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Circulatory System in Children with Localized Scleroderma

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Abstract. The circulatory system was studied in 43 children (ages 3–18 years, mean 10.6 years; 32 girls, 11 boys) suffering from localized cutaneous forms of scleroderma. The following studies were undertaken: general pediatric examination, cardiologic examination including routine electrocardiogram (ECG), 24-h Holter ECG monitoring, echocardiography plus Doppler study, and a treadmill exercise test. Three children found to have congenital heart malformations were excluded from the study. Children with localized scleroderma were often lighter and shorter than their appropriate controls. The most common ECG abnormality was incomplete right bundle branch block, but other ECG and Holter abnormalities were found as well. Abnormal echocardiographic results were obtained in 16 cases. The abnormalities concerned valvar function (in all heart valves but predominantly in the mitral valve). It was found that the children suffering from scleroderma had different indices than controls for left ventricular mass index, mitral valve function and left ventricular filling. During the exercise test (conducted according to Bruce's protocol) we found no difference between patients and controls.

Key words: Localized scleroderma — Heart — Child

Localized scleroderma (cutaneous forms of scleroderma) is often described as a benign disease, limited to the skin, subcutaneous tissue, and sometimes muscles [10, 16–18, 26, 35, 37]. According to Majewski [26], neither visceral nor immunologic changes are usually found (except in patients with linear scleroderma). Spraker [36] noted that treatment is usually not needed for this ''benign'' disease, but he also stated that cutaneous forms of scleroderma are sometimes transformed into scleroderma generalisata (visceralis). At autopsy visceral sclerodermic changes have been described in patients who had been diagnosed clinically, as having only a cutaneous form of the disease, and in cases where no cutaneous abnormalities were found (scleroderma sine scleroderma) [5, 8, 22, 37].

There are few papers concerning, or even mentioning, the cardiologic status of children with cutaneous forms of scleroderma [11, 18, 19, 23, 27, 33, 38, 39], even though these forms of the disease are typical of childhood [1, 4, 6, 8, 10, 12, 19, 20, 25, 29, 34, 39, 40]. The aim of this work was to study the circulatory system in children suffering from cutaneous forms of scleroderma.

Materials and Methods

A total of 43 children aged 3–18 years (mean 10.6 ± 3.8 years) were studied. The types of disease and their sex distribution are shown in Table 1. In each case the diagnosis of scleroderma was established at the University Department of Dermatology in Katowice. The children were also treated in this unit during the period 1990–1993. At the same time they were seen at the University Department of Pediatric Cardiology to assess their general development and study their cardiologic status. At the time of the cardiologic investigation they had been suffering from scleroderma for 3 months to 11 years (mean 3.17 ± 2.7 years).

After careful physical examination the following cardiologic studies were performed: standard electrocardiography (ECG), 24-h Holter ECG (Medilog 4500, Oxford System), echocardiographic and Doppler study (Hewlett-Packard and Toshiba color system), and a treadmill exercise test (according to the Bruce protocol). The results were compared with those obtained from a control group.

Results

The results obtained are presented in Tables 2–6. It is interesting to note that of the 43 children in this study, 3 were suffering from congenital heart malformations (ventricular septal defect & atrial septal defect primum type, patent ductus arteriosus, and atrial septal defect secundum type). These children were successfully operated on and excluded from further analysis.

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Table 1. Clinical characteristics of the children in the study

Disease	Girls (no.)	Boys (no.)	Total (no.)
Morphea	23 (one case of PDA and one case of ASD II)	7	30
Scleroderma generalisata	4	2	6
Scleroderma linearis	1	1	2
Scleroderma *''en coup de sabre''*	4	1 (one case of ASD I + VSD)	5
Total	32	11	43

In the parentheses are details of the children suffering from congenital malformations of the circulatory system. These children were excluded from further study.
ASD I, atrial septal defect, primum type; VSD, ventricular septal defect; PDA, persistent ductus arteriosus; ASD II, atrial septal defect, secundum type.

Table 2. Results of ECG studies in children with localized scleroderma versus controls

Results	Girls		Boys		Total	
	S	C	S	C	S	C
Normal	8	26	1	6	9	32
Abnormal	19	—	8	—	27	—
Doubtful[a]	4	5	—	3	4	8
Total	31	31	9	9	40	40

S, localized scleroderma; C, controls.
The differences are statistically significant ($p < 0.01$).
[a] Doubtful result: isolated incomplete right bundle branch block.

Table 3. Results of 24-h Holter ECG monitoring in children with localized scleroderma versus controls

Results	Girls		Boys		Total	
	S	C	S	C	S	C
Normal	17	15	3	18	20	33
Abnormal[a]	12	8	4	2	16	10
Total	29	23	7	20	36[b]	43

S, localized scleroderma; C, controls.
The difference is close to statistically significant ($p \sim 0.05$).
[a] The following were classified as abnormal results: extrasystoles of supraventricular (>50/24 h) or ventricular origin, bigeminy, trigeminy, among others.
[b] Four children were not studied because of parental objections.

Discussion

There are few other studies with which our results can be compared. It is known that scleroderma is not common during childhood [1, 4, 6, 8, 10, 12, 13, 15–21, 24, 28]. According to Spraker [36], fewer than 3% of patients seen by pediatric rheumatology departments suffer from this disease. The only comprehensive study concerning the circulatory system in children suffering from localized scleroderma was published in 1988 by Własowa [40]. Unfortunately, it was published in Russian and in a journal that is not widely available. Własowa described material collected for a period of 20 years. Hence a large proportion of her material was studied before the introduction of modern technology to pediatric cardiology.

The predominance of girls over boys, as found in our material, is well established in the literature [1, 4, 6, 10, 12, 15–18, 28, 31, 32, 37]. The weight and height of 5 of the 40 children studied were more than 2 standard deviations below the appropriate norms [33]. Unfortunately, Własowa [40] did not investigate the physical development of the children in her study, and in no other study in the accessible literature was the group of children with localized scleroderma large enough to allow study of their development.

Our observation concerning the high incidence of functional heart abnormalities in sclerodermic children seems to be in agreement with the findings of several authors. For example, Ansell et al. [1], Goldman and Kotler [14], and Lee [22] each noted that heart function in adult patients with scleroderma is often affected, though without clinical manifestations. According to these authors, morphologic heart changes can be found at autopsy in about half the patients with scleroderma. Ac-

Table 4. Echocardiography and Doppler studies in children with localized scleroderma versus controls

Results	Girls		Boys		Total	
	S	C	S	C	S	C
Normal	20	22	4	6	24	28
Abnormal[a]	11	1	5	1	16	2
Total	31	23	9	7	40	30

Doppler abnormalities occurred significantly less frequently in the control group of 30 children (one case of mitral valve prolapse and one case of primary/secondary tricuspid valve regurgitation).
Statistical significance: $p < 0.01$.
[a] Valvar function abnormalities: mitral valve regurgitation (15 subjects); tricuspid valve regurgitation (7 subjects); pulmonary artery valve regurgitation (5 subjects); aorta valve regurgitation (3 subjects). Insufficiency of more than one valve was detected in some children.

Table 5. Anatomic and functional indices of the circulatory system (echocardiography and Doppler studies)

Parameter	Subjects		*p*
	Localized scleroderma ($n = 40$)	Controls ($n = 30$)	
Heart rate (bpm)	87.6 ± 15.2	80.3 ± 10.3	<0.05
Right ventricle (mm)	14.8 ± 3.8	15.90 ± 2.74	NS
Left atrium (mm)	24.9 ± 4.1	23.50 ± 2.96	NS
EDD (mm)	40.7 ± 5.3	42.1 ± 3.9	NS
SF (%)	30.3 ± 6.5	35.9 ± 6.8	<0.05
mvcf (L/s)	1.52 ± 0.41	1.51 ± 0.39	NS
$I \times LV_{mass}$ (g/m^2)	78.30 ± 9.15	64.7 ± 12.5	<0.02
E_v/A_v	1.84 ± 0.51	1.85 ± 0.38	NS
E_{int}/A_{int}	2.98 ± 2.00	1.85 ± 0.49	<0.01
A_{int}/T_{int}	0.29 ± 0.09	0.36 ± 0.06	<0.01

EDD (or LVEDD), left ventricular end-diastolic dimension; SF, shortening fraction of left ventricle; mvcf, mean velocity of circumferential fiber shortening; $I \times LV_{mass}$, index of left ventricular mass; E_v/A_v, ratio of E wave maximum velocity to A wave maximum velocity (see Fig. 1); E_{int}/A_{int}, ratio of E wave integral velocity to A wave integral velocity (see Fig. 1); A_{int}/T_{int}, ratio of A wave integral velocity to total integral velocity (see Fig. 1).

Table 6. Results of the physical performance test on a treadmill for children with localized scleroderma versus controls

Performance	Localized scleroderma (no.) ($n = 38$)		Control group (no.) ($n = 30$)	
	Girls	Boys	Girls	Boys
Third degree (6 km/h, 14%)	6	2	6	1
Fourth degree (7 km/h, 16%)	21	4	16	2
Fifth degree (8 km/h, 18%)	2	3	1	4
Total	29	9	23	7

The test was not performed in two children: one was unable to perform it (being only 3 years old) and the other was disqualified because of resting tachycardia.
None of the differences between the groups were statistically significant.

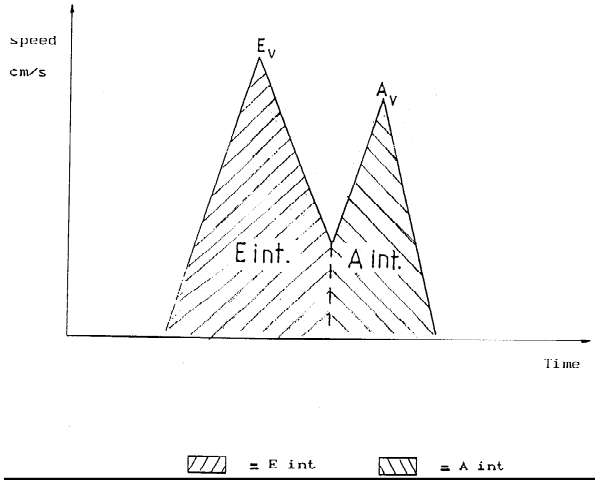

Fig. 1. Schema of blood flow through the mitral valve during diastole: Doppler study.

cording to Szymańska-Jagiełło [37], such changes are even more frequent. Dupuis et al. [7] reported that these patients suffer from *Myocardite sclerodermique*, which is associated with heart fibrosis. These changes may result in electrical disturbances of heart function [1, 7].

In contrast to the reports of other authors, we found no pericardial effusion in our patients. In material described by Własowa [40] the pericardium was ''affected'' in 23.6% of sick children; however, she did not explain exactly what pericardial disorders were observed. Goldman and Kotler [14] believed that clinical manifestations of pericardial involvement can be found in 5–10% of patients with scleroderma, irrespective of age. On the other hand, according to these authors, during echocardiographic examination pericardial abnormalities are detected in 41% of patients. Goldman and Kotler also stated that at autopsy cardiac changes are seen in 33–72% of sclerodermic subjects; and according to Oram and Stokes [29] this rate is even higher—up to 100%. It should be noted, however, that according to the authors mentioned above, visceral changes in scleroderma develop after a long duration of the disease (two to five decades). The same opinion was expressed by Le Roy [23]. On the basis of our results the reportedly high

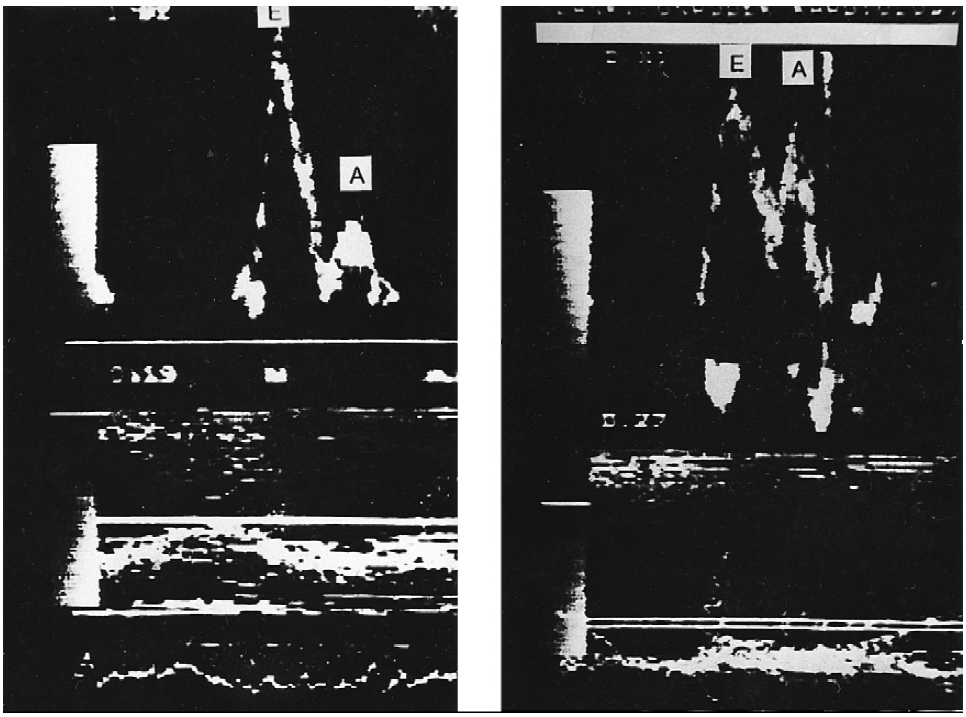

Fig. 2. Typical flow through the mitral valve in a child with localized scleroderma (*left*) and a healthy child (*right*).

incidence of pericardial involvement may be questioned, at least for children. It should be remembered that because the patients in our study were children the mean disease duration was only about 3 years.

In our material we found no cases of evident cardiac hypertrophy (in children who were not suffering from congenital structural heart malformations). On the other hand, it is known that various forms of cardiomyopathy are common in adults suffering from scleroderma. However, statistical analysis of the entire group of our patients revealed a significantly greater index of left ventricular mass than in normal subjects. This result might be interpreted, as a prelude to hypertrophic cardiomyopathy. Ciszewski and Kochanowski [2, 3] found no evidence of cardiac hypertrophy in their adult patients suffering from scleroderma, though they demonstrated a significantly thicker intraventricular septum and left ventricular posterior wall. Their observation seems to be in agreement with our findings.

Our observation of a faster heart rate and larger shortening fraction in children with localized scleroderma compared with controls could be the result of the increased functioning of the sympathetic nervous system, which has been described in adults with hypertrophic cardiomyopathy [11].

Valvar insufficiency, which was common in our patients (16 of 40), has often been detected in adults by other authors [e.g, 9]. It may be a result of enlargement of the valvar rings (an effect of affected functioning of connective tissue).

During echocardiography we found a significantly abnormal pattern of left ventricular diastolic filling in the presence of normal systolic function in patients with scleroderma. The Doppler abnormalities—significantly higher values for E_{int}/A_{int} and lower for A_{int}/T_{int} (Figs. 1, 2) in our patients than in controls—indicate a restrictive pattern of filling [11].

Our finding concerning the alterations in electrical heart function detected by routine and Holter ECG monitoring in sclerodermic children is in good agreement with the results of several investigators. For example, Ansell et al. [1], Goldman and Kotler [14], Riecker [31], and Targa et al. [38] opined that fibrosis of the conducting heart system in patients with scleroderma often results in different types of conduction abnormality (e.g., atrioventricular block or ventricular tachycardia). In Poland Mandecki et al. [27] studied a group of 27 adult subjects with scleroderma and found heart conduction abnormalities in 21; the most common ECG change was incomplete right bundle branch block (as in our study). Ciszewski and Kochanowski [2, 3] found an abnormal ECG in 41 of 66 patients suffering from generalized scleroderma, a frequency similar to that in our material. On the other hand, Targa et al. [38] found a normal ECG in 92.3% of patients with localized scleroderma.

Własowa [40] described supraventricular tachycar-

dia in 12.3% of sclerodermic children, atrioventricular block in 15.8%, and incomplete right bundle branch block in 12.8%. Dupuis et al. [7] reported that the ECG abnormalities in sclerodermic children were mainly nonspecific. These opinions seem to be in agreement with our findings.

Using an exercise test performed according to Bruce's protocol, we found no differences between patients and controls, although this test may not be detailed enough to reveal changes in cardiac performance.

We plan to continue these studies to determine the long-term cardiologic effects of cutaneous forms of scleroderma.

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