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## **SKIN CLINICAL AND MORPHOLOGICAL CHANGES IN PATIENTS WITH SEBORRHEIC KERATOSIS**

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### **Abstract**

The clinical characteristics and morphological features of seborrheic keratosis in 30 patients are presented. In 26 (86.7%) cases, the process was localized only on the covered areas of the skin (back, chest, shoulders), and in 4 (13.3%) cases, it affected the face and neck. The average number of lesions per patient was  $6.5 \pm 2.1$ , with an average size of the largest diameter measuring  $1.7 \pm 0.6$  cm. Morphologically, seborrheic keratosis was manifested in various histological variants (hyperkeratotic, acanthotic, "irritated", mixed), acanthosis, epidermal cell proliferation, primarily of basal cells, as well as the presence of keratin cysts, circulatory disturbances, and immune cell reactions of varying intensity.

**Key words:** seborrheic keratosis; clinic; morphology; inflammation; diagnosis; treatment.

Recent statistical studies indicate skin neoplasms incidence increase among the population of developed countries [1, 2]. Despite the significant number of scientific works devoted to seborrheic keratosis, the question of its morphological nature remains a subject of debate [3, 4].

Terminological differences also complicate the classification of this process, which can lead to diagnostic difficulties among clinicians and pathologists.

Morphological examination remains the “gold standard” of diagnosis because it allows to differentiate seborrheic keratosis from other skin neoplasms [5, 6]. This pathology (also known as basal cell papilloma) is characterized by papillary growths presence covered with dense dark brown crusts that are easily removed [7, 8]. Trauma or inflammatory process can lead to ulceration, which greatly complicates the diagnosis.

Thus, a detailed analysis of seborrheic keratosis both clinical and morphological peculiarities will help to increase diagnostic accuracy, optimize treatment approaches and improve the prognosis for patients.

**The aim of the work** is to determine the clinical and morphological peculiarities of seborrheic keratosis to improve diagnosis, assess the clinical course and select the optimal treatment tactics

### **Material and methods**

A comprehensive clinical and morphological examination of 30 patients aged 48 to 72 years was conducted, including 14 men and 16 women. The average age of the patients was equal to  $58.3 \pm 2.6$  years. All patients provided written agreement for their examination and treatment results use with scientific purposes.

All patients underwent a detailed visual examination, during which the size, borders, color, relief, number of formations and their localization were assessed. The diagnosis was confirmed by histological analysis of the affected skin biopsies.

Skin biopsy was performed with the patients agreement under local anaesthesia (novocaine or lidocaine 0.5% solution). Morphological elements of the rash together with the adjacent unchanged skin were completely excised with a scalpel in aseptic conditions.

Postoperative wounds were sutured with a silk suture, treated with 5% alcoholic solution of iodine and an aseptic dressing was applied. The sutures were removed on the 8th-10th day. The postoperative period in all patients was without complications, the wounds healed with primary tension.

The control group consisted of 20 biopsies of unchanged skin (abdomen, back, limbs) obtained during orthopaedic reconstructive surgeries in somatically healthy individuals aged 21-60 years.

Tissue samples were fixed in 10% neutral formalin solution at +4°C for 24 hrs after which standard histological processing was performed using paraffin embedding. Serial sections with a thickness of  $5 \pm 1 \mu\text{m}$  were made using a “Microm HM325” rotary microtome (Carl Zeiss, Germany)

and stained using various histochemical methods (hematoxylin-eosin, van Gieson's picrofuchsin, Mallory, Weigert, etc.).

Immunohistochemical staining for PCNA (proliferation nuclear antigen) was used to assess the proliferative activity of epithelial cells.

Histological studies were performed using a "Hund H500" microscope (Germany), digital images were obtained using a "DCM510" video camera (USB 2.0, 5 MP CMOS).

Morphological and morphometric study of histological samples was performed in Pathomorphology Department of University Clinic of Odessa National Medical University. Statistical analysis was performed using the programs "Statistica 5.5" (StatSoft Inc., 1999) and MedStat 3 (No. MS 00032).

## Results

Analysis of clinical observations allowed us to establish the following patterns.

Seborrheic keratosis was localized exclusively on closed areas of the skin (back, chest, shoulders) in 26 (86.7%) patients while in 4 (13.3%) patients it was localized on open areas (face, neck). The average number of formations per patient was  $6.5 \pm 2.1$ , and the average diameter of the largest of them was  $1.7 \pm 0.6$  cm. The average age of the first element of the rash appearance was equal to  $14.4 \pm 2.3$  years.

According to the anamnesis, the primary element of the rash was a spot, almost invisible against the background of the surrounding skin. It had clear boundaries, a pink or yellowish tint, a warty (corrugated) surface and was covered with easily removable fatty crusts. Over time, the crusts thickened, became more fissured, and the spot gradually darkened and transformed into a plaque.

The plaques had yellow-brown color and were characterized by a warty or mushroom-like surface covered with a fatty layer. They were raised above the skin level on a wide base. In some cases, dome-shaped formations with a smooth surface were noted, on which white or black keratin "pearls" with a diameter of up to 1 mm, clearly visible during dermatoscopy, could be detected.

Skin preparations from patients with seborrheic keratosis microscopic investigation allowed to identify four main histological variants:

- Hyperkeratotic (20 cases, 66.6%) – characterized by expressed hyperkeratosis and acanthosis;
- Acanthotic (6 cases, 20%) – characterized by significant proliferation of basal cells of the epidermis;
- "Irritated" variant (2 cases, 6.66%) – accompanied by expressed infiltration of inflammatory cells dermis;
- Mixed variant (1 case, 3.33%) – combined the features of several previous types.

Papillomatosis, acanthosis and horny cysts formation were the characteristic morphological features of seborrheic keratosis. The presence of horny cysts and pseudocysts is a key diagnostic criterion for this disease. In some cases, melanin accumulations were noted which could change the clinical appearance of the lesions.

The pathological changes were clearly demarcated and, as a rule, had an exophytic character. The degree of pigmentation in the basal cords varied. On the surface, areas of hyperkeratosis were observed, which formed invaginations filled with keratin. In the deeper layers, horny masses could form horny cysts, which were not always connected to the surface.

Two patients with the “irritated” variant of seborrheic keratosis had microscopic lymphocytic infiltration in the superficial dermis and within the keratosis. They also had more expressed squamous cell differentiation which required differential diagnosis with squamous cell carcinoma and pseudocarcinomatous hyperplasia.

## **Discussion**

The proliferating cells, mostly small and compact, resembled basal cells of the epidermis and were called basaloid. In patients with the “irritated” variant, positive typing of PCNA was observed in almost all layers of the epidermis, with its greatest detection in basal cells.

In patients with the hyperkeratotic variant, cells with a positive reaction to PCNA occupied a significant part of the epithelial layer. In places, individual cells or small groups of cells with a negative reaction were found, located mainly in the superficial layer of the epidermis. The percentage of cells with a positive reaction to PCNA varied from 28% to 75%, the average value for different variants was: hyperkeratotic —  $36\pm2.5\%$ , acanthotic —  $49\pm3.7\%$ , “irritated” —  $70\pm5.1\%$ .

Of particular interest was the expressed vascular reaction manifested in a significant number of vessels with signs of angiogenesis which is a morphological sign of immunosuppression. Cellular infiltrates in most cases were focal and located mainly in the subepithelial and perivascular compartments. The cellular composition included lymphocytes, plasma cells, fibroblasts, histiocytes, segmented leukocytes and a small number of mast cells. In 7 cases, stromal infiltration was absent or represented by single plasma cells and lymphocytes with an admixture of neutrophils.

Thus, seborrheic keratosis is a slowly progressive disease that belongs to skin neoplasms and requires treatment and dispensary observation. This disease is most common in old age and is diagnosed equally often in men and women. In most cases, seborrheic keratosis is localized on closed areas of the skin.

Histological and immunohistochemical studies confirmed that seborrheic keratosis manifests itself in various histological variants among which the most characteristic are papillomatosis,

acanthosis, proliferation of basal cells of the epidermis as well as the formation of horny cysts. Microcirculation disorders and varying intensity of the immunocellular reaction were also revealed.

Morphological features, such as the presence of horny cysts, basaloid cells and a specific vascular reaction, are important indications for the complete removal of skin altered areas with subsequent monitoring of the patient's condition.

It should be noted that early diagnosis and/or preventive measures with wide segments of the population of all age groups are the key in terms of malignant neoplasms early detection. In this regard, pathomorphological studies should be the basis which, with the oncologist correct analysis, will serve as the basis for malignant skin tumors correct, adequate and as earlier diagnosis. At the same time, patients with long-lasting inflammation of unclear genesis should be seriously clinically supervised, because prolonged inflammation, according to fundamental ideas, after a certain period of time might initiate an undesirable and life-threatening oncological diagnosis [9-11].

### **Conclusions.**

1. Seborrheic keratosis is a slowly progressive disease that belongs to skin neoplasms and requires treatment and dispensary observation.
2. Histological and immunohistochemical studies confirmed that seborrheic keratosis manifests itself in various histological variants among which the most characteristic are papillomatosis, acanthosis, proliferation of basal cells of the epidermis as well as the formation of horny cysts.
3. Morphological features, such as the presence of horny cysts, basaloid cells and a specific vascular reaction, are important indications for the complete removal of skin altered areas with subsequent monitoring of the patient's condition.
4. Patients with long-lasting inflammation of unclear genesis should not be omitted from clinical supervision.

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## **Informed Consent Statement**

The retrospective analysis of material was used. Written informed consent from the patients was not necessary to publish this paper.

## **Data Availability Statement**

The data presented in this study are available on request from the author.