International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: SJIF: 5.995
Available Online at www.journalijcar.org
Volume 6; Issue 10; October 2017; Page No. 6670-6672
DOI: http://dx.doi.org/10.24327/ijcar.2017.6672.0993

Research Article

DIGITAL NECROSIS REVEALING SNEDDON SYNDROME

Jamal Fatihi[1]*., Salah Bellasri[2]., Amine Abdellah[3]., Tarik Addiou[1] and Hicham Janah[1]

[1]Department of Internal Medicine, Fifth Military Hospital of Guelmim, Morocco
[2]Department of Radiology, Fifth Military Hospital of Guelmim, Morocco
[3]Department of Cardiology, Fifth Military Hospital of Guelmim, Morocco

ARTICLE INFO

Article History:

Received 15th July, 2017
Received in revised form 19th August, 2017 Accepted 25th September, 2017
Published online 28th October, 2017

Key words:

Sneddon syndrome, digital necrosis, ischemic stroke

ABSTRACT

Sneddon's syndrome is a rare disease defined by the presence of ischemic cerebrovascular events associated with livedo racemosa. It can also affect other organs such as heart, kidneys, eyes and the peripheral nervous system. We herein describe the case of a 28-year old man, who presented with Raynaud's phenomenon, digital necrosis, neurological and cardiac manifestations revealing Sneddon syndrome. We highlight through this case diagnostic and therapeutic challenges of Sneddon syndrome.

INTRODUCTION

Sneddon's syndrome (SS) is a rare non-inflammatory thrombotic vasculopathy characterized by the combination of cerebrovascular disease with livedo racemosa [1]. It mainly affects women between 25 years and 35 years of age (80% of patients) and has a chronic progressive course that causes multiple neurologic and systemic manifestations [2]. Diagnosis of SS is mainly based on skin biopsy and abnormal findings in neurological examination and/or MRI [3]. Long-term anticoagulation has been recommended for cerebral ischemic events, but the optimal management is still unknown. There are controversial results regarding effects of immunomodulatory agents. We report the case of a 28 year old man diagnosed as SS with skin, neurological and cardiac involvement. His clinical course under treatment is described, followed by a discussion of diagnostic and therapeutic options in SS.

Case Report

A 28-year-old man was admitted to our department with a 3-month history of Raynaud phenomenon with digital necrosis, hand tremor and "migraine" headache. He had never smoked, no other vascular risk factors were reported and he wasn't taking any medication. Physical examination was remarkable for obvious digital necrosis of the distal right first finger (Fig.1 and Fig.2) with livedo of the dorsum of both hands (Fig.3). No other skin changes, specifically sclerodactyly or teleangiectasia, were present. His blood pressure was 130/80 mmHg and he was in sinus rhythm. Heart auscultation noticed a systolic murmur on the apex. His neurological examination revealed a stato- kinetic cerebellar syndrome. A MR angiography was performed and revealed multiple white-matter abnormalities at parietal corticosubcortical region suggesting involvement of small vessels with parietal cortex atrophy (Fig.4). The cardiac study included normal ECG, normal supra aortic vessels ultrasound and transthoracic ultrasound which showed significant thickening of the mitral valve leaflets with a secondary moderate mitral regurgitation (Fig.5). Blood tests screen were negative for lupus anticoagulant, immunoglobulin IgG and IgM anti-cardiolipin antibodies, anti-nuclear and anti-double-stranded DNA autoantibodies, thrombocytopenia, leukopenia, VDRL, cryoglobulins, circulating immune complexes, antithrombin-III, protein C, and protein S. The cerebrospinal fluid was normal. The patient was diagnosed as having aPL-negative SS with skin, neurological and cardiac involvement. Antiplatelets and corticosteroid therapy resulted in rapid improvement of digital necrotic lesions.

3 months after discharge the patient had series of epileptic seizures and experimented cognitive disturbances with concentration, attention and memory impairment. Control MRI showed progression of brain lesions. Immunosuppressive therapy was intensified by adding azathioprine to steroids, antiepileptic medication was introduced, antiplatelets were changed by wafarine anticoagulation. The patient did not complain of any new seizure and the neuropsychological status stays stable 7 months later.

Corresponding author:* **Jamal Fatihi
Department of Internal Medicine, Fifth Military Hospital of Guelmim, Morocco

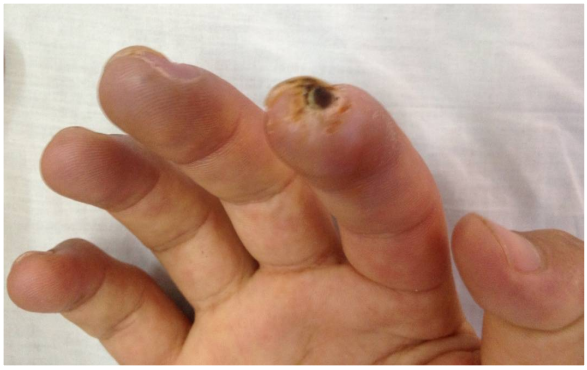

Figure 1 Digital necrosis of the distal right first finger

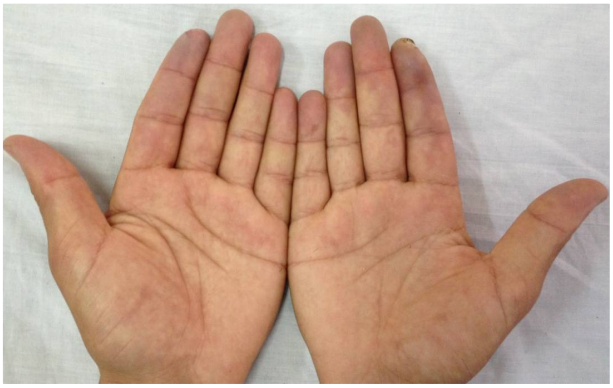

Figure 2 Bilateral acrocyanosis of hands

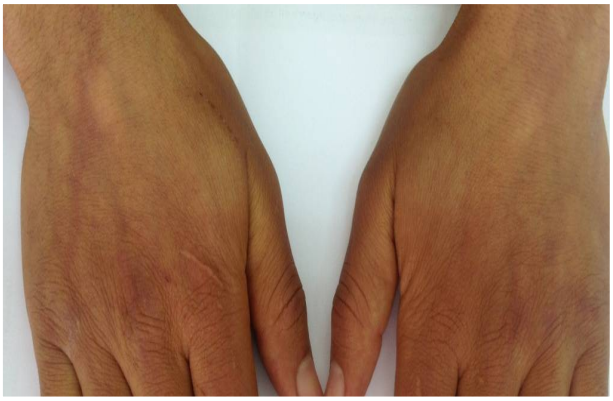

Figure 3 Livedo of the dorsum of both hands

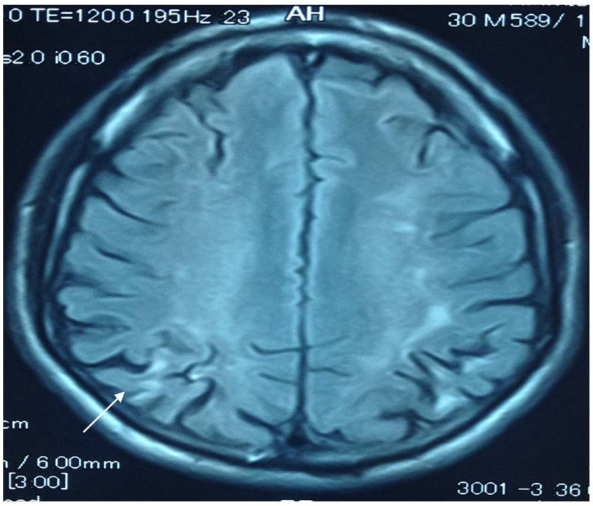

Figure 4 Subcortical parietal white matter abnormalities with cortical atrophy (arrow)

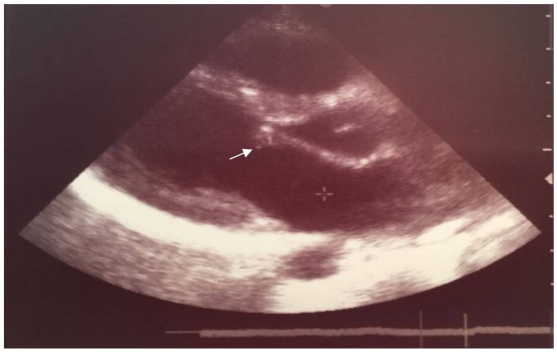

Figure 5 Mitral valve leaflets thickening (arrow)

DISCUSSION

Sneddon's syndrome (SS) is a rare non-inflammatory thrombotic vasculopathy characterized by the combination of cerebrovascular disease with livedo racemosa [1]. Since 1965, the term SS has been introduced by Sneddon to describe the association of livedo racemosa and multiple cerebral infarcts [4]. The estimated annual incidence of SS is four cases per million, the disease predominantly affects women in young adulthood [5]. The pathophysiology of SS is not fully understood, but the presence of antiphospholipid (aPL) antibodies in 50% of patients, as well as the skin and brain biopsy findings, suggests a thrombotic vasculopathy of medium and small arteries [6].

One of the diagnostic hallmarks of SS is livedo racemosa defined as a dusky erythematousto-violaceous, irregular, net-like pattern in the skin. Livedo usually precedes the onset of the neurological picture, sometimes for several decades and can intensify in the acute phase of a neurological complication [1] [2]. Histopathological findings in biopsies of cutaneous lesions in SS have been variously described as thrombosis of subcutaneous arterioles and compensatory capillary dilation with blood stagnation causing livedo [7]. Our patient had, in addition to livedo racemosa, a peripheral vasculopathy manifested by Raynaud's phenomenon and digital infarction.
Stroke is another diagnostic hallmark of SS. Focal acute neurological signs resulting from cerebral ischemic events are more frequent in SS patients. Sudden motor deficit, aphasia, visual field defect and acute encephalopathy are frequent as the first neurological event [8]. Headache represents the most frequent unspecific symptom [9]. Cognitive impairment and psychiatric disturbances can occur in approximately 77% of SS patients and SS can also be a cause of dementia in the young [10]. Focal or secondary generalized seizures are commonly seen in SS, especially in patients with positive Antiphospholipids [11]. Lesions can be more clearly detected by MRI than by CT scan. These lesions are often small and multifocal, located predominantly in the periventricular deep white matter or pons [1]. In our observation, tremor and headache were the first and prominent initial symptoms of cerebrovascular disease before other neurological and skin signs. Cognitive decline appeared early in the course of the disease.

Mitral valve thickening and coronary vasculopathy are the main cardiac manifestations of SS that can be found in literature [12] [13]. Cardiac abnormalities in this context might increase morbidity and mortality. In our case, heart

valve abnormalities were present without coexisting coronary disease.

Any patient suspected of SS should undergo blood tests for lupus anticoagulant, immunoglobulin IgG and possibly IgM anti-cardiolipin antibodies, anti-nuclear and anti-double-stranded DNA autoantibodies, thrombocytopenia, leukopenia, VDRL, cryoglobulins, circulating immune complexes, antithrombin-III, protein C, and protein S. According to the presence or absence of aPL, 2 subtypes of SS have been described subsequently with different possible pathologic mechanisms. The relationship between Sneddon's syndrome and the Antiphospholipid antibody syndrome is not yet well established [2]. Our case was not associated to aPL.

Treatment of patients with SS is still controversial. Categorization of SS patients into two subsets (aPL-positive and aPL-negative) might influence disease management [14]. In both aPL-positive and aPL-negative cases, limited effectiveness or frank inefficacy of various immunotherapies, including steroids and azathioprine, has been repeatedly described. For SS patients with aPL antibodies warfarin is often used. On the other hand, one study demonstrated that SS patients without aPL benefit from antiplatelet therapy [15]. Our patient was aPL-negative and received initially antiplatelets with steroids. Because of the neurological worsening, therapy was intensified by adjunction of azathioprine and antiplatlets were changed by wafarine anticoagulation with resulting clinical improvement.

CONCLUSION

The clinical implication of this observation is that digital necrosis associated with livedo and non specific neurological signs should alert the clinician to look carefully for SS. Early recognition and treatment of this syndrome improves prognosis of this cerebrovascular disease.

References

1. Wu S, Xu Z, Liang H. Sneddon's syndrome: a comprehensive review of the literature. Orphanet *Journal of Rare Diseases* 2014; 9:215
2. Frances C, Papo T, Wechsler B, et al. Sneddon syndrome with or without antiphospholipid antibodies. A comparative study in 46 patients. Medicine (Baltimore) 1999;78:209-19
3. Boesch SM, Plörer AL, Auer AJ, Poewe W, Aichner FT, Felber SR, Sepp NT. The natural course of Sneddon syndrome: clinical and magnetic resonance imaging findings in a prospective six year observation study. *J Neurol Neurosurg Psychiatry* 2003;74:542-544
4. Sneddon IB. Cerebro-vascular lesions and livedo reticularis. *Br. J. Dermatol*. 1965;77:180-185
5. Zelger B, Sepp N, Stockhammer G, Dosch E, Hilty E, Ofner D, Aichner F,Fritsch PO: Sneddon's syndrome. A long-term follow-up of 21 patients. *Arch Dermatol* 1993; 129:437-447.
6. Dominguez F, Pieske B, Kelle S. Cardiac manifestations of Sneddon's syndrome. *International Journal of Cardiology* 2015; 190: 275-276.
7. Devos J, Bulcke J, Degree H, Michielsen B. Sneddon's Syndrome: Generalized Livedo reticularis and Cerebrovascular Disease. *Dermatology* 1992;185:296-299
8. Martins da Silva A, Rocha N, Pinto M, Alves V, Farinha F, Correia A.P, Coelho T, Magalhaes M. Tremor as the First Neurological Manifestation of Sneddon's Syndrome. *Movement Disorders* 2005; 20:248-251
9. Tietjen GE, Al-Qasmi MM, Shukairy MS. Livedo reticularis and migraine: a marker for stroke risk? Headache 2002; 42:352-355.
10. Adair JC, Digre KB, Swanda RM, Hartshorne MF, Lee RR, Constantino TM, Knoefel JE. Sneddon's syndrome: cause of cognitive decline in young adults. *Neuro Psychiatry Neuropsychol Behav Neurol* 2001; 14:197-204.
11. Quenardelle V, Willaume T, Benoilid A. A first seizure revealing Sneddon's syndrome. *Rev Neurol* 2014; 170:55-57
12. Kalashnikova LA, Nasonov EL, Borisenko VV, Usman VB, Prudnikova LZ, Kovaljov VU, Kushekbaeva AF. Sneddon's syndrome: cardiac pathology and antiphospholipid antibodies. *Clin. Exp. Rheumatol*. 1991; 9: 357-361
13. Scheuermann S, Schlundt C. STEMI of the anterior wall associated with Sneddon's syndrome, Herz 2014;39: 352-353
14. Flöel A, Imai T, Lohmann H, Bethke F, Sunderkötter C, Drost DW. Therapy of Sneddon Syndrome. *Eur Neurol* 2002;48:126-132
15. Dutra LA, Braga-Neto P, Pedroso JL, Graziani O, Barsottini P. Sneddon's syndrome: case report and review of its relationship with antiphospholipid syndrome. *Einstein* 2012;10(2):230-2

How to cite this article:

Jamal Fatihi *et al* (2017) 'Digital Necrosis Revealing Sneddon Syndrome', *International Journal of Current Advanced Research*, 06(10), pp. 6670-6672. DOI: http://dx.doi.org/10.24327/ijcar.2017.6672.0993

****