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*The liver and its ultrasonographic picture in children
suffering from vitiligo*

Vitiligo is a disfiguring skin disease that affects about 1% of the general population (1, 2). It is an acquired melanin pigmentary disorder manifesting itself in expanding depigmented lesions of the skin (3). This disease is characterized by the depigmentation of the skin due to the destruction of melanocytes (4). To date, the etiopathomechanism of vitiligo has not been convincingly elucidated and a number of seemingly mutually opposed hypotheses with equal likelihood still coexist (3). Due to the observed variation in clinical manifestations of the disease, it seems likely that the etiology of vitiligo may differ among patients. Therefore, several theories on vitiligo etiopathogenesis have been combined to formulate a convergence theory for vitiligo. This theory states that stress, accumulation of toxic compounds, infection, autoimmunity, mutations, altered cellular environment and impaired melanocyte migration and/or proliferation can all contribute to vitiligo etiopathogenesis in varying proportions (3).

There has been put forward a hypothesis that autoimmune mechanisms are involved in the pathogenesis of vitiligo (5). Initially vitiligo was considered a disorder confined to the epidermis only. However, some reports suggest it may affect the whole organism (6-9). There is evidence indicating the coexistence of vitiligo and liver diseases, like hepatitis type C (10, 11) or the onset of vitiligo induced by, for example interferon used in the treatment of hepatitis type C (4, 12, 13). Sacher et al. (14) report the simultaneous occurrence of chronic active hepatitis associated with vitiligo, nail dystrophy, alopecia and a new variant of LKM antibodies. Vitiligo in adults is associated with an increased incidence of autoimmune diseases such as alopecia areata, diabetes mellitus, pernicious anemia, Addison's disease, and Hashimoto thyroiditis. Vitiligo may appear as part of polyglandular autoimmune syndrome that may include selective IgA deficiency (1, 7, 8, 10, 15, 16).

Schallreuter et al. (9) proved that enzymatic defect observed in vitiligo patients manifesting itself in lack of the capacity to synthesize the melanins from L-tyrosine via

the essential activity of tyrosinase leads to an accumulation of the non-enzymatic byproduct 7-tetrahydropterin (7-BH₄) in the epidermis, and an increased synthesis of catecholamines in keratinocytes, leading to an excess of norepinephrine in both the plasma and urine of these patients.

In an ultrasonographic examination we attempted to analyze whether a morphological enlargement of the liver occurs in children with vitiligo.

The aim of this work was to make ultrasonographic measurements of the liver in three lines in the group of 38 vitiligo children and to compare with the measurements of the organ in the sex-and age-matched control group of children with a mild form of pityriasis capitis of the head.

MATERIAL AND METHODS

Thirty-eight vitiligo children (23 boys and 15 girls, ages 7-15, median age 10.8±2.0 years) and 43 of the control group (18 boys and 25 girls, ages 7-15, median age 10.5±2.2 years) were enrolled in this study which was conducted by the Pediatric Ward of the Clinic of Dermatology in Lublin. The enrollment excluded patients with disseminated vitiligo. The characteristics of the examined group are presented in Table 1. Vitiligo was of

Table 1. Characteristics of the examined groups

Group	n	Parameter	M	SD	MIN	MAX	p
C	43	age (years)	10.5	2.2	7	15	>0.5
V	38	age (years)	10.8	2.0	7	15	
C	43	weight (kg)	37.4	12.9	18.5	75.0	>0.2
V	38	weight (kg)	34.4	8.6	18.0	50.0	
C	43	height (cm)	143.2	16.2	110.0	173.0	>0.4
V	38	height (cm)	141.0	13.9	115.0	170.0	
C	43	BMI (kg/m ²)	17.6	3.2	13.4	28.6	>0.3
V	38	BMI (kg/m ²)	17.1	2.3	12.6	23.6	
C	43	L1 (cm)	12.3	1.5	10.1	16.0	-
V	38	L1 (cm)	12.3	1.5	9.0	14.8	-

C	43	L2 (cm)	11.1	1.4	8.7	14.0	-
V	38	L2 (cm)	10.7	1.5	6.7	13.1	-
C	43	L3 (cm)	9.4	1.3	6.8	12.0	-
V	38	L3 (cm)	9.1	1.5	5.7	12.8	-

C – control, V – vitiligo, M – the mean value, MIN – minimum, MAX – maximum, SD – standard deviation, p – probability, BMI – body mass index, L1 – measurement in the right front armpit line, L2 – measurement in the central line of the right clavicle, L3 – measurement in the central line of the body, n – number

type “B”. The skin lesions covered the skin of the trunk and/or limbs and they did not affect more than 25%–38% surface of the whole body.

In additional examinations there were found no deviations in the analysed population, no cases of hepatitis or contagious or infectious diseases which might affect the immunological system and the size of the liver. The children were not previously treated with any general or skin drugs. Ultrasonography (US) was performed on a Siemens Sonoline Sx and Siemens Sonoline Elegra apparatus with a 3.5 MHz transducer.

In order to estimate the size of the liver there were made the measurements in 3 oblong surfaces of the right liver lobe in two vertical lines (in the right front armpit line and in the central line of the right clavicle and of the left liver lobe in one plane (in the central line of the body in the section going through the long axis of the aorta). The obtained results were compared with those in the control group. The values were expressed in the ratio of percent of the expected values for the child's height and for three measurements of the liver in relation to the values in the control group (paper is being published). A t-Student test was used for the statistical analysis.

RESULTS

The results have been presented in Tables 2 and 3. In Table 2 we present the frequency of the changes of the liver size in vitiligo patients compared to the norm of the liver size in the control group expressed in percentile for three measurements in respective lines (L1, L2, L3). The frequency of vitiligo cases with the enlarged liver compared to the norm presented in the table suggests that over 92% measurements (from 92.1% for L2 and L3 to 94.7% for L1) is within a wide range of the norm (from 2.5 to 97.5 percentile). The results beyond a wide range of the norm in vitiligo patients were observed only occasionally. According to a normal distribution it is expected to be ca 5%. For the liver measurement in L1, only one case was stated below 2.5 percentile and one case over 97.5 percentile. The diminishing of the liver in L2 below 2.5 percentile was

Table 2. Frequency of the changes of the liver size in vitiligo patients with reference to the norm expressed in percentiles

n=70	<2.5		2.5 a 16.0		16-84		84-97.5		>97.5		2.5-97.5	
	f	%	f	%	f	%	f	%	f	%	f	%
L1	1	2.6	4	10.5	26	68.4	6	15.8	1	2.6	36	94.7
L2	3	7.9	5	13.2	25	65.8	5	13.2	0	0	35	92.1
L3	2	5.3	7	18.4	22	57.9	6	15.8	1	2.6	35	92.1
EV		2.5		16.7		66.7		16.7		2.5		95

f – frequency, EV – expected values

Table 3. The sizes of the liver in vitiligo patients expressed in percent of the expected values in the control group

n=38	MIN	MAX	M	SD	SE	Δ	t	p
L1	81.1	119.9	100.7	9.75	1.581	+0.7	0.443	>0.60
L2	67.2	116.4	97.4	11.98	1.944	-2.6	1.337	>0.15
L3	67.6	123.9	97.9	14.35	2.328	-2.1	0.902	>0.30

M – the mean value, MIN – minimum, MAX – maximum, SD – standard deviation, SE – standard error, Δ – the difference of the mean values with the standard values of our own control group taken as 100%, t – the value of t-function, p – probability, n – number

observed in three children (7.9%), no cases of enlargement were observed. In L3 determining the left lobe of the liver, the diminishing of the organ below 2.5 percentile was observed in two children (5.3%) whereas its enlargement over 97.5 percentile was observed in one child only (2.6%). Thus, no considerable deviations from a wide range of the norm of the liver size in vitiligo patients were observed.

In Table 3 we present the range of values of three measurements of the liver in three respective lines (L1, L2 and L3), the mean value M, the standard deviation SD, the

standard error SE, the difference of the mean values with the standard values of our own control group taken as 100% (Δ), the value of t-function and probability (p). The range of values for the liver measured in the front right armpit line (L1) was from 81.1 to 119.9%, on the average $100.7\pm 9.75\%$ of the expected values. The values in L1 compared to those in the control group were not statistically significant $p>0.60$. The range of values of the liver measured in the central line of the right clavicle (L2) in the group of children with vitiligo was from 67.2% to 116.4% values in the control group, on the average 97.4 ± 11.98 , and when compared with the control group, it was not statistically significant $p>0.15$. The range of values of the liver measured in the central line of the body in the section going through the long axis of the aorta in the group of children with vitiligo was from 67.6% to 123.9%, on the average $97.9\pm 14.35\%$ values in the control group. In comparison with healthy children no statistically significant difference was stated $p>0.30$.

DISCUSSION

Although vitiligo has long been considered a disorder confined to the skin, there is now positive evidence that it also involves the extracutaneous compartment of the "melanocyte organ." Vitiligo is a puzzling disorder characterized by a disappearance of epidermal and/or follicular melanocytes caused by unknown mechanisms (2).

Multiple hypotheses have been put forward to explain vitiligo. An inherited tendency to develop depigmentation may involve the inherent aberrancies that have been observed in nonlesional vitiligo melanocytes *in vivo* as well as *in vitro*. These abnormalities potentially render vitiliginous melanocytes more vulnerable to assaults from extracellular factors. Such factors include keratinocyte physiology, extracellular matrix composition, humoral and cellular immunity and environmental agents (15). Certain chemicals can induce vitiligo. These chemical agents are catechols and phenols, which are toxic to melanocytes *in vitro* and *in vivo* (7). In none of our patients these compounds were found.

Husebye et al. (16) have stated that of 15 patients with vitiligo, 12 (80%) had antibodies and autoantibodies against the enzyme aromatic L-amino acid decarboxylase (AADC) of pancreatic beta-cells and in patients with hepatitis those antibodies were found in 92% in those with hepatitis. There were also reports on the existence of antithyroid antibodies, antigastric parietal cell antibodies, thyroid diseases and pernicious anemia (7). Ficner et al. (6) have investigated deficiency of protein dimerization cofactor of HNF1 (transcription factor hepatocyte nuclear factor 1) -DCoH/PCD (pterin-4 alpha-carbinolamine dehydratase) activity in the liver and have stated that it causes an atypical hyperphenylalaninemia and deficiency in human epidermis is related to the depigmentation disorder vitiligo.

Despite the existence of the above data suggesting the existence of some correlations between the size of the liver and the development of vitiligo, neither the enlargement of

the organ measured in three lines of the body nor changes in the structure of the organ when compared with the examined control group of healthy children, were found.

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SUMMARY

The size and the structure of the liver in 38 children with vitiligo and 43 healthy children suffering from a mild form of pityriasis capitis were measured in an ultrasonographic examination and then compared. In the examined group there were found single cases beyond the norm. No changes in the structure of the liver parenchyma were stated in any of the vitiligo cases. For the liver measured in L1 there were stated 94.7% cases of vitiligo within the range from 2.5 to 97.5 percentile values in the control group. For the liver measured in L2 – 92.5% cases from 2.5 to 97.5 percentile values in the control group and for the liver measured in L3 – 92.1% cases of vitiligo were within the range 2.5 do 97.5 percentile values in the control group.

Wątroba i jej obraz ultrasonograficzny u dzieci chorujących na bielactwo

Za pomocą badania ultrasonograficznego zmierzono i porównano wielkość i rozmiar wątroby 38 dzieci chorujących na bielactwo i 43 zdrowych dzieci cierpiących na łagodną formę łupieżu głowy. W badanej grupie przekroczenie normy stwierdzono jedynie w pojedynczych przypadkach. U żadnego z chorych z bielactwem nie stwierdzono obecności jakichkolwiek nieprawidłowości struktury wątroby. Wymiar wątroby w linii L1 w 94,7% mieścił się pomiędzy 2,5 a 97,5 percentylem obliczonym dla grupy kontrolnej, a w linii L3 w zakresie tym mieściło się 92,1% przypadków.