2. Клінічна медицина

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**Norwegian scabies in HIV-infected PERSONES: clinical features, diagnostics and treatment**

HIV infection poses a global threat today. An estimated 36,9 (34,3-41,4) million people are living with HIV/AIDS, and there are some 2 (1,9-2,2) million new infections each year. Every day, more than 6800 people become infected with HIV and more than 5700 die, mostly because they have no access to HIV prevention, treatment and care services. More than 39 million people worldwide died from diseases that developed on the background of Acquired Immunodeficiency Syndrome [1]. According to WHO / UNAIDS Ukraine continues to be a region with high levels of HIV in Central Asia and Eastern Europe [2]. During 1987-2016 among the citizens of Ukraine 287,968 HIV - positive people were registered including 88,075 AIDS cases and 39,885 deaths from AIDS-related diseases [3].

Currently, dermatologists along with other doctors are at the forefront of diagnosis of HIV infection and AIDS. This is because lesions of the skin and mucous membranes are most often affected by HIV infections. On the other hand lesions on the skin and mucous membranes  can be the first sign of HIV infection [4].

Mucocutaneous findings occur throughout the course of HIV infection. The spectrum of skin lesions and mucous membranes in HIV infection is quite wide. They can be divided into three main groups: neoplasms, infections (viral, bacterial, fungal and parasitic) and other dermatoses with unclear pathogenesis [4, 5].

A broad spectrum of presentations of scabies occurs in the HIV-infected population. Scabies may present as atypical or crusted forms [6, 7].

Norwegian (crusted) scabies was first described by Norwegian scientists Woesk and Dantelssen in 1847 in leprosy patients. In previous years the occurrence of the disease was rare, but in recent years, cases of "Norwegian" or "crusted" scabies have become more common due to HIV infection.

Norwegian scabies is caused by the same mite (Sarcoptes scabiei) that causes common scabies. It proved an untenable assumption that Norwegian scabies was caused by a different form of human mite or mite of animals. The identity of the causative agent of both common and Norwegian scabies is evidenced by the appearance of a typical form of the disease in medical personnel, family members and other persons who were in contact with patients with Norwegian scabies. Patients with Norwegian scabies are very contagious. Local epidemics, often arising around them, have been described.

In the pathogenesis of Norwegian scabies, the leading mechanisms appear to be immune mechanisms. This peculiar and severe variant of scabies is more common in people weakened by severe diseases (leukemia, tuberculosis, lupus erythematosus, scleroderma), in people with peripheral sensitivity disorders (leprosy, syringomyelia, paralyzes, tabes dorsalis), in people with constitutional anomalies of keratinization, in mentally retarded people (Down's syndrome, senile dementia, etc.), in persons with immune deficiency due to long-term treatment with cytostatics and corticosteroid hormones and in HIV-infected patients as well as AIDS patients.

Crusted scabies is a severe, debilitating disease. It is an uncommon condition, most often presenting in immunocompromised individuals, such as those with HIV infection, especially in association with a low CD4 cell count [8], as well as the elderly. The infection is characterized by considerably high numbers of mites where multiplication continues unhindered, producing thousands to millions of mites.

The clinical picture shows hyperkeratotic skin crusts that may be loose, scaly and flaky, or may have thick and adherent presentation. The crust contains high numbers of mites (up to 200 mites per 1 cm2). Large hyperkeratotic crusted masses in various areas of the skin are a characteristic clinical sign of Norwegian scabies. Crusts in the form of a shell can also cover significant areas of the skin, limiting movement and causing painful sensations. When the crusts are removed, large damp erosive surfaces are exposed. Hyperkeratosis of the palms and soles often develops.It creates a similarity to the hyperkeratotic form of psoriasis.

The distribution of lesions may be localized or extensive and often in atypical patterns including the neck, face, scalp, eyelids and under the nails [9, 10].

The hair loses its shine, becomes dull, dry, ash-gray and this often marks the development of alopecia. Also, nail plates thicken, become loosened and are easily broken. An unpleasant sour smell often emanates from the patient. Usually the disease has a generalized nature with a rise in body temperature and the appearance of erythroderma. It is very important to know that in some cases there may be a complete absence of itching [11].

 The disease is often complicated by secondary pyoderma, lymphadenitis and is accompanied by eosinophilia, leukocytosis and an elevated ESR.

During histological examination of skin biopsy, in the thickened stratum corneum, a large number of burrows are seen in multilayered rows; the granular layer is absent in these areas. Acanthosis and parakeratosis can be seen. In the papillary layer of the dermis there are few inflammatory changes.

Norwegian scabies progresses chronically and without antiparasitic treatment can last for years. However, with timely initiated adequate treatment, the disease quickly regresses.

Differential diagnosis should be carried out to exclude pyoderma, eczema complicated by pyoderma and hyperkeratotic form of psoriasis.

Treatment. Scabies, especially crusted scabies, is associated with considerable patient distress due to itching and potential stigma, as well as being an entry point for secondary bacterial infection of the skin, which is a significant risk for morbidity and even mortality. Therefore, prompt resolution of the skin manifestations is a priority to patients and their families.

Permethrin appears to be the most effective treatment for scabies infection. It has been tested against topical crotamiton and oral ivermectin in RCTs and it appears to be superior in terms of minimizing treatment failure in participants with a clinical diagnosis of scabies. A few trials show no difference in cure rates between permethrin and topical benzyl benzoate. However, no serious adverse effects leading to death or permanent disability were reported. Ivermectin is currently the only oral treatment for scabies that is in routine use. It appears to be more effective than both placebo and lindane but is less effective than permethrin. The limited data on crusted scabies in HIV-infected patients suggest a good effect of oral ivermectin. Local ivermectin resistance needs to be assessed and considered.

Treatments should be based on severity with separate recommendations for the severe form of scabies with a very high mite burden including crusted scabies and for the classic mild/moderate type. For mild/moderate disease in association with HIV infection, treatment efficacy appears to be similar to individuals in the HIV-negative population. A Cochrane review [12] included 22 studies involving 2,676 people without HIV (both children and adults)where one study was a controlled trial with a placebo, six studies including children, three studies including adults, and 13 studies including both children and adults. In HIV-negative study subjects with non-crusted scabies, topical permethrin appeared to be more effective than oral ivermectin (three trials). Permethrin appeared to be the most effective topical treatment for scabies and ivermectin appeared to be an effective oral treatment. Currently there is no data on the best treatment for scabies in association with HIV. There is also no evidence that treatment of HIV-associated crusted scabies is different from treatment of non HIV-associated crusted scabies. The use of oral ivermectin (200 μg/kg in two doses, one to two weeks apart) was found to be successful in several reviews [13,14,15]. Keratolytics were shown to be useful in reducing the mite burden of scabies in all cases. According to Guidelines on the treatment of skin and oral HIV-associated conditions in children and adults (WHO, 2014) [16]:

* For scabies in HIV-infected children and adults (including pregnant women) topical application of permethrin 5% (two applications) is recommended. If permethrin is not available, benzyl benzoate (at least two applications) should be used. If there is poor response to treatment, or permethrin treatment is not feasible, then oral ivermectin at 200 µg/kg is recommended.
* For severe or crusted scabies in HIV-infected children ≥15 kg and adults:
* Two doses (with one to two weeks in-between) of oral ivermectin;
* If ivermectin is not available, then treat with topical permethrin 5% (or alternatively benzyl benzoate) until clinically clear, as longer treatments may be required.
* For severe or crusted scabies in HIV-infected children <15 kg:
* Topical permethrin 5% (or alternatively benzyl benzoate) until clinically clear, as longer treatments may be required.
* In addition, a keratolytic, such as 5% salicylic acid, may be used to remove scale bulk.

In addition to individual patient management, contact tracing and treatment are necessary to prevent spread of disease and ensure treatment success. All family members and people in close contact should be treated simultaneously. In close-contact communities such as nursing homes, hospitals, schools and prisons, all patients and staff are required to have treatment. In addition household items such as clothes, towels and bedding should be washed in hot water, dried and ironed [21].

The use of ART in HIV-infected patients with reconstitution of the immune system will probably reduce the frequency of crusted scabies.

Conclusion: A broad spectrum of presentations of scabies occurs in the HIV-infected population. Scabies may present as atypical or crusted forms. Crusted scabies is a severe, debilitating disease [4, 7, 16].

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