

тим більше, що деякі з них (розумова відсталість, кретинизм) практично незворотні. Таким чином, у розвитку зобної ендемії велику роль відіграють екологічні умови відповідного регіону. Індуктором тиреоїдної патології в цілому є йододефіцит, як прямий, так і відносний, основною причиною якого є техногенне забруднення навколишнього середовища (фтористі з'єднання, радіонукліди і ін.). Тобто зобна ендемія або йододефіцит має регіональні відмінності, які пов'язані з екологічними умовами цього чи іншого регіону.

Ключові слова: щитовидна залоза, патологія щитовидної залози, йододефіцитні захворювання, йод, фтор, забруднення радіонуклідами.

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отсталость, кретинизм) практически необратимы. Таким образом, в развитии зобной эндемии большую роль играют экологические условия соответствующего региона. Индуктором тиреоидной патологии в целом является йододефицит, как прямой, так и относительный, основной причиной которого является техногенное загрязнение окружающей среды (фтористые соединения, радионуклиды и др.). То есть зобная эндемия или йододефицит имеет региональные различия, связанные с экологическими условиями этого или иного региона.

Ключевые слова: щитовидная железа, патология щитовидной железы, йододефицитные заболевания, йод, фтор, загрязнение радионуклидами.

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COMMON LABORATORY DIAGNOSTIC DATA ANALYSIS OF PATIENTS WITH DUPUYTREN'S CONTRACTURE AT THE STAGES OF PATHOLOGICAL PROCESSES IN PALM APONEUROSIS

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The study of the characteristic features of laboratory data in patients with Dupuytren's contracture, which in the past was verified as having been exposed to ionizing radiation, showed that in the examined patients with Dupuytren's contracture there is a concordance of the fibrous process in the palmar aponeurosis and liver, and the pathological process in the liver is one of the primary pathogenetic links in the formation of contracture. It was revealed that there is a relationship between the degree of fibrous liver damage and the biochemical blood parameters of patients with Dupuytren's contracture.

Key words: Dupuytren's contracture, liver fibrosis, connective tissue, ionizing radiation.

The work is a fragment of the research project "Determination of the connective tissue pathology etiopathogenesis in victims after radiation accidents based on which the pathogenetic justification for the victims treatment will be developed", state registration No. 0118U002106.

Frequent connective tissue pathology symptoms regularity is diagnosed as neuromuscular affect and lesions of the joint, which may be characterized by muscle weakness, myalgia, arthralgia, arthritis (mostly observed symmetrical joint damage). This fact is proved by the logical progress of symptoms of various extrahepatic manifestations, among which the DC often comes to the fore in the clinical picture and a significant number of experts consider DC as a typical stigma for patients with chronic alcoholic hepatitis [3, 4, 5].

The worldwide studies of the impact of ionizing radiation on the connection tissue were carried out, but those studies were carried out in experiments at significant irradiation doses for a very short time without regard to radionuclide incorporation.

Statistics points out the increase in the prevalence of clinically manifested pathology of connection tissue in individuals exposed to ionizing radiation and scientists describe such phenomena [2, 4, 6].

The purpose of the study was to identify the typical peculiarities of common laboratory data of patients with Dupuytren's contracture who had been exposed to ionizing radiation (this fact was verified and confirmed by state register records) at different stages of the pathological process in the liver with determination of typical morphological changes till pathological changes in the tissues of the palm aponeurosis.

Materials and methods. The results of our work are based on the integrated dynamic supervision data of the individuals (accident liquidators of the Chernobyl nuclear power plant (ChNPP)) with Dupuytren's contracture (DC) performed on the basis of the clinic of radiation registry of the National Academy of medical Sciences (NAMS) of Ukraine in 2002 through 2012. The study used case follow-up cards and patient's chart stored in the archive of the National Research Center for Radiation Medicine (NRCRM) of NAMS of Ukraine, military hospital in Irpin and surgical departments of the Kyiv City Emergency Care Hospital (KCECH).

To achieve the purpose, we examined 188 patients (male, aged 41-71 years) with DC, which were treated in the hospital of NRCRM of NAMS of Ukraine, the military hospital in Irpin and surgical departments of the KCECH. All patients were operated because of calculous cholecystitis.

The duration of the pathological process in the liver and palmar aponeurosis for all the patients was as follows: up to 5 years; 5 to 10 years; 10 and more years. Depending on the liver fibrosis stage (F) the patients were divided into 3 groups. The first group included 110 patients who had the I-st stage of liver fibrosis (F1); the second group – included 59 patients with II-nd stage of liver fibrosis (F2); the third group included 19 patients who had III-rd stage of liver fibrosis (F3).

All the patients passed through laboratory blood analysis, fiber test using BioPredictive method (France), elastometry and liver biopsy.

All calculations were carried out according to the requirements and criteria of the evidence-based medicine, and the results are within the range of probability.

Mathematical methods of parametric statistics were applied to estimate the statistical probability of materials obtained during the study. The study was performed in the circumference of the necessary and sufficient, selection of each trait was by performed by the method of irreversible randomization and the formation of controlled randomized groups (clusters) applied parametric statistics methods using the Student's coefficient and determining the mean errors in each cluster.

Results of the study and their discussion. The analysis of DC degree variation with liver fibrosis stage showed that the inspected patients with liver fibrosis stage F1 were dispersed among DC degrees I, II and III in about the same quantity. Among patients with stage of liver fibrosis F2 the DC degree II was found in almost half of cases (49.2%). At the same time among patients with liver fibrosis stage F3 the majority of individuals (57.9%) had DC degrees III. The mean age of patients with DC and liver fibrosis stage F1 was 47 ± 0.7 years old. 47% of the inspected patients were in the age cohort of 41-50 years, 29% – 51-60 years; the rest – 61-70 years (table. 1).

The mean age of patients with second stage of liver fibrosis (F2) was 49 ± 0.8 years: 30% of the studied patients were within the age cohort of 41-50 years, 39% – 51-60 years; the rest – 61-70 years. The mean age of patients with DC and third stage of liver fibrosis (F3) was 49 ± 0.9 years. Among patients of this group 37% were in the age of 41-50 years, 29% – 51-60 years, and the rest – within the age of 61-70 years.

Table 1

Variation of Dupuytren's contracture degree with liver fibrosis stage

DC degree	Liver fibrosis stage		
	F1 (n=110)	F2 (n=59)	F3 (n=19)
I (n=62)	42 (38.2%)	18 (30.5%)	2 (10.5%)
II (n=65)	30 (27.3%)	29 (49.2%)	6 (31.6%)
III (n=61)	38 (34.5%)	12 (20.3%)	11 (57.9%)
Total	110 (100%)	59 (100%)	19 (100%)

All the inspected were passing through blood tests until the appearance of clinical symptoms and during the treatment. Till clinical manifestations the inspected patients' leucogram was characterized by a tendency to increase the total number of white blood cells, increase in blood relative of band, segmented neutrophils and the percentage decreasing of lymphocytes. ESR was 1.8 times higher than the reference.

At the same time for patients with DC moderate activity of chronic hepatitis the deviations of blood values received from the clinical blood analysis were often observed: reducing the number of red blood cells in 41.3% of cases, hemoglobin – 36.9%, leukocytes – 41.3%, neutrophils – 58.7%. The eosinophilia was found in 65.2% of patients, relative lymphocytosis (absolute lymphocyte content was maintained at a physiological level) – in 6.5% and acceleration of erythrocyte sedimentation – in 50%.

When biochemical indices were studied the raised index of gamma glutamine transferase (GGT) was registered in all the patients, and high levels of alkaline phosphatase (ALP) – in 58 (44.6%) patients. 88 (66.6%) patients had a protein synthesis dysfunction in liver as hypo-, dysproteinemia, reduction of prothrombin.

Comparison of the mean values of basic hematological parameters appointed by analysis procedure for patients suffering from DC with liver fibrosis revealed slight deviations from the control group (table 2.).

An increased number of leukocytes, lymphocytes, eosinophiles, monocytes and decreased content of segmented and stab neutrophils was detected in patients with DC with liver fibrosis stage F1. However, none of the mean values of the aforementioned parameters have exceeded significantly the accepted standards. The analysis of the frequency of clinical blood test parameters deviations from the reference

demonstrated that the platelet count was reduced in 9 (8%) patients, neutrophils – in 26 (24%). 13 (12%) patients had a slight eosinophilia. Other indices of peripheral blood deviated from the reference occasionally.

Table 2

Peripheral blood hematological indicators for patients with Dupuytren's contracture depending on liver fibrosis degree

Indices	Study groups				Reference range
	F1 (n=110)	F2 (n=59)	F3 (n=19)	Control (n=45)	
leukocytes, $\times 10^9/l$	6.2 \pm 0.16 p<0.05	5.9 \pm 0.18	6.4 \pm 0.44 p<0.05	5.63 \pm 0.17	4.0-8.8
lymphocytes, %	38.03 \pm 0.76	39.5 \pm 1.37	37.2 \pm 1.56	37.23 \pm 0.57	19-37
lymphocytes, $\times 10^9/l$	2.34 \pm 0.07 p<0.05	2.3 \pm 0.1 p<0.05	2.35 \pm 0.17 p<0.05	1.31 \pm 0.23	1.5-2.4
erythrocytes, $\times 10^9/l$	4.9 \pm 0.04	4.8 \pm 0.05	4.9 \pm 0.08	4.73 \pm 0.05	4.0-5.5
hematoglobulins, g/l	150.2 \pm 0.99	148.3 \pm 1.53	151.7 \pm 3.19	146.40 \pm 1.58	130-160
platelets, $\times 10^9/l$	255.6 \pm 4.79	242.6 \pm 4.77	258.9 \pm 6.98	251.80 \pm 5.24	180-320
segmented neutrophils, %	51.2 \pm 0.83 p<0.05	49.5 \pm 1.31 p<0.05	53.7 \pm 1.65	56.17 \pm 0.65	47-72
stab neutrophils, %	0.8 \pm 0.09 p<0.05	0.8 \pm 0.14 p<0.05	0.47 \pm 0.16 p<0.05	1.60 \pm 0.16	1-6
eosinophiles, %	3.1 \pm 0.25 p<0.05	2.98 \pm 0.28	2.21 \pm 0.44	2.31 \pm 0.27	0.5-5
basophils, %	0.24 \pm 0.05	0.34 \pm 0.08	0	0.31 \pm 0.09	0-1
monocytes, %	6.3 \pm 0.25 p<0.05	6.7 \pm 0.36 p<0.05	6.3 \pm 0.47 p<0.05	2.37 \pm 0.35	3-11

Note. p – is the probability of a difference compared to the control group.

Similar, but less numerous changes (compared with control group), namely an increased number of lymphocytes, monocytes and decreased content of segmented and stab neutrophils were detected in patients with DC with liver fibrosis stage F2. Just as in the group of F1, the mean values of changed indices didn't significantly differ from the reference ones. Indices of the deviation frequency analysis based on clinical blood test showed that platelet count was reduced in 8 (13%) patients and neutrophils count - in 22 (38%).

7 (12%) patients had a slight eosinophilia. Other indices of deviations from the reference were fixed occasionally.

Patients with liver fibrosis stage F3 who suffered from DC had the indices main value that differed from the reference ones in the following: the increased number of leukocytes, lymphocytes, monocytes; the decreased number of stab neutrophils. However, the only index, namely, the content of stab neutrophils was significantly reduced compared to the lower limit of reference. The analysis of the frequency of deviations of the clinical blood test parameters from the reference ones demonstrated that the neutrophils number was reduced in 3 (15.8%) patients. 2 (10.5%) patients had slight eosinophilia. Other indices of clinical blood test deviated from the reference occasionally.

Since in the vast majority of patients with DC the key indices of peripheral blood were within the reference, it is possible to summarize that the found tendency to change notably the tendency to leuko-, lympho-, eozyno- and monocytosis and neutropenia is not clinically significant. The only notable and the most probabilistic breach which should be admitted is moderate stab neutropenia in patients with DC and with the liver fibrosis stage F3, but in our opinion, such an infringement is directly associated neither with any pathological process in the liver nor with the development of contractures.

The study of the biochemical blood tests results of the affected by DC revealed the presence of moderate cytologic and dysproteinemic syndromes (table. 3).

For the patients with DC and liver fibrosis stage F1 a significant increase of alanine aminotransferase ALT, aspartate aminotransferase AST and ALP was revealed when the average values were compared with reference group indicators.

It should be noted that this increase was significant not only in comparison with the reference group, but also in comparison with the upper limit of the admitted standards.

The fact that a significant increase in serum iron and γ -globulin content of protein fractions and reduction of albumin by comparison with the control and reference limits was fixed for patients with DC and fibrosis stage F1. In addition, the thymol test indicator tended to grow but it didn't exceed the upper limit, so this trend cannot be considered as clinically significant.

Frequency analysis of biochemical blood parameters deviation from the reference values showed that 89 (81%) patients with DC and first degree of fibrosis had the raised level of ALT, 68 (62%) patients had the raised level of AST, 77 (70%) – of ALP, 88 (80%) – of serum iron, 63 (57%) of β -globulins and

63 (57%) of γ -globulins relative content. 34 (31%) patients had the increased thymol level. The reduced content of albumin in the group of first degree of liver fibrosis (F1) was observed in 62% of cases.

Table 3

Biochemical blood indicators variations with liver fibrosis degree for patients with Dupuytren's contracture

Indices	Study groups				Reference range
	F1 (n=110)	F2 (n=59)	F3 (n=19)	Control (n=65)	
ALT, units/l	157.2±12.9 p<0.001	130.9±16.3 p<0.001	168.9±27.4 p<0.001	29.4±2.4	8-54
AST, units/l	73.1±6.3 p<0.01	71.4±9.7 p<0.01	70.7±11.4 p<0.01	25.3±2.2	16-40
ALP, units/l	131.3±5.7 p<0.01	124.3±8.8 p<0.01	119.5±13.6 p<0.01	52.7±3.9	36-92
PTI, %	88.5±1.1	88.7±2.2	89.8±2.9	92.5±6.3	80-105
Total protein, g/l	75.25±0.9	76.3±0.9	75.9±1.2	72.3±3.8	63-87
Thymol test, units	3.6±0.3 p<0.05	3.2±0.4	4.7±0.8 p<0.05	2.0±1.0	0-4
Serum iron, μ M /l	37.8±4.4 p<0.001	24.3±3.2	25.7±2.1 p<0.05	17.8±3.6	10.5-25.0
Globulins, g/l	30.5±0.7	30.8±1.2	33.2±1.2	26.0±4.5	17-35
Albumins, g/l	44.9±0.5	44.9±0.6	42.7±0.6	42.5±6.3	30-55
Albumins, %	48.6±0.7 p<0.05	51.3±1.2	53.4±1.9	55.9±1.8	52.0-65.0
α_1 - globulins, %	3.9±0.14	4.4±0.3	3.6±0.3	3.5±0.6	2.5-5.0
α_2 - globulins, %	10.6±0.3	9.75±0.3	9.6±0.7	9.4±0.8	7.0-13.0
β - globulins, %	15.0±0.4	13.3±0.4	13.5±0.9	12.0±1.1	8.0-14.0
γ - globulins, %	22.4±0.5 p<0.05	21.7±0.8	20.4±1.0	18.7±1.7	12.0-18.0

Note. p – the probability of a difference compared to the control group.

A significant increase of ALT, AST and ALP was revealed in patients with DC and liver fibrosis stage F2 like the group of patients with F1. There weren't other changes in the indices according to the mean values comparison results.

Frequency analysis data of biochemical parameters deviation from the reference values showed that 46 (78%) patients with DC and second stage of fibrosis (F2) had the raised value of ALT, 29 (49%) patients had the raised value of AST, 37 (63.5%) – of ALP, 29 (50%) – of serum iron, 19 (33%) of β -globulins and 29 (50%) – of γ -globulins relative content.

Thymol exceeded the reference values in 14 (23%) cases. As well as in the case of the patients with F1, 62% of the patients with the liver fibrosis stage F2 had the decreased albumin relative content.

Like patients with fibrosis stage F1 and F2, patients with DC and liver fibrosis of the third stage (F3) had a significant increase of ALT, AST and ALP, and of the thymol test index. It was revealed by biochemical blood analysis. These changes were found significant when they were compared to the control and the upper limit of the reference. At the same time the raised level of serum iron was found only after the main values had been compared, but it was inconspicuous compared to reference limits.

Patients with liver fibrosis of the third stage (F3) had the increased ALT in 17 (88.9%) cases, AST – in 12 (63.1%), ALP – in 13 (68.7%), serum iron – in 9 (50%) cases, the relative content of β - and γ -globulins – in 5 (28.6%) and 8 (42.9%) cases, respectively. Thymol exceeded the reference values in 60% of cases. The albumin relative content was reduced in 4 (21.4%) cases of the group with the third stage fibrosis.

The data of our study correlated to some extent with the data of on the pathogenetic features of fibrosis development, but the development rates were 30% less than our findings which can be explained by the impact of ionizing radiation [2, 7]. The role of liver and hepatogenic fibrosis in the development of DC is indicated also in the study [5], however, the correlation between liver disease and fibrosis was significantly lower (6.8%) in these studies. The role of fibro genes has also been thoroughly examined in [8], whose data on fibrogenesis correlated with our results but did not take into account the ionizing factor. The relationship of DC and factors of liver injury were pointed out, but there was no verification of the fibrosis itself in his work indicating correlation of liver fibrosis and DC, but this was not proven at a probable level [9]. Similar opinion was stated in the works by some researchers, however, all indices were 29-50% lower due to the fact that the studied contingent was not exposed to ionizing radiation [1]. Data analysis indicates that there is some correlation of liver pathology and palm aponeurosis, but there is no data on patients with irradiation, so the correlation of indices is not correct [9]. Thus our studies have almost no analogues at present.

Conclusions

1. Based on the study results one can say with high probability that there is a coherence between two processes: palmar aponeurosis and liver fibrosis process on the one hand and the pathological process in the liver on the other hand. It is one of the primary pathogenetic elements which form the Dupuytren's contracture.

2. The examined patients having Dupuytren's contracture had an association between the stage of liver injury and fibrous blood biochemical indicators. The patients with Dupuytren's contracture and the liver fibrosis stage F1 had the most notable changes in biochemical blood parameters. These changes demonstrate the active development of the pathological process in the liver. Patients from group F1 should be classified as "prospectively dangerous", and palm deformity should not be considered as completed.

3. According to the results of biochemical examination, patients with the liver fibrosis stage F2 have stabilization of the pathological process in the liver, which is often accompanied by the formation of the second degree of Dupuytren's contracture. Such patients may be considered as the most "biochemically stable".

4. For patients with the liver fibrosis stage F3 pathological processes in the liver are less active than in those with F1, but deeper than in F2 patients, and they are mostly associated with the formation of Dupuytren's contracture of stage III.

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Реферат

АНАЛІЗ ЛАБОРАТОРНИХ ДАНИХ У ХВОРИХ НА КОНТРАКТУРУ ДЮПУЙТРЕНА НА ЕТАПАХ ФОРМУВАННЯ ПАТОЛОГІЧНОГО ПРОЦЕСУ У ДОЛОННОМУ АПОНЕВРОЗІ

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Визначення характерних особливостей загальнолабораторних даних хворих на контрактуру Дюпюїтрена, які в минулому верифіковано зазнали впливу іонізуючого опромінення, показало, що у обстежених хворих на контрактуру Дюпюїтрена має місце конкордатність фіброзного процесу в долонному апоневрозі та печінці і патологічний процес у печінці є однією з первинних патогенетичних ланок формування контрактури. Виявлено, що існує асоціація між ступенем фіброзного ураження печінки та біохімічними показниками крові хворих на контрактуру Дюпюїтрена.

Ключові слова: контрактура Дюпюїтрена, фіброз печінки, сполучна тканина, іонізуюче опромінення.

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АНАЛИЗ ЛАБОРАТОРНЫХ ИССЛЕДОВАНИЙ У БОЛЬНЫХ С КОНТРАКТУРОЙ ДЮПУИТРЕНА НА ЭТАПЕ ФОРМИРОВАНИЯ ПАТОЛОГИЧЕСКОГО ПРОЦЕССА В ЛАДОННОМ АПОНЕВРОЗЕ

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Изучение характерных особенностей данных лабораторных исследований у больных с контрактурой Дюпюитрена, которые в прошлом были верифицированы как подвергшиеся воздействию ионизирующего излучения, показало, что у обследованных больных с контрактурой Дюпюитрена имеет место конкордатность фиброзного процесса в ладонном апоневрозе и печени. При этом патологический процесс в печени является одним из первичных патогенетических звеньев формирования контрактуры. Виявлено, что существует взаимосвязь между степенью фиброзного поражения печени и биохимическими показателями крови больных контрактуры Дюпюитрена.

Ключевые слова: контрактура Дюпюитрена, фиброз печени, соединительная ткань, ионизирующее облучение.

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