

Demodecosis: Clinical Picture and Early Diagnosis

^{1,2}A. Kubanov, ²Y. Gallyamova and ²A. Grevtseva

¹State Scientific Center of Dermatovenereology and Cosmetology,
Ministry of Health of Russia, Korolenko Str. 3, Bldg. 6, 107076 Moscow, Russia

²Russian Medical Academy of Postgraduate Education,
Ministry of Health of Russia, Barrikadnaya, Str. 2/1, 123995 Moscow, Russia

Abstract: The study presents the current data of scientific literature on the prevalence and etiology of demodecosis. Modern theories of pathogenesis of the disease are specified; clinical picture of the disease is described and treatment methods are presented in the study. Demodecosis is a wide-spread chronic disease, mainly on facial skin. Mites of genus *Demodex* are part of the skin microflora and the vast majority of people do not have any clinical symptoms and complaints, however, the mites support the severity of the inflammatory process in dermatoses such as acne, rosacea, perioral dermatitis and may cause an independent disease.

Key words: Antiparasitic therapy, demodex, demodecosis, papulopustules dermatoses, literature survey, treatment

INTRODUCTION

Papulopustules dermatoses which localize mainly on facial skin (acne, rosacea, perioral dermatitis) remain the important problem in dermatovenereology. Among various causes of the development of these diseases a certain part is assigned to the parasitic theory (Baima and Sticherling, 2002). According to this theory, follicular mite (*Demodex*) is the cause for the formation of papules and pustules on facial skin. The mite belongs to genus *Demodex*, Demodicidae family, suborder Trombidiformes, class Acariformes. For the first time, the mite was revealed by F. Berger in earwax of acoustic meatus of a person in 1841, the same year F.G.J. Henle revealed the mite on a person's skin. A year after in 1842 G. Simon established the existence of the parasite in hair follicles and for the first time described the morphological properties, calling them *Acarus folliculorum* (from Greek "folliculorum mites"). Later G. Simon (1842) and Owen (1843) attributed the found mites to genus *Demodex*. Much later, after more than half a century English acarologist Hirst (1917-1923) identified 21 species and several subspecies of mites of the *Demodex* genus at animals. Later, studying mite parasitizing on human skin, Akbulatova (1963) discovered and described two forms: *Demodex folliculorum longus* and *Demodex folliculorum brevis* (Akbulatova, 1963).

Demodecosis is a widespread chronic disease, located mainly on facial skin. According to various sources, the prevalence of demodecosis among adults is from 25-100% (Segal *et al.*, 2010; Ruffli and Mumcuoglu,

1981) and the incidence of the disease ranks the seventh place on frequency of skin diseases. Demodecosis makes 10.5% in the structure of acne form dermatose. The frequency of demodex complications at patients with rosacea occurs in 88.7% and with perioral dermatosis in 58.8% cases.

Mites of *Demodex* genus are equally spread among all races and all age groups (Mahe, 1998). Only rare cases of mite detection at newborns were described (Jansen and Plewig, 1996; Gutierrez, 2000) and as a whole a low level of dissemination is registered at children. In all probability, this is due to lower production of sebum at children in comparison with adults (Peric *et al.*, 2010). Thus, at patients younger than 20 years the prevalence of *Demodex* mites is 13-20% and to 70 years it increases up to 95-100%. At patients after 45 years the activity of mites is supported by age-related changes of skin and glands, climacteric hormonal changes and also various somatic pathologies. The greatest number of *Demodex* cases is seen at people in the age group of 20-40 years. In laboratory studies, *Demodex folliculorum longus* is detected more frequently than *Demodex folliculorum brevis* (Baima and Sticherling, 2002) in the ratio at men 4:1, at women 10:1 (Bohdanowicz and Raszeja-Kotelba, 2001).

ETIOLOGY AND PATHOGENESIS

As many researches show, even if there are some mites on the skin, the clinical picture does not always develop. On this basis, it can be argued that mites of the

genus *Demodex* are opportunistic parasites (Mahe, 1998). So far, the exact reasons resulting in pathogenicity of mites of the genus *Demodex* are not set, existed theories are diverse and contradictory (Wolf *et al.*, 1988).

The most common opinion that one of the starting factors of the disease development is disorder of skin microflora. Following this theory, the development of pathogenic of a mite is favored by changes in the functions of the sebaceous glands with further changes in the composition of sebum and microbiocenosis that leads to skin disbacteriosis. Starting factor for the disease development is disorder of corynebacterium symbiosis and opportunistic pathogenic microflora as well as strengthening of microbial colonization, owing to changes in number of superficial lipids.

According to many researchers, the success of therapy with metronidazole which does not possess direct anti-parasite effect is due to the fact that *Demodex* shows its pathogenic properties as carrier of microbes and viruses into the deeper parts of hair follicles and sebaceous glands (Wolf *et al.*, 1988). Additional factor for the development of inflammatory purulent-necrotic process is the possibility of entry pathogenic pyococcus and *Pityrosporum* spp. into the deeper layers of follicles and sebaceous glands when mites move (Clifford and Fulk, 1990; Wolf *et al.*, 1988).

Other theories of the development of skin inflammation at demodocosis are also noteworthy. *Bacillus (Bacillus oleronius)* which was found on the surface of a mite as a result of its activity is capable to increase the activity of mites (Forton and Seys, 1993) and also stimulate other microorganisms (streptococcus, staphylococcus, propionbacterium acne, fungi genus *Malassezia*) (O'Reilly *et al.*, 2012), produce pro-inflammatory proteins 62 and 83 kDa, triggering cascade of immune reactions (Li *et al.*, 2010).

A favorable factor for the occurrence of demodocosis is the presence of nidus of infection, gastrointestinal disorders, liver and nervous system disorders, endocrine glands disorder and prolonged use of topical corticosteroids. Many authors have noted the connection of incidence rate in spring and summer period with high insolation and changes in environmental temperature. Most likely, it can be explained by the fact that production of vitamin D causes the increased synthesis of cathelicidins (LL-37) under the influence of ultraviolet radiation, supporting the activity of inflammatory process (Peric *et al.*, 2010; Persi and Rebora, 1985; Schaubert and Gallo, 2008).

The reactivity of the immune system plays a major role in the invasion of demodex mites. Several researchers have shown that *Demodex folliculorum* is more common

at patients of decreed groups, for example at hemodyalesis and T-cell lymphomas (Ozdemir *et al.*, 2005; Nakagawa *et al.*, 1996), at primary or secondary immunodeficiency (Gothe, 1989), AIDS, acute lymphoblastic leukemia and other malignancies (Kaya *et al.*, 2013), after corticosteroid therapy (Boge-Rasmussen *et al.*, 1982) or after cytostatic treatment (Bosch *et al.*, 1997).

According to many researchers, imbalance in cytokine cascade is the factor for the development of mites' invasion, maintenance of pathological process activity, as well as inefficiency of the carried-out therapy. It was revealed the presence of infiltrates of eosinophils and typical granulomas which consisted of CD4⁺ T-helpers around *Demodex* mites (Rufli and Buchner, 1984), the rise of readiness of lymphocytes to apoptosis and increased number of NK cells with Fc-receptors (Akilov and Mamcuoglu, 2004), reduction of absolute lymphocyte count and rise of IgM level (El-Bassiouni *et al.*, 2005).

Mites, having difficult life cycle are capable to express different antigens at certain stages of their development, thus causing various immune reactions. At the same time, the parasites themselves are protected from their owner's metabolite by chitinous shell. Chitin of mites causes the activation of Toll-like receptors of keratinocytes, triggering the cascade of inflammatory reactions of the immune response (Yamasaki *et al.*, 2011). Back in 1984 Rufli and Buchner (1984) showed in their study that dermal granulomatoes infiltrate round mites is represented mainly by T-helpers, thus supporting the hypothesis about the importance of the cell-mediated immune response in the pathogenesis of this disease.

ASPECT OF THE DISEASE

The source of demodocosis infection is a human being (patient or carrier) and pets. Mites are parasitic on dogs, horses and cattle. Demodocosis can be primary and proceed as independent disease as well as secondary as a result of already existed skin diseases (rosacea, perioral dermatitis, seborrheic dermatitis and etc.) (Fig. 1 and 2).

The main localization of mites is sebaceous glands of facial skin, ear auricles, back, chest, tarsal glands, skin follicles in nipples, rarely in the back (Akbulatova 1963). Atypical localizations where demodex can be found are penis, buttocks, ectopic sebaceous glands, mucous membrane of a mouth. Stcherbatchoff having found mites in ciliary follicles of a person's eyelids, proved the role of the mite in the development of blepharitis and blepharoconjunctivitis. Ethio-pathogenetic influence of mites in eyes diseases is great and now is described by many researchers (Whiting, 1993).



Fig. 1: a, b) Rosacea, complicated by demodex



Fig. 2: a, b) Acne, papulopustular form, complicated by demodex

The disease occurs suddenly. Subjectively, patients have feelings of itching, burning, crawling, fullness and heat. Pathological skin process is localized mainly in the T-zone of the face. Classic clinical manifestations of demodex infection is Pityriasis folliculorum; it is accompanied by feelings of itching and heat, skin becomes thinned taking a form of papyrus paper (Baima and Sticherling, 2002). Acne-form type is characterized by a predominance of papules on facial skin and the presence of papulopustular elements and diffuse erythema speaks for rosacea-like type (Baima and Sticherling, 2002). Clinical picture of Demodex gravis has similarity with granulomatous rosacea and also is characterized by the presence of granulomas in derma (Baima and Sticherling, 2002).

Interestingly, different types of mites cause various clinical picture which is presumably, connected with the sizes of mites. At detection of *Demodex folliculorum*, erythema and desquamation of epithelium is often observed, at detection of *Demodex brevis* symmetric papulopustular elements are observed (Akilov *et al.*, 2005).

At eye disease hyperkeratosis with scales on ciliary border and desquamation around eyelashes is marked. Patients complain of itching and feeling of a Foreign body in eyes (Kheirkhah *et al.*, 2007a, b; Lacey *et al.*, 2009).

In scientific literature there is an assumption concerning the role of demodex in the formation of androgenic alopecia (Mahe, 1998). Perhaps, the mechanism of alopecia is connected with the formation

of infiltration in hair follicle caused by Demodex mites. T-lymphocytes, activated by inflammation, induce synthesis of collagen which ultimately leads to fibroid degeneration of hair follicle (Whiting, 1993).

Prolonged chronic demodecosis is characterized by skin thickening, feeling of tightening, decreased skin elasticity and softness, presence of serous or sanious crusts. Secondary pyococcus infection is accompanied by the appearance of large pustules, nodular elements, macro abscesses which can lead to face disfiguration.

DIAGNOSIS OF DEMODECOSIS

Diagnosis of demodecosis can be performed by several methods. Laboratory diagnosis is the simplest method. During it the acarogram which is based on calculation of larvae, nymphs, eggs and imago is formed. It is possible to detect a mite on the damaged skin area at extraction of follicle content or at extraction of eyelashes or eyebrows without damaging hair follicles (Hom *et al.*, 2013). The studied material is placed on the glass slide with 10% alkali solution (glycerol is used in order to determine activity of mites), covered with glass slide and examined under low magnification microscope. It is recommended to add fluorescein color liquid into studied material for more accurate microscopic calculation of detected mites (Kheirkhah *et al.*, 2007a, b). Microscopic method is the only method for the detection of mites in hair follicles (Fig. 3).

The criterion of mites' activity is presence of >5 adult individuals, larvae and eggs per 1 cm². One mite on 2-4 eyelashes is considered to be the norm in the diagnosis of demodecosis of eyelashes.

The advantage of this methodology is the ability to analyze multiple lesions as well as removing mites not only from the surface of the skin but also directly from the sebaceous glands. Here is another problem it is not always possible to reach mites in the depth of sebaceous glands. In this regard, scraping is not a highly informative method and does not prove the absence of mites (Crawford *et al.*, 2004). The disadvantages of this method are epithelium trauma, examination of small scaled lesions, relative painfulness of the manipulation and discomfort after epilation.

To evaluate the carried-out therapy, repeated acarograms are made in order to count number of mites and determine their activity. If only waste products and empty egg shells are found in scraping, the repeated study is conducted because during the treatment demodex moves to zones which did not undergo acaricide treatment. In such cases, most commonly mites are located at the age of the scalp.



Fig. 3: Mites of Demodex genus, light microscopy

Another modified method of diagnostics is carrying-out surface biopsy ("scotch-test") (Crawford *et al.*, 2004). A drop of cyanoacrylate adhesives (BF-6, sulfacrylate) is placed on the degreased cover slide and then pasted on the affected area on 1 min. In the second, variant the scotch-tape is used (1cm² in size) which after removal is glued to the cover slide. At removal of cover slide or scotch-tape, the layer of epidermis, contents of sebaceous glands with available mites remain on their surface. Then, a solution of alkali is applied, covered over with cover slide and examined under a microscope at low magnification. In comparison, with direct microscopic examination, this method allows to diagnose demodecosis in most number of cases (Askin and Seckin, 2010). The advantage of this method is the conduction of this manipulation in any part of skin as well as its ease of use. Epithelium trauma, difficulty in obtaining material from nose wings, incomplete sterility of the received materials are the disadvantages of the method.

The more informative method of demodex diagnosis is skin biopsy with subsequent histology of the obtained materials. For this purpose, a small portion of skin is taken by puncture (punch) or excisional (scalpel) methods, then fixed in 10% neutral formalin solution, firmed with paraffin and stained with hematoxyline and eosin. Histological study has a lot of advantages. In particular, it is possible fully to see the sebaceous gland and surrounding areas. At retrospective pathomorphological study of scalp biopsies in 15% of cases there was a combination of demodecosis with fungal, inflammatory lesions, nevi and fibrosis (Karaman *et al.*, 2008). The main drawback of this method is skin trauma with the formation of a scar as well as inability to study a large skin area.



Fig. 4: Demodex mites, confocal laser scanning microscopy

As a diagnostic tool to identify demodex Segal *et al.* (2010) proposed to use a dermatoscope. Dermatoscope Method allows to visualize mites on skin surface as well as enlarged skin vessels (Whitfeld *et al.*, 2011; Segal *et al.*, 2010). Another non-invasive method of assessing the presence of demodex mites is the use of optical coherence tomography which allows to assess *in vivo* the condition of the patients' skin in two views (Maier *et al.*, 2012).

With the advent of confocal laser microscope a new method of patients' examination for the presence of mites has become available. Confocal laser scanning microscopy allows to visualize surface skin layers *in vivo* and get extensional four dimensional image. The advantage of this method is high informational content, noninvasiveness and therefore, the absence of discomfort for patients (Fig. 4).

TREATMENT OF DEMODECOSIS

Currently, standardized medical guidelines for the treatment of demodocosis do not exist. When choosing a therapy, a clinical picture of the disease, its severity and concomitant abnormality of the patient should be considered.

Until now for many years, the most effective drug in the treatment of Demodocosis has been metronidazole which is a derivative of nitroimidazole group (Patrizi *et al.*, 1997). Metronidazole has a pronounced anti-inflammatory (Persi and Rebora, 1985), antiedemic (Jansen and Plewig, 1996) and immunomodulatory effect. The standard treatment with metronidazole is 250 mg three times a day for 2-4 weeks.

Another drug of choice is ornidazole, prescribed by the scheme of 500 mg twice a day, treatment courses for 10 days. The medication has antiparasitic and bacteriostatic actions, increases activity of neutrophils, stimulates the adrenergic structures and enhances the reparative processes (Barnhorst *et al.*, 1996).

Outer therapy must also include antiparasitic means. Metronidazole ("Klion", "Metrogil") in the form of an ointment or gel 2% applied for 14 days is mostly common used. As an alternative therapy the benzyl benzoate ointment can be used (Baima and Sticherling, 2002; Beridze *et al.*, 2009).

In order to achieve the elimination of mites acaricide medications are administered. Permethrin from pharmacological group of pyrethroids, possessing antiparasitic effect has proved its efficiency (Forton and Seys, 1993). A small amount of ointment is applied a thin layer to the affected skin. The ointment is washed with water in 24 h. In most cases a single application is enough, but in case of ineffectiveness (the emergence of new elements of the rash, continuation of itching), the procedure is recommended to repeat after 14 days.

If there are papulopustular rash, classic reduction ointments and pastes should be assigned (zink-ichthyol ointment (Fulk and Clifford, 1990), 1-2% tar ointment and 1-2% ichthyol ointment, 1% ichthyol-resorcinol paste) (Junk *et al.*, 1998).

However, despite a successful therapy with classic means, resistant to therapy and relapsing forms of demodocosis are more and more frequent in practice of dermatologist. In this regard, new methods and treatment techniques are developing. For example, Beridze *et al.* (2009) recommends using a combined method of cryotherapy with "Rosamet" cream (metronidazole, 1%).

In case of acne form type of demodocosis or resistance to antiparasitic medications, it is expedient to use systemic retinoids (isotretinoin) at a dosage 0.1-0.5 mg kg⁻¹ of body weight per day for 2-4 months (Forton, 2012).

CONCLUSION

General preventive measures are observation of hygienic requirements, adequate and rational facial treatment, good nutrition and rest. It is important to use protective means against ultraviolet radiation as well as limiting sun exposure (Wang *et al.*, 2004).

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