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Improvement of Methods for Early Diagnosis of Basalcellskincancer

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Annotation: Basalcellcarcinoma of the skin is the most common skin tumor. Its incidence is currently growing and in the structure of keratinocyte tumors, BCCaccounts for 80%. The study involved 80 patients (49 men and 31 women) aged 39to 87 years (mean age 63 years) with clinical manifestations of basal cell skincancer, they underwent dermatoscopy and biopsy of the affected skin areas. Theproposed minimally invasive diagnostic test using liquid nitrogen irrigation of thelesion has a potential advantage over routine research methods and can be used in the early diagnosis of BCC.

Keywords: Basal cellcarcinoma of the skin,early diagnosis.

Background: Basal cell carcinoma of the skin is the most common skin tumor. Its incidence is currently growing and in the structure of keratinocyte tumors, BCC accounts for 80%.

Materials and methods: 80 patients (49 men and 31 women) aged 39 to 87 years (mean age 63 years) with clinical manifestations of basal cell skin cancer, dermatoscopy, biopsy of affected skin areas.

Results: The proposed minimally invasive diagnostic test using liquid nitrogen irrigation of the lesion has a potential advantage over routine research methods and can fill the gaps in the verification of the diagnosis of BCC.

The relevance of the study of basal cell skin cancer is dictated by the fact that this tumor is the most common, and its incidence is currently growing. In the structure of keratinocyte tumors, BCC accounts for 80%. To date, the incidence of BCC has increased significantly, and the ratio of CCC to CCM is already 2:1 [1,5]. According to the literature, in comparison with squamous cell (squamous RCC/SCC), CCC affects a relatively younger population, however, according to the results of some studies, the average age of patients with CCC was higher than in the group of patients with SCC. So, on average, people aged 40 to 70 years are susceptible to BCC, however, according to Bath-Hextalletall. the incidence among the younger population is increasing [3,7,8].

The second urgent problem in the study of CCB is the economic costs of treating patients, and they directly depend on the duration of the patient's curation [2]. Detection of a tumor in the debut will significantly reduce the volume and duration of treatment. This dictates the need to increase the oncological alertness of the population, as well as to optimize the diagnostic algorithm of the disease [9]. The complexity of diagnosing BCC in the early stages is determined by the low specificity of the clinical manifestations of the neoplasm.

The purpose of our study was to substantiate the significance of a diagnostic test for CRC in the initial stage in order to improve diagnostic measures.

The objectives of the study were to study the clinical, dermatoscopic and histological characteristics of patients with basal cell skin cancer in order to improve the accuracy and speed of diagnostic measures.

Materials and methods of research: The research base consisted of patients with clinical

manifestations of basal cell skin cancer. All participants in the study were examined and treated at the dermatological department of the St. Petersburg State Pediatric Medical University, the Department of Pathological Anatomy with a course of forensic medicine, the Republican Clinical Leather Hospital of the Republic of Uzbekistan and the Tashkent City Oncological Dispensary.

For the period from 2014 to 2021 80 patients (49 men and 31 women) aged 39 to 87 years (mean age 63 years) were examined and included in the study. A prospective study was conducted in 35 people from 2017 to 2021; a retrospective study was conducted in 45 people. The inclusion criterion was the clinical picture - the presence of an erythematous pink spot with uneven clear boundaries and possible slight peeling on the surface. The lesions were predominantly acral in location (hands and face), but localization in other areas was acceptable. At the initial stage, all patients underwent history taking, physical examination, dermatoscopy, and diagnostic skin biopsy from the lesion. The next stage of the study was the formation of a new diagnostic algorithm for CBC at an early stage, namely the development of a new diagnostic test.

Based on the history, physical examination and dermatoscopy, all patients were divided into four groups. The first group included 35 patients with a clinical diagnosis of basal cell carcinoma (21 men and 14 women), the second included 20 patients with squamous cell skin cancer (10 men and 10 women), and the third included 16 patients with actinic keratosis (10 men and 10 women). 6 women). The fourth group with an unverified diagnosis included 9 patients (6 men and 3 women).

Table #1 Gender and age characteristics of study participants

Group/	БКК (n=35)	ПКК (n=20)	АК (n=16)	Unverified diagnosis(n=9)
characteristic	48-87 (65,87)	48-78 (61,55)	39-70 (56,5)	48-67 (58,4)
Age	21 14	10 10	10 6	6 3

In each case, clinical and dermoscopic assessment of the neoplasm was carried out using the HEINEDELTA 20 TDermatoscope DermliteDL3N (Heine Optotechnique GmbH&Co.KG, Germany) and 10x optical zoom Derm Lite FotoIIPro (Samsung Electronics Co., Ltd., Yeongtong-Gu. Suwon-Shi, South Korea).

All patients underwent cryotherapy. Before irrigation with liquid nitrogen, we treated the lesion with alcohol, and to make the procedure less painful, we used a 2% lidocaine solution or EMLA ® cream (Lidocaine 2.5% + Prilocaine 2.5%). Then a cryo-tip (usually type C, Cry-AC, Brymill®) was placed at a distance of 5-10 mm from the skin surface and liquid nitrogen was directed to the center of the treated field 10 times (exposures, cooling limit and depth 5 mm - 20° C) up to 1-2 minutes.

12 hours after the procedure, we performed a dynamic assessment of clinical and dermoscopic signs relative to the initial ones, and then excised the neoplasm in order to determine the histological changes associated with the procedure and verify the diagnosis. In the case of the formation of translucent or pearly papules, the test was considered positive.

Results of own studies: All patients participating in the study had a similar clinical picture: the process of skin lesions was limited and was represented by single erythematous spots/plaques of pink color, with clear boundaries, localized on the skin of the face or hands, less often on the trunk. Slight peeling was determined on the surface of the elements. All patients had no complaints about subjective sensations (itching/burning/pain) in the area of the lesion.

Based on the data obtained during an objective examination, taking anamnesis, the patients were diagnosed with a clinical diagnosis: basal cell skin cancer in 43.75% of cases (35/80), squamous cell skin cancer in 25% of cases (20/80), actinic keratosis - in 20% (16/80).

The first group included 35 patients diagnosed with basal cell skin cancer (21 men and 14 women, aged 48 to 87 years, mean age 65.86). Clinical manifestations of patients of the 1st group were characterized by the presence of a flat pink erythematous spot/plaque with clear boundaries, up to 2

cm in diameter (n=35/35, 100%). In 16 (46%) patients, peeling was noted on the surface of the elements. In 17 (48.5%) patients, the elements were located on the skin of the face (68.6%), in 6 patients in the area of the dorsal surface of the hands (17.14%), in 12 patients the neoplasm was localized on the skin of the trunk (34.3%).). From the anamnesis it is known that 27 patients (77%) came for a consultation about a neoplasm within 1 month after they noted its appearance, the remaining 23% - on average, sought help after 2 months. 4 patients (11.4%) had a family history.

The second group included 20 patients with squamous cell skin cancer (10 women and 10 men aged 48 to 78 years, mean age 61.55 years). In patients of group 2, in 100% (20/20) of cases, the rashes were represented by an erythematous pink plaque with clear boundaries, of various shapes. The vast majority of rashes were localized on the skin of the face, in particular, in the temporal and frontal regions 85%), in 3 out of 20 patients the neoplasm was located on the dorsal surface of the hands (15%). In 1 patient (5%), a family history was recorded.

The third group included 16 patients with actinic keratosis (6 women and 10 men aged 39 to 70 years, mean age 56.5 years). Among patients of group 3, all rashes were represented by erythematous red spots, with intense peeling on the surface and heterogeneous color. Compared with groups 1 and 2, desquamation was recorded in patients of the third group in 100% of cases (16/16). None of the participants in group 3 complained of subjective sensations within the lesions (0/16, 0%). In all participants of group 3, rashes were localized on the skin of the face (16/16, 100%). Three noted the gradual progression of the elements in the form of their increase in size (3/16, 18.8%).

The fourth group consisted of patients with unverified clinical diagnosis. Among them were 6 men and 3 women aged 48 to 67 years, the average age was 58.4. In all participants of the group, the rashes were limited in nature and were represented by an erythematous flat spot of pink / red color, with clear boundaries, of various shapes. Peeling on the surface of the element was noted in 3 patients (33%) In 7 patients (77.8%), the element was located on the skin of the face, while in 1 - on the skin of the left hand (11%) and in 1 - in the back area (eleven%). Twopatients (2/9, 22%) had a familyhistory.

Table 2 Clinical characteristics of patients

sign	Basal cell carcinoma (n=35)	Squamous cell skin cancer (n=20)	Actinic keratosis (n=16)	Patients with unverified diagnosis (n=9)
Hereditary	4(11,4%)	1(5%)	0/16(0%)	2/9(22%)
anamnesis	35(100%)	20(100%)	16(100%)	9(100%)
1-3 phototype	0(0%)	0(0%)	0(0%)	0(0%)
4-6 phototype	14/35(40%)	7/20(35%)	3/16(18,8%)	4/9(44%)
History of sun exposure (presence of burns 2	3/35(8,6%)	1/20(5%)	2/16(12,5%)	0/9(0%)
degrees)	1/35(2,9%)	1/20(5%)	0/16(0%)	0/9(0%)
Oncological	0/35(0%)	0/20(0%)	0/16(0%)	0/9(0%)
anamnesis	33/35	20/20(0%)	9/16(56,3%)	9/9(100%)
More than 1 element	(94,3%)			
Localization in	2/35(5,7%)	0/20(0%)	7/16(43,8%)	0/9(0%)
facial areas	17(48,6%)	17/20(85%)	16/16(100%)	7/9(77,8%)
Localization in the limbs	6/35(17,1%)	3/20(15%)	0/16(0%)	1/9(11%)
(brushes)	12/35 (34,3%)	0/20(0%)	0/16(0%)	1/9(11%)
Localization in	35/35(100%)	20/20(100%)	16/16(100%)	9/9(100%)
trunk area	0/35(0%)	0/20(0%)	0/16(0%)	0/9(0%)
flat	16/35(46%)	16/20(80%)	16/16(100%)	3/9(33%)

All study participants underwent dermatoscopy of the lesion at the stage of the initial visit.
Among the participants of the 1st group, the most common symptom was branched (tree-like)

vessels, which were observed in 24/35 patients (68.6%). This sign characterizes the vascular pattern of the neoplasm. Against an erythematous background, also in a number of cases (8/35, 22.9%), shiny red-white structureless areas were noted. Teleangiectasias characteristic of long-term basaliomas were noted in 3 cases out of 35 (8.6%). Short white streaks were also frequently recorded.

– in 14 cases out of 35 (40%). Superficial white/yellow scales were found in 16 patients (45.7%). Leaf-like areas were found in one patient (2.9%). Pigmented structures were found in 1 patient (2.9%) and included multiple blue-gray globules, dots, and blue-gray nests.

In all patients of the second group, the erythematous background of lesions was noted first of all (20/20, 100%). For patients of group 2, a separate dermoscopic pattern was identified - "strawberry pattern/pattern". It was observed in 18/20 patients (90%). It is also noteworthy that all without exception had superficial white/yellow scales (20/20, 100%). Most patients had concentric structures (15/20, 75%), shiny red-white structureless areas (11/20, 55%). In 8 patients out of 20, short white streaks (40%) were found, in three - branched vessels (15%) and vessels surrounding the hair follicle. Hyperkeratotic hair follicles were found in three patients (3/20, 15%), and 6/20 had hyperkeratosis/amorphous keratin. Ulceration was found in 4/20 patients (20%), and one had multiple small erosions (5%).

Among the patients of group 3, the main signs were also the erythematous background of the lesions and the "strawberry pattern", it was found in all participants in the group (16/16, 100%). 2 patients had unstructured red-white areas (2/16, 12.5%). Most of the participants in the group showed signs of hyperkeratosis: superficial white/yellow scales (13/16, 81.25%), hyperkeratosis/amorphous keratin (10/16, 62.5%), hyperkeratotic follicles (8/16, 50%) . Four patients had short white streaks (4/16, 25%), one (1/16, 6.25%) had multiple small erosions, and one had ulceration (1/16, 6.26%).

Patients of group 4 also demonstrated an erythematous background of lesions (9/9, 100%). 5 patients had short white streaks (56%), 4 had red-white, shiny, unstructured areas, 2/9 had leaf-like areas (22%), and one had concentric structures (11%). Branched vessels were found in 3 patients (3/9, 33%), telangiectasias in 1 (1/9, 11%), and vessels surrounding the hair follicle in 3/9 patients (33%). Among the pigment inclusions, gray-blue nests were found in 2 patients (22%), dots - in 3/9 patients (33%), multiple gray-blue globules - in 2 patients (22%). Hyperkeratosis was noted in 2 individuals (2/9, 22%), superficial white and yellow scales in 4/9 individuals (44%).

During the analysis of histological preparations, the diagnosis was verified in 88.75% of cases (71/80). In particular, the diagnosis of basal cell skin cancer was made in 43.75% of cases (35/80), squamous cell skin cancer - in 25% of cases (20/80), actinic keratosis - in 20% (16/80). In 9 patients, the diagnosis made by the pathologist did not correspond to the final one. Three main groups of patients were identified: basal cell skin cancer, squamous cell skin cancer and actinic keratosis.

A study using a new diagnostic test for basal cell skin cancer was conducted prospectively. It involved 18 patients of group 1 (10 men and 8 women, mean age 63.5 years) with a clinical diagnosis of basal cell skin cancer, 9 patients of the second group (6 men and 3 women, mean age 61.9 years) with a clinical diagnosis squamous cell skin cancer and 6 patients of group 3 (3 men and 3 women, mean age 59.6 years) with a clinical diagnosis of actinic keratosis.

When assessing tissue changes through dermatoscopy after 12

– 24 hours after irrigation of the lesion with liquid nitrogen, the formation of translucent/pearl papules along the periphery of the lesion occurred in 16/18 patients of group 1 (89%). Moreover, in 11 patients (11/16, 68.75%) pearly papules were noted, in 5 - translucent (7/18, 31.25%). In the second group, 7 patients out of 9 (78%) had a negative result, while 2 had a nonspecific result (22%). Group 3 patients showed a negative result (6/6, 100%).

The specificity of the test was 88.24%, sensitivity - 88.89%, positive predictive value - 88.89%, negative predictive value - 78.94%. Based on the data obtained, the test can be recognized as valid and practically applicable.

To control the results after the test, all subjects underwent a skin biopsy from the lesion. As part of the histological substantiation of the mechanism of the test, it was revealed that it is based on the phenomenon of tumor retraction. As a result of irrigation with liquid nitrogen, a nonspecific inflammatory reaction is formed within 12-24 hours, due to which stromal edema develops. Against the background of the difference in the density of the tissues of the stroma and tumor nests, the tumor tissue is forced upward and a gap is formed between the basaloid nests and the stroma, which dermoscopically corresponds to the formation of translucent/pearl papules.

In all patients of group 1, a sign pathognomonic for basal cell carcinoma was determined - a "palisade" of basal keratinocytes (35/35, 100%), and the vast majority had artifactual gaps or the phenomenon of tumor retraction (32/35, 91.4%). In one case, the patient had cellular atypia/polymorphism (1/35, 2.9%), apoptotic cells (5/25, 14.3%) and mitoses (8/35, 22.9%) were also infrequently isolated. In most patients, the tumor was limited to the papillary dermis (29/35, 82.9%), and invasion into the reticular dermis was observed in 6 individuals (6/35, 19.4%). One patient was reported to have melanocytes (1/35, 2.9%). Hyperkeratosis was determined in half of the iced patients (16/35, 45.7%). Another symptom characteristic of basal cell carcinoma, tumor neovascularization of the superficial layers of the dermis, was detected in 31 cases (31/35, 88.6%). In all patients, the ratio of tumor parenchyma to stroma was >1 (35/35, 100%), in 8 cases stromal fibrosis of the dermis was noted (8/35, 22.8%). In most patients, the inflammatory infiltrate was represented by lymphocytes (30/35, 85.7%), histiocytes (30/35, 85.7%), in one case melanophages were noted (1/35, 2.9%). Tumor thickness was less than 1 mm in 29 participants of the group (29/35, 82.6%), in

6 - up to 2 mm (6/35, 19.4%), infiltrative growth was also observed in 6 patients (6/35, 19.4%). It should be noted that the "palisade" of basal keratinocytes and the presence of an artificial fissure are pathognomonic signs of basal cell carcinoma, and they were determined in all patients of group 1, respectively.

Tissue changes in patients of group 2 included: cellular atypia/polymorphism (20/20, 100%); the presence of apoptotic cells (3/20, 15%), the presence of mitoses (5/20, 25%); limitation of the papillary dermis (16/20, 80%), the presence of invasion into the reticular dermis (4/20, 20%), ulceration - moderate and severe destruction of the epidermis in 5 cases out of 20 (25%); hyperkeratosis (20/20, 100%); horny cysts (4/20, 20%); tumor neovascularization of the superficial layers of the dermis (3/20, 15%); stromal fibrosis of the dermis in 4 cases out of 20 (20%); diffuse dermal fibrosis (1/20.5%); the infiltrate was represented by: lymphocytes and histiocytes in each case (20/20, 100%); tumor thickness up to 1 mm (16/20, 80%); tumor thickness up to 2 mm (4/20, 20%); ratio of tumor parenchyma to stroma >1 (20/20, 100%); infiltrative growth (20/20, 100%). A distinctive histological feature of patients of the second group was the presence of anaplasia/polymorphism of keratinocytes of varying degrees.

When analyzing histological preparations of patients of group 3, the following signs were found: cellular atypia/polymorphism (16/16, 100%); apoptotic cells (2/16, 12.5%); the presence of mitoses (9/16, 56.25%); restriction to the papillary dermis (16/16, 100%); ulceration - moderate and severe destruction of the epidermis was found in 1 case (1/16, 6.25%); hyperkeratosis (16/16, 100%); tumor neovascularization of the superficial layers of the dermis (2/16, 12.5%); inflammatory infiltrate is represented by lymphocytes and histiocytes in all patients (16/16, 100%); tumor thickness up to 1 mm (16/16, 100%).

The final diagnosis, formed on the basis of the results of an objective examination, histological examination and response to ongoing therapy, made it possible to verify the nosology of 4 groups of patients: 4 patients had a pigmented form of basal cell carcinoma, two had Bowen's disease (22%), 1 had lichenoid keratosis (11%), two patients had eczematid (22%).

Table 3 Histological signs of patients of experimental groups

(moderate and severe destruction				
epidermis)	16/35 (45,7%)	20/20(100%)	16/16(100%)	5/9(56%)
Hyperkeratosis	0/35(0%)	4/20(20%)	0/16(0%)	2/9(22%)
Horny cysts	31/35(88,6%)	3/20(15%)	2/16(12,5%)	1/9(11%)
Tumor neovascularization of superficial layers	8/35(22,8%)	4/20(20%)	0/16(0%)	2/9(22%)
dermis	0/35(0%)	1/20(5%)	0/16(0%)	0/9(0%)
Inflammatory infiltrate is represented by: -lymphocytes - histiocytes - melanophages -leukocytes	30/35(85,7%) 30/35(85,7%) 1/35(2,9%) 0/35(0%)	20/20(100%) 20/20(100%) 0/20(0%) 0/20(0%)	16/16(100%) 16/16(100%) 0/16(0%) 0/16(0%)	9/9(100%) 9/9(100%) 2/9(22%) 0/9(0%)
Tumor thickness up to 1	29/35 (82,6%)	16/20(80%)	16/16(100%)	9/9(100%)
mm	6/35(19,4%)	4/20(20%)	0/16(0%)	0/9(0%)
Tumor thickness	0/35(0%)	0/20(0%)	0/16(0%)	0/9(0%)
up to 2 mm	35/35(100%)	20/20(100%)	Not applicable	Not applicable
Tumor thickness	6/35(19,4%)	20/20(100%)	0.16(0%)	0/9(0%)

Dermoscopy has significantly improved the process of making a diagnosis of CCC. Through the efforts of many researchers, a number of patterns and signs have been formed, noting which, one can assume the diagnosis of BCC. However, the probability of misdiagnosis in early-stage basal cell skin cancer also remains high. The next diagnostic step is to perform a histological examination. The two main features that the pathologist relies on - the "peripheral palisade" of basaloid cells and the phenomenon of tumor retraction - as it turned out, may be absent in patients with recently manifested BCC, which also leads to an erroneous diagnosis.

Conclusion: Thus, the proposed minimally invasive diagnostic test has a potential advantage in comparison with routine research methods and can fill the gaps in the verification of the diagnosis in this case. It is also worth noting that a histological examination in patients with a recent manifestation of BCC, when the neoplasm is represented by an erythematous spot, may be of little information due to the fact that the specific signs of the neoplasm have not yet formed. So, in addition to histological examination, it is necessary to select more accurate differential diagnostic criteria for the diagnosis of BCC.

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