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Value of computed tomography and magnetic resonance imaging in diagnosis of central nervous system involvement in systemic sclerosis

Wartość tomografii komputerowej i rezonansu magnetycznego w diagnostyce zmian w centralnym układzie nerwowym u pacjentów z twardziną układową

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Summary

Background: Systemic sclerosis is an autoimmune connective tissue disease characterized by vascular abnormalities and fibrotic changes in skin and internal organs. The aim of the study was to investigate involvement of the central nervous system in systemic sclerosis and the value of computed tomography (CT) and magnetic resonance imaging (MRI) in evaluation of central nervous system involvement in systemic sclerosis.

Material/Methods: 26 patients with neuropsychiatric symptoms in the course of systemic sclerosis were investigated for central nervous system abnormalities by computed tomography (CT) and magnetic resonance imaging (MRI).

Results: Among these 26 symptomatic patients lesions in brain MRI and CT examinations were present in 54% and in 50% patients respectively. Most common findings (in 46% of all patients), were symptoms of cortical and subcortical atrophy, seen in both, MRI and CT. Single and multiple focal lesions, predominantly in the white matter, were detected by MRI significantly more frequently as compared to CT (62% and 15% patients respectively).

Presence of brain atrophy and focal lesions in CT and MR correlated with disease duration (both $p<0,0001$), extent of skin involvement ($p<0,01$) and presence of pulmonary fibrosis in the course of the systemic sclerosis ($p=0.001$).

Conclusions: These data indicate that brain involvement is common in patients with severe systemic sclerosis. MRI shows significantly higher than CT sensitivity in detection focal brain lesions in these patients.

Key words: Scleroderma • Raynaud Phenomenon • Brain • Computed Tomography • Magnetic Resonance Imaging

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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, gastro-intestinal tract and kidneys [1]. Nearly all patients with systemic sclerosis are affected by episodic vasospasm within distal extremities (Raynaud phenomenon). Repeated attacks of Raynaud phenomenon may contribute to vascular abnormalities in systemic sclerosis by a mechanism of reperfusion injury of the endothelium [2]. Several data indicate that the phenomenon is not restricted to extremities. It can also occur in internal organs, such as lung and heart [3]. Generalized vasospastic tendency and vasculopathy might also have an effect on the central nervous system [4].

However, till now only a limited number of studies, have addressed the issue of central nervous system involvement in SSc [5, 6, 7, 8]. Impaired cerebral blood flow was shown by Cutolo et al. [9]. Cases of cerebritis [10] and intracerebral hemorrhage [11, 12] and mental disorders [13] were reported in a few papers in patients with SSc. Clinical neuropsychiatric symptoms are relatively rare in SSc. These include headaches, vertigo, loss of consciousness, hypo-/dysmnesia, depressive, mild cognitive impairment and organic brain damage syndromes, transient ischaemic attacks (TIA) and cerebral infarction with paresis [14].

Brain lesions can be detected with contemporary imaging techniques, including computed tomography (CT), magnetic resonance (MRI) and single photon emission computed tomography (SPECT) [15 ,16, 17, 18].

The aim of this study was to investigate the frequency of brain abnormalities in SSc and to assess the value of computed tomography and magnetic resonance imaging in evaluation of central nervous system involvement in systemic sclerosis.

Materials and methods

Patients. 26 patients with neuropsychiatric symptoms in the course of SSc, aged 27–72, were enrolled into the study. All patients met the American College of Rheumatology criteria for the diagnosis of SSc: 17 patients were affected by the diffuse cutaneous variant (dSSc) and 9 by the limited cutaneous variant (lSSc) of the disease. The group (tab. 1.) included 25 females and 1 male. Mean age was 50 years (range 27–72, SD 12 years). Mean disease duration was 10 years in the observed group of patients (11 years in lSSc subset and 9 years in dSSc subset). The control group included 26 age- and sex-matched healthy volunteers. Patients with other than SSc risk factors of vascular brain disease (hypertension or diabetes) were excluded from the study. No abnormal CT findings were obtained in the control group. MRI technique (FLAIR sequence) revealed widening Virchow-Robin spaces in 3 patients (aged range 50–60 years).

Clinical evaluation. Complete clinical evaluations including accurate assessment of neurologic condition were performed in all SSc patients. In particular, cutaneous involvement was scored according to Rodnan. The presence of Raynaud phenomenon was examined in all patients. A variety of tests were utilised to evaluate internal organ involvement: cine esophagraphy and/or eosophagus scyntygraphy, gastroscopy, colonoscopy, chest X-ray, pulmonary function tests, HRCT of lungs, electrocardiography and echocardiography. Basic laboratory tests and serological screening for antinuclear antibodies, anticardiolipin antibodies and lupus anticoagulant antibodies (IgG and IgM classes) were performed with the use of enzme linked immunosorbent assay.

CT and MRI. In all patients brain CT and MRI examinations were performed. CT examinations consisted of 3mm slices for posterior fossa and 7mm for the rest of the brain. No contrast media was administered. MRI examinations consisted of SE and FSE sequences, T1-, T2-weighted and FLAIR images of 5mm slices with 0,5mm gap. In 5 cases DWI were performed for the exclusion of early stroke. In 3 cases paramagnetic i.v. contrast media was administered (0,2ml/kg).

Statistical analysis. In order to compare clinical, laboratory and imaging findings, the obtained data were stratified by the presence or absence of certain clinical features

Table 1. Main clinical data of patients in the studied group.
Tabela 1. Charakterystyka kliniczna pacjentów w grupie badanej.

	lSSc(n=9)	dSSc(n = 17)
Mean age (yrs)(range; SD)	49 (32–61; 12,8)	50 (27–72; 12)
Females/males ratio	9/0	16/1
Mean disease duration (yrs) (range; SD)	11 (4–26; 7,2)	9 (1–23; 6,3)
Rodnan skin score (mean value, range; SD)	12,5 (1–22; 7,8)	17 (1–22; 6,3)
(yrs) (mean value, range; SD)	15 (4–26; 7,2)	10 (1–23; 6,3)
Onset of skin sclerosis (yrs) (mean value, range; SD)	11 (1–22; 7,8)	9 (1–22; 6,3)
Interval between the onset of Raynaud's phenomenon and skin sclerosis(yrs) (mean value, range; SD)	8 (1–18; 6,8)	4 (0–20; 6,5)
Skin sclerosis	100%	100%

(neuropsychiatric, cardiac, pulmonary, renal, gastric and articular/muscular manifestations). Similar stratification was performed for the presence of antinuclear antibodies. For the analysis of CT and MRI findings the following classification was employed: the presence and intensity of cortical and cortico-subsortical atrophy, as well as the presence of focal lesions was assessed (no focal lesions, single focal lesion, 2–5 focal lesions, >5 focal lesions, confluent lesions). CT and MR images were analyzed independently. The results are presented as percentage and mean, and confidence interval was 95%. Data analysis included mean values. Significant differences between the subsets of patients were analyzed using the nonparametric Mann-Whitney U test. Correlation coefficients between chosen clinical features of the disease were determined by Spearman's correlation test. Probability values <0.05 were considered significant.

Results

All patients enrolled into the study exhibited neuropsychiatric symptoms, among which the most common were depression, TIA, headache, vertigo, organic brain damage syndrome and hypo-/dysmnesia.

Changes in MRI and CT examinations were detected in 14 (54%) and in 13 (50%) patients, respectively.

Among patients with depression, cortical and subcortical atrophy of moderate degree was found in 6 (35%) individuals. Atrophy of significant degree was detected in one individual (6%). Additionally, single focal lesions were found in 5 patients (29%) according to MRI and in 2 patients (12%) according to CT. Among these patients multiple focal lesions were detected in 2 individuals (12%) on MRI and in one individual (6%) on CT. Diffuse periventricular white matter lesions were revealed in 2 patients by MRI and in 1 patient by CT. In patients with depression, more focal lesions were detected with MRI (7 individuals, 41%) than with CT (3 individuals, 18%).

In 2 patients with organic brain damage syndromes, cortical and subcortical atrophy lesions of moderate degree were detected in both cases in CT and MRI images. Focal white matter lesions were observed on MR images only.

In the patients with TIA history (4 individuals), cortical and subcortical atrophy of moderate degree were present in 2 cases (visualized with both techniques). Single focal lesions were revealed with both techniques in one patient. Multiple focal lesions were found in 1 patient with MRI only (CT scan was normal). Additionally, diffuse periventricular white matter hyperintensities were detected with both techniques in one patient.

In the subset of patients with headaches and vertigo, imaging studies revealed no morphological changes.

There were no significant differences between clinical features of brain involvement in both disease subsets, diffuse SSc or limited SSc. Imaging techniques revealed similar distribution of brain lesions in both subtypes.

Disease duration correlated with the presence of atrophy on CT and MR images ($p=0,0001$) and with the presence of focal lesions, where a very strong correlation ($p=0,0001$) was found for MRI images only. Additionally, a correlation between the disease duration and the presence of diffuse lesions in CT ($p=0,008$) and MRI ($p=0,007$) was recorded.

Interestingly, the presence of pulmonary manifestations, characteristic for SSc also corresponded with abnormal CT ($p=0.012$) and MRI ($p=0.001$) findings.

Investigation of antibody profile revealed presence of antinuclear antibodies in 96% SSc patients. There was no significant correlation between the presence of antinuclear antibodies (Topo I or ACA) and brain involvement, as assessed by either CT or MRI.

Statistically significant correlation was recorded between profound skin sclerosis and the presence of focal lesions on CT and MRI ($p<0.05$).

Discussion

Vascular abnormalities in skin, subcutaneous tissue and internal organs, such as lung, heart, gastro-intestinal tract and kidneys are common findings in patients with SSc. A major abnormality in this regard are episodic vasospasm attacks, contributing to vascular abnormalities by a mechanism of reperfusion injury of endothelium. Several data indicate that this phenomenon might also have an effect on the central nervous system in SSc. However, neurologic involvement in SSc was only infrequently reported. Studies showed impaired cerebral blood flow, cases of cerebritis and central nervous system vasculitis, as well as neuropsychiatric symptoms [6,7,8,9]. Symptoms, such as headaches, vertigo, loss of consciousness, hypo-/dysmnesia, depressive and organic brain damage syndromes, transient ischaemic attacks (TIA) and cerebral infarction with paresis were reported in patients with SSc [13]. Lesions visible on CT and MRI are the consequence of complex (multifactorial) pathogenesis leading to vasculopathy and brain damage.

From a pathological point of view mentioned above white matter lesions are the result of WM degeneration, ischemic demyelination and reactive gliosis. Although cortical atrophy seems to be a consequence of central nervous system vasculopathy

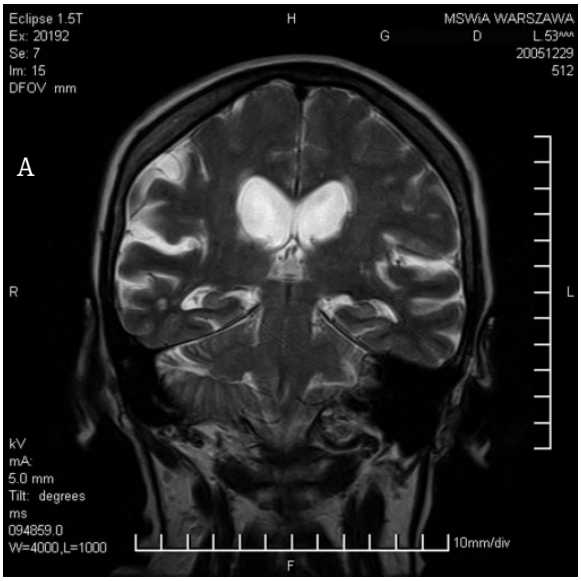
In this study the value of CT and MRI in diagnosis of central nervous system involvement in SSc was assessed. Our results show that MRI is a more sensitive imaging technique than CT for detecting single focal changes (white matter hyperintensities). In patients presenting clinical neuropsychiatric symptoms, alterations in MRI were detected in 54% patients whereas CT scan abnormalities were present in 50% patients. Most prominent findings were cortical and subcortical atrophy. MRI was an especially valuable tool for detecting single and multiple focal lesions(white matter hyperintensities). MRI technique(T2 ,FLAIR) showed in the regard a fourfold higher sensitivity compared to CT.

Also diffuse periventricular lesions were detected in 2 patients by MRI and in only 1 patient by CT.

Studies performed in other connective tissue diseases, predominantly systemic lupus erythematosus, show that disorders of coagulability, especially the presence of antiphospholipid antibodies, might promote much more advanced cerebral ischaemic changes [19]. This study revealed a strong correlation between lung involvement and abnormalities in brain CT and MRI 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.

This hypothesis might be confirmed by our finding that there is a significant relationship between profound skin sclerosis and the presence of focal brain lesions on CT and MRI in SSc patients.

In conclusion, our data indicate that brain abnormalities are common in patients with severe SSc. MRI and CT are equally effective in detecting cortical and subcortical atrophy in SSc, however MRI shows significantly higher than CT sensitivity in detection of focal white matter brain lesions in these patients.



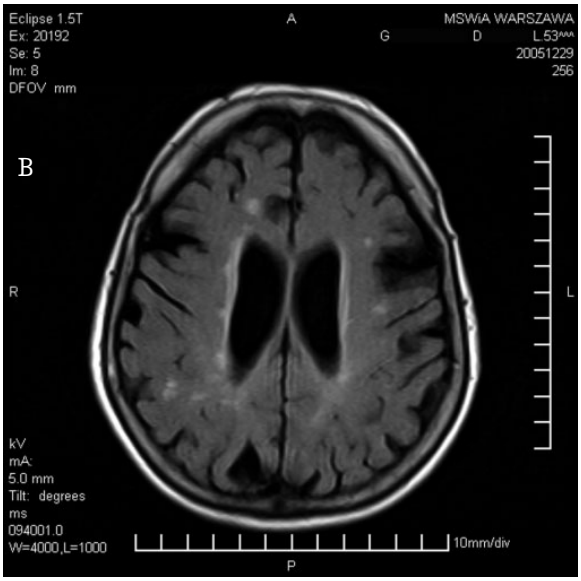


Figure 1 a, b. 61 year-old woman with 14 year history of SSc and TIAs (episodic left haemiparesis and dysphasia). MRI, FSE, T2-weighted and FLAIR images: mild atrophy with ventricular enlargement, vasogenic scar in right parietotemporal region, multiple focal lesions in periventricular, deep and subcortical location.

Rycina 1 a, b. 61-letnia kobieta z 14-letnim wywiadem i TIA (incydenty niedowładu lewostronnego i zaburzeń mowy). MRI, FSE, obrazy T2-zależne, sekwencja FLAIR: zanik korowo-podkorowy nieznacznego stopnia z poszerzeniem układu komorowego, blizna naczyniopochodna w prawej okolicy ciemieniowo-skroniowej, liczne ogniskowe zmiany okołokomorowe w strukturach głębokich oraz zlokalizowane podkorowo.

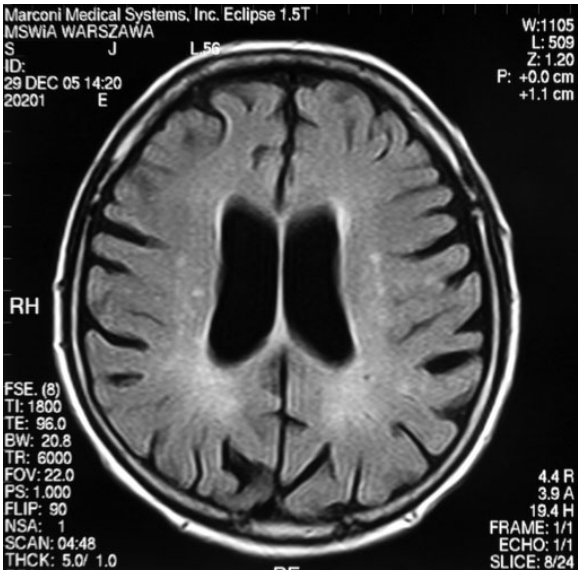
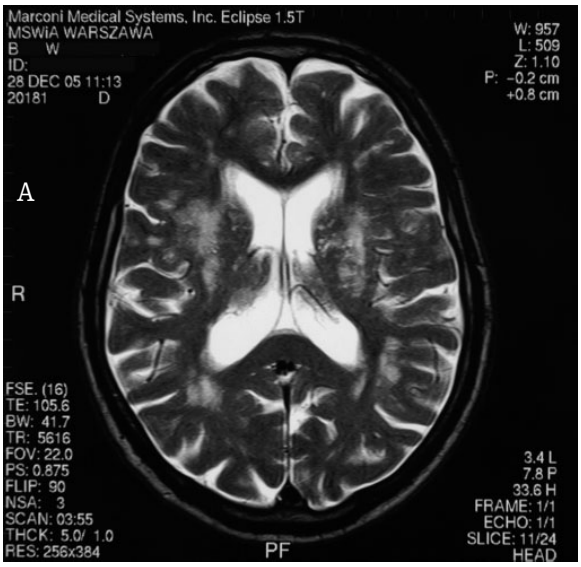


Figure 2. 41 year-old woman with 15 year history of SSc and 2 year history of depression and vertigo. MRI, FSE, FLAIR image: moderate atrophy with mild ventricular enlargement and sulci widening, multiple white matter focal lesions and areas of myelin damage with subsequent gliosis.

Rycina 2. 41-letnia chora z 10-letnim wywiadem twardziny układowej oraz depresją i zawrotami głowy od 2 lat. MRI, FSE, sekwencja FLAIR: zanik korowo-podkorowy miernego stopnia z nieznacznym poszerzeniem układu komorowego oraz bruzd. Liczne ogniska w istocie białej mózgu, obszary uszkodzenia mieliny i następowej glikozy.



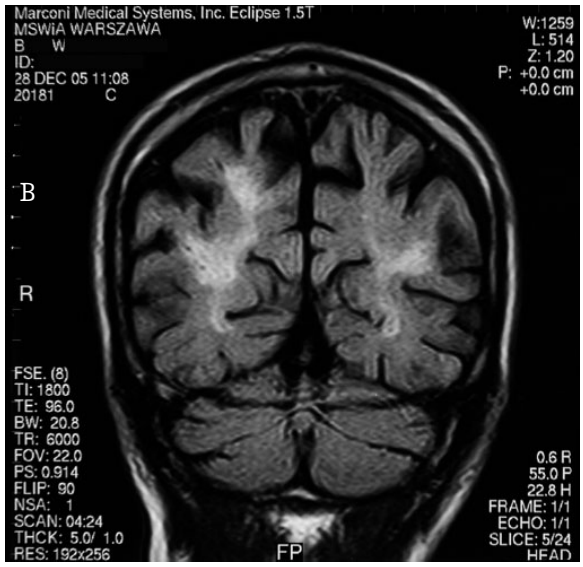
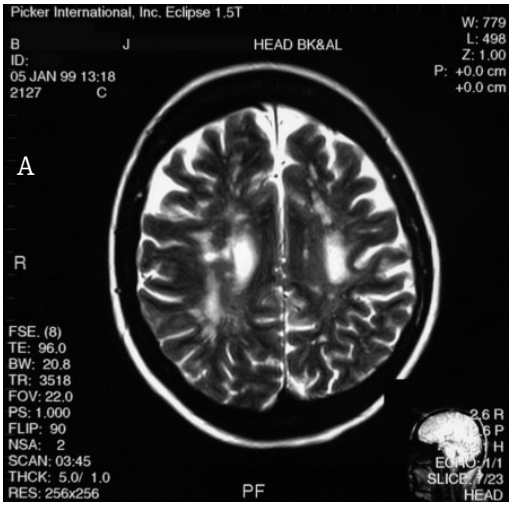
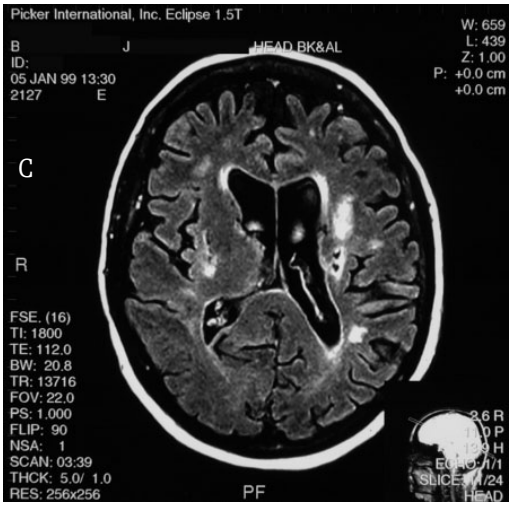


Figure 3 a, b. 53 year old woman with 16 year history of SSc and 3 year history of depression and severe episodes of headache; no focal deficits on neurologic examination; CT revealed mild/moderate atrophy:MRI, FSE, T2-weighted and FLAIR images: mild/moderate atrophy, multiple confluent focal lesions of leukoaraiosis type.

Rycina 3 a, b. 53-letnia kobieta z 16-letnim wywiadem twardziny układowej. Od 3 lat depresja i silne bóle głowy, w badaniu neurologicznym bez cech ogniskowego uszkodzenia OUN. W badaniu TK nieznacznego/miernego zanik korowo-podkorowy. MRI, obrazy FSE, T2-zależne, sekwencja FLAIR: zanik korowo-podkorowy nieznacznego/miernego i liczne zlewające się zmiany okołokomorowe o typie leukoaraiosis.





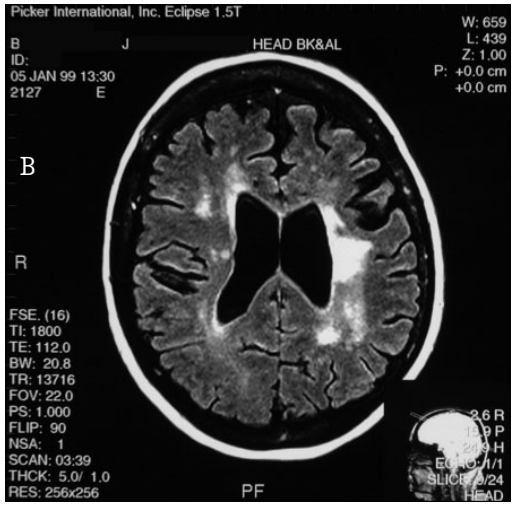


Figure 4 a, b, c. 58 year old man with 23 year history of SSc, complaining on memory loss and concentration deficits with detorioration of daily functions from 3 years; periodical severe headache and vertigo; episode of right sided haemiparesis 4 years ago: MRI, FSE, T2-weighted and FLAIR images: multiple, partialy confluent focal lesions localized in periventricular and subcortical white matter as well as in deep structures of both haemispheres; moderate atrophy predominantly in frontal and frontotemporal regions.

Rycina 4 a, b, c. 58-letni mężczyzna z 23-letnim wywiadem twardziny układowej. Od 3 lat zgłasza osłabienie pamięci, zaburzenia koncentracji i coraz gorsze funkcjonowanie w życiu codziennym. Okresowo silne bóle i zawroty głowy, przed 4 laty epizod niedowładu prawostronnego. MRI, FSE, obrazy T2-zależne, sekwencja FLAIR: liczne ogniska zlokalizowane w podkorowej istocie białej, okołokomorowo i w strukturach głębokich półkul mózgu, częściowo zlewające się ze sobą. Zanik umiarkowanego stopnia, zwłaszcza w okolicach czołowych i czołowo-skroniowych.

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