. This is how this syndrome is differentiated from other disorders [6]. She had hypertension which can be seen in 15-65% of patients with Sneddon syndrome [7,8]. Though in our patient autoimmune markers were negative, less often, there is association of other autoimmune disorders such as systemic lupus erythematosus (SLE), Behcet’s disease, or mixed connective tissue disease with SS [6]. Cerebral angiography was normal in our patient but it can be abnormal in 75% of the patients with Sneddon syndrome [9]. SM Boesch, et al. undertook a prospective longitudinal study on the clinical course of SS in 13 of 17 previously published patients with definite SS. Their mean (SD) age at diagnosis of SS was 36 (7.5) years [7]. Our patient was also of the same age group, that is, 35 years. In the same study 85% patients had headache (11 of 13 patients) and this was the most frequent unspecific symptom observed during follow up. 62% patients (8 of 13 patients) had vertigo and dizziness. Three patients, that is 23% of patients had migraine without aura [8]. As already mentioned earlier our patient had headache of migranous type. She had increased anger and agitation since last 4 years. In the study by SM Boesch, et al. large number of patients (77% that is 10 patients) had loss of concentration ability, memory disturbances, or emotional impairment but according to mini mental state examination none of the patient was demented (mean (SD) 28 (2) points) [7]. Our patient also had episodes of TIA which was followed by ischemic stroke. SM Boesch, et al. in their study reported 7 patients (54%) had TIA and duration was of less than one hour. Motor deficit was more common (75% of patients) and involved the middle cerebral artery in 84% of patients as was seen in our patient. At entry into the study eight patients had one or more (case 2 had four infarcts) chronic infarcts as was the case of our patient who had acute as well as chronic infarcts in MRI [7]. We conclude that though it is rare recurrent territorial infarctions and catastrophic clinical course can occur in patients of SS. Boortz-Marx in his study suggested the role of inflammation by granulomatous leptomeningeal infiltration in SS [10]. In turn, Pinol-Aguade and Geschwind in their study found no evidence of vasculitis and they demonstrated thrombosis and recanalisation in meningeal and cerebral vessels in their cases [11]. Recurrant TIA can be contributed to relapsing obstruction and then recanalization process in cerebral arteries [12]. Larger studies of SS patients are required to establish the potential mechanism of this syndrome and its manifestations.

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