ETIOLOGY AND LEVELS OF DIAGNOSIS OF MALIGNANT TUMORS OF THE OUTER NOSE SKIN

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The paper analyzes the epidemiological indicators of the incidence of nasal skin cancer in Ukraine and Europe according to the National Cancer Registry of Ukraine in 2015 - 2018. The main etiological factors that cause the growth of nasal cancer and the role of various factors in the carcinogenesis of squamous cell carcinoma are considered.

Data on methods of early diagnosis are given and the role of timely diagnosis that affects the quality of life of the patient is determined.

To prevent cancer of the external nose, the expediency of state aid in eliminating the effects of harmful environmental factors that cause the development of malignant neoplasms is discussed. The author offers suggestions for early detection and improving the diagnosis of malignant tumors of the skin of the outer nose.

**Keywords:** malignant neoplasms, external nose, epidemiological indicators, diagnosis.

The modern development of medicine involves the constant improvement of methods of diagnosis, treatment and prevention of diseases according to the requirements of evidence-based medicine. It is known that malignant diseases are one of the most important modern medical, biological and socio-economic problems in the world.
Today, cancer is a global problem, as diseases in the later stages of development lead to disability and a significant reduction in the duration and quality of life of patients.

However, it should be emphasized that there is a low medical culture of the population, which seeks help late. And also lack of oncological vigilance at doctors of the first link.

Statistics show that every year about 2.9 million new cases are registered in developed countries and more than 3 million in developing countries. According to Schart FM, Gabbe C. the morbidity of skin cancer in Germany among men is second only to lung cancer, and among women breast cancer, which is 93.4 and 55.8 per 100,000 population, respectively [7, 10, 11, 12, 13].

In recent years, there has been an increase in the number of superficial epithelial malignancies of the head and neck in all countries. Especially the two most common cancers - basal cell and squamous cell [2]. In Ukraine, 1 million new cases of cancer are registered annually [2, 3, 7], in Russia malignant skin tumors rank 3rd after lung cancer [1].

Thus, annually in Ukraine more than 20,000 cases of superficial malignant neoplasms of the head and torso are diagnosed, which is 44.5 cases per 100 thousand population [2, 5, 6]. Thus, annually about 100 new cases per 100,000 population [2, 3, 6].

It is known that squamous cell skin cancer and other malignancies can develop on any part of the skin.

Squamous cell skin cancer (synonyms: squamous cell carcinoma, squamous cell epithelioma, epidermoid cancer, squamous cell carcinoma) is a malignant epithelial tumor of the skin that develops from keratinocytes.

The first historical data on the causes and clinical manifestations of squamous cell skin cancer date back to 1775, when the English physician Percival Pott described the clinical picture of scrotal cancer in London
chimney sweeps. He found that the cause of the disease is the chronic effect of soot on the skin. Thus, the work of P. Pott was the first to identify a chemical carcinogen.

Today, there are well-known factors of exogenous and endogenous nature that cause the development of precancerous changes and the development of malignant tumors in the skin of the face and torso, i.e., that lead to tissue malignancy.

To understand the development of the pathological process due to the action of harmful agents, it is important to know not only the structure of the skin, but also changes as a result of harmful actions. This knowledge allows the clinician to understand the etiopathogenesis of the disease, to show timely cancer vigilance and to determine the tactics of such conditions.

The action of harmful agents (cancer risk factors) on the components of the skin: the epidermis, dermis and related structures can give impetus to the development and growth of malignant tumors.

It is known that malignant tumors of the skin most often develop in exposed areas of the skin, which are exposed to UV-solar radiation or artificial tanning (insolation), as well as the action of chemical agents (contact with soot, sulfur, resins, tar and arsenic), thermal agents and physical irritations. Most of the factors are a risk of developing a malignant disease and are related, one way or another, to a person's lifestyle.

But the prolonged effects of UV radiation from the sun and artificial tanning, as well as constant mechanical injuries to nevi, birthmarks and skin scars in most cases lead to skin cancer. The effect of ultraviolet radiation does not end on the epidermis of the skin, but penetrates into the much deeper layers of the skin - the dermis and subcutaneous fat.

It is known that the human body is protected from aggressive sunlight by producing a pigment that makes the skin color darker, and the more a person is in the sun, the darker the skin.
On the one hand, tanning is a kind of protective reaction of the body against the effects of sunlight on the internal subcutaneous tissues.

On the other hand, the prolonged effect of UV radiation from the sun and artificial sunburn provokes diseases such as melanoma and squamous cell carcinoma.

Today it is noted that regardless of skin color most often sick people who spend a long time in the sun (fishermen, agricultural workers, etc.). In addition, the carcinogenic effects of solar radiation are facilitated by the effects of sea (salt) cold wind, which causes dry skin. However, the harmful effects of these factors on the body can be reduced by increasing the protection of exposed areas of the body.

Also, the effect of ionizing radiation was detected after the discovery of the action X-rays, on the body of radiologists who worked without protection, who were affected by skin cancer. It is also known that prolonged exposure to the radioactive zone often causes neoplasms of hematopoietic organs, but this factor should not be excluded from the probable causes of malignant skin lesions.

Today, attention is also paid to the identified genotypes of human papillomavirus (HPV) and skin neoplasia. There are 5 types of HPV (Alpha, Beta, Gamma, Mu and Nu). Cutaneous HPV was detected in all 5 types of viruses. Most members of the genus Beta have been isolated from patients with liquid genodermatosis - verruciform epidermodysplasia (BE). The association between HPV and human skin cancer has been evident in patients with BE for 10 years (Pfister H., 2012). Studies by H. Pfister have shown that human papillomaviruses Beta cause benign and malignant tumors not only of the skin but also of the mucous membrane.

For example, in patients with actinic skin keratosis, HPV persists much more than in tumors. Therefore, higher viral loads in actinic keratosis foci are consistent with the carcinogenic role of cutaneous HPV in different
stages of skin cancer. The oncogenic potential of HPV Beta is explained by blocking apoptosis by the viral protein E6 and interfering with cellular mechanisms of DNA repair. E7 proteins disrupt the regulation of the cell cycle and promote invasive growth.

Thus, when HPV blocks apoptosis, the skin keratinocytes out critical mutations in oncogenes and genes of the tumor suppressor survive and proliferate.

Endogenous causes include all liver diseases that reduce and disrupt the body's antioxidant defenses by promoting growth of formations on the skin of exogenous origin. It is known that against the background of specific diseases can cause skin cancer (RS). RS in these specific diseases is highly malignant. This cancer has a pronounced infiltrative type of growth and is prone to recurrence.

For example, tuberculosis of the skin, especially lupus tuberculosis. Tuberculous lesions of the skin of the auricle often appear as hematogenous, if the original complex - elsewhere (in the lungs, intestines, etc.). Tuberculous lesions of the skin of the auricle have three forms: nodular, ulcerative and less common form of perichondritis. Therefore, all forms of tuberculosis need to be differentiated from skin cancer. Damaged areas are sharply separated from healthy skin, soft to the touch, the skin that covers them retains its normal appearance for a long time, and then acquires a red-blue hue. Eventually, the skin may become covered with ulcers again.

Histological examination reveals changes characteristic of tuberculosis: tubercles, giant cells, small cell infiltration and vortex decay. Against this background, skin cancer can develop. Approximately 2–4% of lupus patients subsequently developed skin cancer. Treatment is specific general and local. RS can also occur on the background of syphilitic gum. Syphilis of the skin of the auricle can occur in all three forms. Ear rubber
sinks occur in isolated cases. The pathogenesis of cancer on the background of humus syphilis is similar to the process in tuberculous lupus. Treatment is specific to the general. But in these cases it is necessary to differentiate tuberculosis and syphilis by Wassermann’s reaction and to carry out histologic and bacteriological research.

Sometimes there is cancer that develops from the appendages of the skin: hair follicles, sebaceous and sweat glands, and finally, we should not forget the hereditary predisposition to the appearance of both benign and malignant skin tumors.

Thus, the above indicates that malignant tumors the skin of the outer nose, ears and torso may develop as a result of the action of provoking factors and their prolonged action (harmful exogenous agents) and because the face (outer nose and ears) and other parts the torso is an open area.

But, there is a group of factors that medicine cannot effectively counteract yet. This is a genetic predisposition.

Analyzing the statistics of the Cancer Registry of Ukraine, among the diseases in Ukraine we can identify the main types of malignant skin lesions, which are called - white cancer: basal cell carcinoma and squamous cell skin cancer and the most malignant skin tumor - melanoma.

Therefore, despite the improvement of methods of diagnosis and treatment, the absolute frequency of death from squamous cell carcinoma remains. Due to the direct correlation between the effectiveness of diagnostic and treatment and the stage and morphology of the cancer process, several levels of diagnosis of malignant skin tumors are known: early, timely and late.

Today in Ukraine, the diagnosis of skin tumors is carried out according to European standards only in a specialized unit, ie oncologists. It is too late! The problem of early and high-quality diagnosis of malignant diseases of the skin of the face, torso and their treatment worries many
researchers, both in Ukraine and in Europe. This is due to the increase in the number of patients with malignant skin neoplasms in recent years.

The system of standardization of medical care is focused on the development of medical - technological documents that help the doctor to act effectively in specific clinical situations, avoiding ineffective and erroneous interventions. Clinically and morphologically distinguish benign and malignant skin formations. Diagnosis according to the protocol of diagnosis "malignant lesion of the skin" is established in a specialized medical institution on the basis of histological or cytological conclusion on the basis of biopsy examination of the pathological formation.

Examination of primary patients is performed by family doctors, who in case of suspicion of malignant skin tumors should refer patients for 5 days for secondary (specialized) medical care.

This requires a clinical justification that confirms the signs and symptoms that may indicate basal cell, squamous cell skin cancer or melanoma of the skin:
1. The excrescence of pink color, which is flat formation with an increase in the periphery and the presence of crusts in the center.
2. The red spot or area of irritation, especially on the face, neck, shoulders.
3. The brilliant knot of mother-of-pearl color.
4. The open ulcer or erosion that does not heal for more than 5 weeks.
5. The cicatricial area with a shiny surface and fuzzy contours.

Regardless of the level of diagnosis, all primary care patients should undergo a full range of examinations and tests: general blood test, blood glucose, coagulogram, blood on Wassermann reaction, X-ray or CT scan of the lungs and bacteriological examination and direct to a specialized unit to conduct histological examination.

Questions of modern diagnostics of superficial skin neoplasms of the face and torso are relevant because the diagnosis is made late stages of
skin cancer leads to reduced quality of life and low survival of patients. Unfortunately, at the stage of early development of the disease, patients do not seek medical help.

The early diagnostics should be made at the primary level, which is based on the detection of clinical symptoms of the tumor and the use of special clinical diagnostic methods necessary for the diagnosis of malignant neoplasms as soon as possible and the choice of treatment. This level of diagnosis is to detect malignant skin tumors in situ or in the I- and clinical stages of the disease, when the tumor does not metastasize. If a malignant disease is suspected, the primary care physician should refer the patient to a specialized unit, which establishes the final diagnosis. But this implies that adequate treatment can guarantee complete recovery of the patient.

The timely diagnostics is should be made at the primary level, which is based on the detection of clinical symptoms of the tumor and the use of special clinical diagnostic methods necessary for the diagnosis of malignant neoplasms as soon as possible and the choice of treatment. This level of diagnosis is to detect malignant skin tumors in situ or in the I- and clinical stages of the disease, when the tumor does not metastasize. If a malignant disease is suspected, the primary care physician should refer the patient to a specialized unit, which establishes the final diagnosis. But this implies that adequate treatment can guarantee complete recovery of the patient.

The late (untimely) diagnostics is the diagnosis of malignant neoplasms at stages T3 and T4, which indicates an unfavorable prognosis and complexity, or the impossibility of treatment according to a radical program. Especially in the presence of regional or distant metastases.

The late (untimely) diagnostics is 100 percent dependent only on the patient and family. At T3, and T4 of malignant process of skin and especially at T4 and when there is a metastasis, really testifies to not possibility of carrying out treatment not under the radical program, and with
the palliative purpose, ie treatment will be directed on reduction of a cancer intoxication and improvement of life.

Thus, to achieve and perform the first two levels of diagnosis requires a high culture of the population and a high level of professionalism of the medical staff. In both cases, there should be constant and clear oncological alertness.

First of all, the largest arsenal of clinical examination of cancer patients should be used in cancer vigilance: more detailed history taking, non-invasive diagnostic methods: dermatoscopy, ultrasound diagnostic scanning, confocal laser scanning microscopy, thermal differential test and, if necessary- biopsy.

Here are the responsibilities of a primary care physician:
1. The collection of complaints and detailed anamnestic data.
2. The examination of the skin and lymph nodes.
3. The ultrasound of lymph nodes to determine their differentiation.
4. If malignant skin disease is suspected, the patient should be referred to specialists - dermatologist and oncologist.

Today, a unified protocol for the management of patients with suspected skin cancer helps to determine the choice of consultant for adequate treatment of Unified Clinical Protocol of Medical Care (UKPMD) "Basal cell and squamous cell skin cancer and melanoma" by its form, structure and methodological approach to use requirements of evidence-based medicine created in accordance with the methodology approved by the order of the Ministry of Health of Ukraine dated 28.09.2012 № 751 “On creation and implementation of medical and technological documents on standardization of medical care in the system of the Ministry of Health of Ukraine ”, registered with the Ministry of Justice of Ukraine on November 29, 2012 for 2001/22313.
Detailed collection of medical history with the identification of possible causes (harmful factors), encouraging the development of skin cancer and with the definition of hereditary factors. After that, dermatoscopy is an examination of identified and individual skin formations using a specialized dermatoscope, which allows without surgery to "look" inside the mole (formation), assess its type, structure and determine whether it is benign or whether it is necessary to remove it. The dermatoscope magnifies the image of the formations 10 times and allows you to "look" under the stratum corneum.

Dermatoscopy is a modern method of diagnosing skin tumors, which is used in leading clinics in Europe and America. This method of research allows you to visualize the smallest structures of the epidermis, which are difficult to distinguish with the naked eye.

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**Dermatoscopy** (epiluminescent microscopy - skin surface microscopy) is a non-invasive diagnostic method of visual assessment of skin lesions, allowing to study of morphological and subepithelial structures with different magnification. The method is based on the use of a dermatoscope - an optical device with a built-in backlit lens - and the use of immersion oil, which allows to obtain images of intradermal structures with a size of 0.2 μm. The method, according to the citation index, has become the most popular and significant over the past 15 years. This fact can be explained by high diagnostic efficiency, availability of manual dermatoscopes, as well as simple methods of skin examination. Today,
advanced digital video systems are widely used to capture images and assess skin structure.

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Next, if there is insufficient diagnostic information, you need to use other diagnostic methods.

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The use of a digital dermatoscope has a number of benefits: the function of polarization, the ability to store images in a computer archive and the use of modern analytical software. According to various authors, the coincidence of the dermatoscopic result with the morphological diagnosis is about 90%.

Ultrasound diagnostic scanning is not widely used in dermatoncology due to the technical costs (sensor frequency 3 - 10 MHz does not allow to obtain images of the structures of the epidermis, dermis and hypodermis).
Only recently, thanks to the creation of instruments with a sensor frequency of 20 - 100 MHz (high-resolution digital ultrasound imaging) it is possible to study all layers of the skin with high measurement accuracy at different intervals, to document all features without tissue damage.

**Confocal laser scanning microscopy** is an in vivo non-invasive diagnostic method that allows obtaining images of the layers of the epidermis from the surface of the dermis with a resolution close to conventional light microscopy. The method has two indisputable advantages: the ability to obtain a lifetime image at the cellular level and the demonstration of the image in 4 dimensions - height, width, depth, and time.

However, today there is equipment for confocal laser scanning microscopy, which is massive, which limits its use on hard-to-reach parts of the skin due to the difficulty of fixing the lens. In addition, the images obtained by confocal laser scanning microscopy of the skin layers are oriented parallel to the skin surface, which makes it difficult to analyze the results based on their comparison with classical biopsy data.

These modern diagnostic methods (high-resolution digital ultrasound imaging and confocal laser scanning microscopy) are currently of limited use in Ukraine and developing countries due to the high cost and lack of training.

In our opinion, the use of the method of laser-induced fluorescent and spectral diagnosis of squamous cell skin cancer is particularly promising. The method is based on the use as a photosensitizer of 5-aminolevulinic acid or Photolon, allowing to determine the boundaries of tumors and the degree of hyperreactivity of its cells.

**Thermal Differential test** is a biological test based on the temperature difference between tumor tissue and healthy skin. Researches are carried out by means of the electrothermometer with the definition of temperature in 5 - 8 points of the struck zone. At the same time, the
difference of temperature between the struck and healthy parts of the skin in one degree should be noted. Informative is when there is a difference of 1 degree.

**Biopsy.** The final method of skin disease research is the morphological examination of the material after total removal of the tumor lesion or biopsy. Biopsy should not be performed in cases of color changes in the tumor and the presence of aggressive infiltrative growth. In these cases, it is possible to conduct a cytological examination or examination of the material after extensive removal.

It is generally known that the results of the histological examination in the diagnosis of skin tumors are more informative than the data of cytological examination (smears or scrapings from the surface of the tumor ulcer or punctate from the tumor). Therefore, it is advisable to perform a biopsy.

**DIFFERENTIAL DIAGNOSIS OF MALIGNANT TUMORS SKIN WITH INFECTIOUS DISEASES**

A family doctor, dermatologist and oncologist should be consulted on the differential diagnosis of skin diseases with infectious diseases that are aggressive and long.

But at the initial stage of diagnosis it is necessary to exclude HIV infection (with a contagious mollusk - a giant on the background of HIV infection) and only then consider the causes of the disease.

Infectious diseases that need to be differentially diagnosed include: syringoadenoma, rhinophyma, rosacea - erythematous-papular form, actinic keratosis of the skin and erythematous of the skin (discoid lupus).

Taking into account the pathogenesis of cancer on the background of humus syphilis, similar to the process in lupus tuberculosis, should be to carry out differential diagnostics with the use of additional ones’ examinations for tuberculosis and syphilis.
The tuberculous type of leprosy, which forms papular plaques that are objectively similar to depigmented spots, should be especially diagnosed skin. In these cases, you need to differentiate with leprosy.

It should also be considered as a cause of skin cancer as a result of the action of certain drugs that suppress the immune system. These are antitumor, anti-inflammatory drugs with corticosteroids.

The clinical course of infectious diseases at some stages of development is clinically similar to malignant signs of skin disease, so it is necessary to make a differential diagnosis. For example: syringadenoma - a tumor of the sweat glands (apocrine and eccrine) is more often localized on the skin. Characteristic long-term course. Objective: dense, bluish papules with ulcers. Complaints of patients with itchy skin, pain and ulcers. Malignancy accounts for about 2.5% of cases.

Conclusions:
1. In Ukraine, more than 20,000 cases of superficial malignant neoplasms of the head and torso are diagnosed annually, which is 44.5 cases per 100 thousand population. This fact indicates the shortcomings of prevention and timely diagnosis.
2. The use of a set of diagnostic methods: medical history, visual examination (non-invasive objective clinical semiotics): dermatoscopy, confocal laser scanning microscopy, thermodifferential test, ultrasound and invasive diagnostics: cytological and morphological examination allowed to establish and diagnose treatment according to a radical program.
3. Constantly spend
4. Eliminating environmental illiteracy and increasing state control over the level of environmental pollution will help reduce the number of malignant skin lesions.

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