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Detection of asymptomatic brain involvement in systemic sclerosis

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Summary

Background: Systemic sclerosis is a chronic connective tissue disease, characterized by vascular changes, accompanied by fibrosis of the skin and internal organs. Neuropsychiatric symptoms are considered rare in these patients. Objectives The aim of the study was to evaluate frequency of morphological brain abnormalities in those patients with systemic sclerosis, who demonstrate no clinical symptoms of central nervous system involvement.

Material/Methods: 24 patients with systemic sclerosis, who had no neurological or psychiatric abnormalities were included into the study. In all patients brain magnetic resonance imaging was performed. Fluid-attenuated inversion-recovery and fast spin-echo magnetic resonance imaging sequences were used.

Results: In 37% (9/24) of these patients brain magnetic resonance images revealed abnormalities. These included: cortical and subcortical atrophy (4/24), single focal lesions (5/24) or diffuse lesions (2/24). In 3 patients simultaneous presence of more then one of these abnormalities was detected. Brain computer tomography revealed abnormalities in 2/24 (8%) of patients.

Conclusions: Our results indicate, that the central nervous system may be involved in systemic sclerosis despite lack of neuropsychiatric symptoms. Brain magnetic resonance imaging allows early detection of these abnormalities. We suggest to perform brain magnetic resonance in all patients of systemic sclerosis before introducing treatment.

Key words: brain • magnetic resonance imaging • scleroderma • systemic sclerosis

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Background

Systemic sclerosis (SSc) is a chronic connective tissue disease of autoimmune etiology, characterized by progressive fibrosis and vascular abnormalities in the skin, subcutaneous tissue and internal organs, such as lung, heart, gastrointestinal tract and kidneys [1]. Nearly all patients with SSc are affected by the Raynaud phenomenon, an episodic vasoconstriction in distal extremities. Research confirms that in SSc vascular dysfunction is not restricted to extremities, but is widespread and may affect blood vessels in all internal organs [2,3]. Furthermore, repeated attacks of Raynaud phenomenon may contribute to vascular abnormalities by a mechanism of reperfusion injury of the endothelium [4].

Even though generalized vasospastic tendency might have an effect on the central nervous system, clinical neuropsychiatric symptoms are considered rare in patients with SSc.

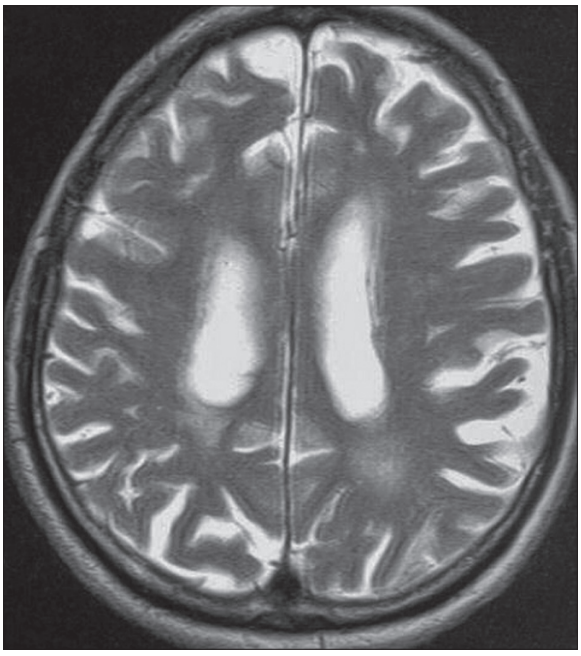

Figure 1. Asymptomatic focal brain lesions in a 41-year female old patient with SSc.

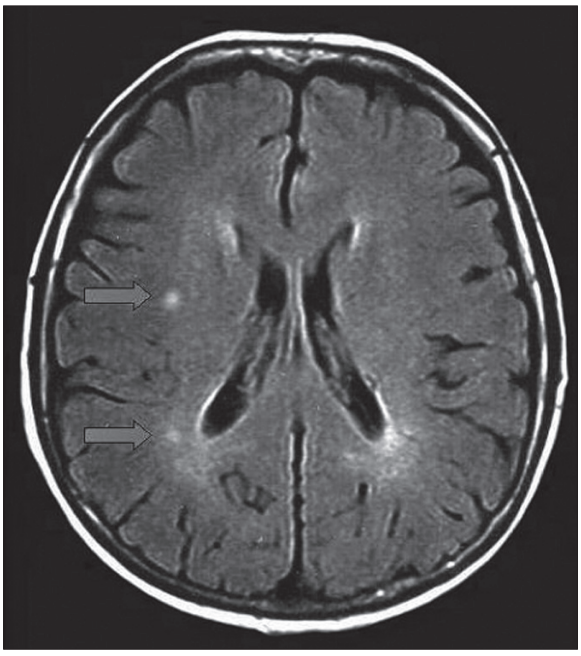

Figure 2. Asymptomatic cortical and subcortical atrophy in a 55-year old female patient with SSc.

These include sporadic occurrence of headache, vertigo, loss of consciousness, hypo-/dysmnesia, depressive and organic brain damage syndromes and transient ischaemic attacks [5,6]. Impaired cerebral blood flow was shown in a proportion of these patients [7–9]. Anecdotal cases of cerebritis [10], intracerebral hemorrhage [11,12] and mental disorders [13] were reported in patients with SSc.

In general brain lesions can be detected with diverse contemporary imaging techniques, including computer tomography (CT), magnetic resonance (MRI) and single photon emission computed tomography [14–16].The aim of this study was to investigate the possible presence of brain abnormalities in SSc patients who demonstrate no neurologic or psychiatric symptoms upon clinical investigation and to assess the value of computer tomography versus magnetic resonance imaging in evaluation of these abnormalities.

Material and Methods

A number of 54 consecutive patients with systemic sclerosis visiting our scleroderma out-patient division, were investigated for clinical neuropsychiatric symptoms. All patients met the American College of Rheumatology criteria for the diagnosis of SSc [17]. The presence on any neurological or psychiatric abnormality was regarded as exclusion criterion. Excluded from the study were also patients with coexisting other than SSc risk factors of vascular brain disease, such as hypertension or diabetes. After this pre-selection 24 patients with SSc were included into the study. 16 of them were affected by diffuse SSc and 8 by limited SSc. The group included 22 females and 2 males. Mean age was 49 years (range 26–69, SD 11 years).

Mean disease duration was 10 years. The control group included 24 age- and sex-matched healthy volunteers.

Complete clinical evaluation was performed in all patients. Cutaneous involvement was scored according to Rodnan's modified criteria [18]. The presence of Raynaud phenomenon was examined in all patients. Internal organ involvement was assessed by: eosophagus scyntygraphy (for esophagus dysmotility), chest X-ray, pulmonary function tests, HRCT of lungs (for lung fibrosis), electrocardiography and echocardiography (for cardiac involvement). For statistical analysis abnormalities in organ function were recorded in a "present" or "absent" manner. Basic laboratory tests and serological screening was performed. Presence of antinuclear antibodies, anticardiolipin antibodies and lupus anticoagulant antibodies (IgG and IgM classes) was evaluated with the use of enzyme linked immunosorbent assay.

In all patients brain CT and MRI was performed. Fluid-attenuated inversion-recovery (FLAIR) and fast spin-echo (FSE) MRI sequences were used. For statistical analysis of CT and MRI findings, the presence and intensity of cortical and cortico-subcortical atrophy (none, minor, major), as well as the number of focal lesions (no focal lesions, single focal lesion, 2–5 focal lesions, >5 focal lesions) were assessed. CT and MR images were analyzed independently.

Statistical analysis was performed by means of the non-parametric Mann-Whitney U test. Correlation coefficients between chosen clinical features were determined by Spearman's correlation test. Values lower than 0.05 were considered significant. Statistical analysis was performed by author JC of this publication. The study protocol was approved by the ethics committee. All patients gave written informed consent for participation in this study.

Results

Among 24 patients with no clinical symptoms of brain involvement, 37% (9/24) presented abnormalities in brain

MRI. In these patients following abnormalities were detected: minor degree cortical and subcortical atrophy in 3/24 (12.5%), major degree cortical and subcortical atrophy in 5/24 (21%), single focal lesions in 2/24 (8%), multiple focal lesions in 2/24 (8%) and diffuse brain lesions of leukoaraiosis type in 2/24 (8%) cases. In three patients cortical and subcortical atrophy coexisted with focal lesions. Figure 1 shows asymptomatic focal brain lesions in a 41-year old patient with SSc. Asymptomatic cortical and subcortical atrophy in a 55-year old patient with SSc is presented in Figure 2. MR imaging technique (FLAIR sequence) revealed Virchow-Robin spaces in 2/24 (8%) of healthy controls. Cortical or subcortical athophy or focal lesions were not observed in healthy controls.

CT revealed abnormalities in 2/24 (8%) of patients. In both cases major degree cortical and subcortical atrophy was detected. In one patient additionally multiple focal lesions were found. No abnormal CT scans were obtained in the control group.

Data analysis revealed a statistically significant correlation between disease duration and presence of atrophy in MR images ($p<0.01$), as well as presence of focal lesions ($p<0.01$). Abnormal MRI findings corresponded with pulmonary fibrosis ($p<0.01$) and cardiac manifestations ($p=0.01$). A borderline statistical correlation ($p=0.049$) between extent of skin indurations expressed as Rodnan score and the presence of atrophy in MRI was recorded. No other, statistically significant correlations between brain abnormalities in MRI or CT and clinical symptoms or laboratory results could be detected. There was no relationship between the tendency to develop asymptomatic brain abnormalities and the presence, bloodconcentration or type of antinuclear antibodies.

Discussion

Neuropsychiatric abnormalities are considered rare in SSc. In our study 55% (30/54) of SSc patients presented clinical neuropsychiatric symptoms of various degree. Out of the remaining 24 patients, who presented no neuropsychiatric symptoms upon detailed neurologic and psychiatric investigation a number of 9 (37%) showed abnormalities in brain MRI. These were: mild to severe cortical and subcortical atrophy, single focal lesions or diffuse lesions of leukoaraiosis type. In the same group of 24 patients CT images revealed abnormalities in only 2 (8%) cases. Both patients exhibited major degree cortical and subcortical atrophy. In one patient additionally multiple focal lesions were found. These data indicate a significant advantage of MRI over CT in diagnosing brain abnormalities in SSc. MRI was an especially valuable tool for detecting single and multiple focal lesions. MRI technique showed in this regard a fourfold higher sensitivity as compared to CT. Focal lesions detected in MRI were is some cases accompanied by hiperintensive regions and atrophic lesions found in areas supplied by main brain arteries, what may indicate a role of vascular abnormalities in mechanism leading to the development of brain lesions in these patients. Studies performed in connective tissue diseases, predominantly systemic lupus erythematosus and scleromyxoedema show that disorders of coagulability, especially the presence of antiphospholipid antibodies, might facilitate ischaemic changes.[19–21] In our study, no thrombotic changes were observed. No correlation between the presence of antiphospholipid antibodies and brain abnormalities was detected.

Our study reveals that disease duration and lung involvement strongly correlate with abnormalities in MRI brain scans. It may be suggested that brain ischaemic lesions in SSc might be secondary to generalized hypoxia resulting from lung fibrosis. One may also hypothesize that both, profound lung involvement and significant brain abnormalities in SSc might be a general manifestation of a more severe disease process related to slowly progressing vasuloscopathy, characteristic of SSc.

Conclusions

In conclusion, our results indicate, that the central nervous system is involved in SSc more often than it might be suspected based on symptomatology only. Early diagnosis may be obtained by means of the MRI technique and we suggest to consider performing brain MRI in every patient with SSc before choosing therapeutic strategy for the patient

References:

1. Sakkas LI: New developments in the pathogenesis of systemic sclerosis. Autoimmunity 2005; 38: 113–16
2. Herrick AL: Pathogenesis of Raynaud's phenomenon. Rheumatology (Oxford), 2005; 44: 587–96
3. Kahaleh MB: Vascular involvement in systemic sclerosis (SSc). Clin Exp Rheumatol, 2004; 22: S19–23
4. Sicinska J, Rudnicka L: Raynaud's disease and Raynaud's phenomenon in connective tissue diseases. Pol Arch Med Wewn, 2002; 108: 1011–22
5. Hietaharju A, Jaaskelainen S, Hietarinta M et al: Central nervous system involvement and psychiatric manifestations in systemic sclerosis (scleroderma): clinical and neurophysiological evaluation. Acta Neurol Scand, 1993; 87: 382–87
6. Angelopoulos NV, Drosos AA, Moutsopoulos HM: Psychiatric symptoms associated with scleroderma. Psychother Psychosom, 2001; 70: 145–50
7. Cutolo M, Nobili F, Sulli A et al: Evidence of cerebral hypoperfusion in scleroderma patients. Rheumatology (Oxford), 2000; 39: 1366–73
8. Nobili C, Cutolo M, Sulli A et al: Brain functional involvement by perfusion SPECT in systemic sclerosis and Behcet's disease. Ann NY Acad Sci, 2002; 966: 409–14
9. Pizova NV: Cerebral vascular pathology in systemic sclerosis. Zh Nevrol Psikhiatr Im S S Korsakova, 2004; 104: 19–23
10. Wise TN, Ginzler EM: Scleroderma cerebritis, an unusual manifestation of progressive systemic sclerosis. Dis Nerv Syst, 1975; 36: 60–62
11. Yukawa H, Kubo Y, Otawara Y et al: A case of left occipital lobe hemorrhage in a patient with progressive systemic sclerosis: evaluation of cerebral angiography and histology. No Shinkei Geka, 2000; 28: 1003–7
12. Andonopoulos AP, Maraziotis T, Rigas G et al: Multiple spontaneous intracerebral hemorrhages in a patient with progressive systemic sclerosis. Rev Rhum Engl Ed, 1998; 65: 437–40
13. Shiraishi H, Koizumi J, Suzuki T et al: Progressive systemic sclerosis with mental disorder. Jpn J Psychiatry Neurol, 1991; 45: 855–60
14. Broderick DF: Neuroimaging in neuropsychiatry. Psychiatr Clin North Am, 2005; 28: 549–66

15. Duncan JS: Brain imaging in idiopathic generalized epilepsies. Epilepsia, 2005; 46: 108–11
16. Peterson PL, Axford JS, Isenberg D: Imaging in CNS lupus. Best Pract Res Clin Rheumatol, 2005; 19: 727–39
17. Lonzetti LS, Joyal F, Raynauld JP et al: Updating the American College of Rheumatology preliminary classification criteria for systemic sclerosis: addition of severe nailfold capillaroscopy abnormalities markedly increases the sensitivity for limited scleroderma. Arthritis Rheum, 2001; 44: 735–36
18. Clements P, Lachenbruch P, Siebold J et al: Inter and intraobserver variability of total skin thickness score (modified Rodnan TSS) in systemic sclerosis. J Rheumatol, 1995; 22: 1281–85
19. Walecki J, Sierakowski S, Lewszuk A et al: MR in neurological syndromes of connective tissue diseases. Med Sci Monit, 2002; 8(6): MT105–11
20. Shergill B, Orteu CH, McBride SR, Rustin MH: Dementia associated with scleromyxoedema reversed by high-dose intravenous immunoglobulin. Br J Dermatol, 2005; 153: 650–52
21. Hasegawa M, Nagai Y, Tamura A, Ishikawa O: Arteriographic evaluation of vascular changes of the extremities in patients with systemic sclerosis. Br J Dermatol, 2006; 155: 1159–64