THE IMPORTANCE OF DIFFERENTIAL DIAGNOSING IN TREATMENT OF MARGINAL BLEPHARITIS WITH DEMODEX ETIOLOGY

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Abstract. *Human Demodex mites play a significant role in the skin microbiome's evolutionary hierarchy, with their presence typically being harmless. However, human demodicosis, a unique skin disease, can resemble various inflammatory skin conditions, leading to confusion in medical literature. The proposal suggests categorizing demodicosis into primary and secondary forms, with primary demodicosis manifesting in different ways, such as spinulate demodicosis, papulopustular/nodulocystic demodicosis, ocular demodicosis, and auricular demodicosis. Secondary demodicosis is often linked to immunosuppression. Treatment approaches lack strong evidence, and the optimal acaricide concentrations are yet to be determined. Enhancing in vitro or ex vivo culture models is crucial for future research. The potential role of bacterial endosymbiosis with Demodex mites in demodicosis pathogenesis requires further investigation through clinical studies and experiments to validate the hypothesis.*

Keywords: *demodecosis, Demodex folliculorum, Demodex brevis, keratoconjunctivitis, blepharitis, Sociodemographic.*

INTRODUCTION

Demodecosis, the parasitic inflammatory disease of blepharon, partially margins and follicules, is caused by several types of microorganism that could symbiotic with human organism. To prove that, Human Demodex mites (Demodex folliculorum and Demodex brevis) hold a high rank in the evolutionary and phylogenetic hierarchy of the skin microbiome, although in most people their presence is of no consequence. While human demodicosis is a skin disease sui generis, it can mimic many other inflammatory dermatoses, such as folliculitis, rosacea and perioral dermatitis, leading to unspecific and confusing descriptions in the literature. Here, we propose to classify human demodicosis into a primary form and a secondary form, which is associated mainly with immunosuppression. The clinical manifestations of primary demodicosis may include (i) spinulate demodicosis, currently known as pityriasis folliculorum, involving sebaceous hair follicles without visible inflammation; (ii) papulopustular/nodulocystic or conglobate demodicosis with pronounced inflammation affecting most commonly the perioral and periorbital areas of the face; (iii) ocular demodicosis, inducing chronic blepharitis, chalazia or, less commonly, keratoconjunctivitis; and (iv) auricular demodicosis causing external otitis or myringitis. Secondary demodicosis is usually associated with systemic or local immunosuppression. Treatment is only weakly evidence based, and the most effective concentrations of acaricides remain to be determined. Optimization of an in vitro or ex vivo culture model is necessary for future studies. Endosymbiosis between certain bacteria and Demodex mites in the pathogenesis of demodicosis deserves more attention. Further clinical observations and experiments are needed to prove our hypothesis[1].

Despite the fact that the etiology of this disease is well-researched, the main problem ahead of medical staff would be differential diagnosing and treatment, especially in infants. The reason why differential diagnosing in treatment is one of main problems is that the clinical symptoms of ocular demadicosis resembles the symptoms of other inflammatory diseases of blepharon.

METHODS

There were performed several researches basing on information taken from PubMed, Google Scholar, MEDLINE, Scopus databases. The most relevant author`s articles were selected to clarify the significance of accuracy of diagnosing the marginal blepharitis linked to Demodex infestation in treatment. In addition to that, the research information clinical cases, gathered from 20 patients in Central Regional Policlinics in our own practice from 2021 to 2022, will be given below.

RESULTS AND DISCUSSION

One of the basic methods in diagnosing of Demodex caused Marginal blepharitis in young ages is microscopical learning of dermal scrapping samples taken from blepharons of patients. The diagnosis of demodicosis is mainly based on clinical evaluation and confirmed by microscopic detection of Demodexmites in epilated eyelashes. Thus, the clinical diagnosis is imprecise. Symptoms such as blepharitis, blepharoconjunctivitis, ocular rosacea, eyelash disorders, and chalazia may be suspicious for Demodexinfestation. CD is a reliable diagnostic sign.23 Under slit-lamp examination, CD has the appearance of solidified exudative excretions around the base of the eyelashes. Demodex detection can be easily performed by ophthalmologists or technicians. Briefly, two eyelashes with CD per eyelid are removed with fine forceps under a slit lamp. Sampling of eyelashes with CD is more likely to yield good results than random epilation.43 Under a light microscope, one drop of saline is applied with a pipette to the edge of the coverslip before examination. For those with retained CD, adding one drop of fluorescein solution, peanut oil, or 75% alcohol can help the embedded Demodex to migrate out. The biggest question is the cut-off number of mites detected. As Demodex mites can be found in asymptomatic populations, it remains unclear how many eyelashes should be sampled and how many mites are capable of inducing pathologic changes. Recently, in vivo confocal laser scanning microscopy (CLSM) has been used to detect Demodexinfestation.44 Demodex mites present as roundish or lengthy cone-shaped structures under CLSM. However, it is difficult to distinguish the two types of Demodex mites under CLSM in most cases. In addition, cooperation of the patient is highly required. Diagnosis of demodicosis in children is challenging, if not problematic, because of their poor cooperation during epilation. CD in children is not as obvious as that in adults. Furthermore, the Demodex count in children tends to be lower than that in adult patients,23 presumably because of the relatively shorter infestation period. Therefore, sampling of a much higher number of eyelashes in children than advised in adults may be warranted to establish the diagnosis of ocular demodicosis, especially when CD is not apparent. However, given that demodicosis is thought to be nil or very rare in the normal pediatric population,29 detection of any number of mites is significant[2]. Even if the express methods like ELISA, FISH has great popularity in diagnostics, those methods is not used because of its less informativeness comparing to microscopical research. Another research type that fulfills the data in diagnosing could be Sociodemographic data research. Sociodemographic data including age, sex, economic status, and general hygiene were noted. Medical history was noted for any previous treatment taken, duration of previous treatment, response to previous treatment, and current complaints. Complete ocular examination was done

including best corrected visual acuity, anterior segment examination noting the presence of blepharitis with or without cylindrical dandruff (CD), the presence of conjunctival inflammation, corneal signs with quadrant of corneal vascularization, laterality, opacities, thinning and infiltrate; lens status, presence of glaucoma, and retinal pathology were also noted.[3] When it comes to say about Anamnesis Morbi, it has great impact on proof diagnosing of any diseases, so the same situation in our case.

A single-center observation study from May 2021 to November 2022 was conducted by us in Regional Central Policlinics, Uzbekistan district, Ferghana region, Republic of Uzbekistan. According to the clinical researches of 20 patients (12 men, 8 women aged between 2-7.5 years old) with several clinical symptoms resembling blepharitis with other etiologies, such as bacteria, fungi, viruses.

Demographic and Clinical Characteristics ***Table-1***

Number	Age	Male	Symptoms
1	3.5	M	Itching, redness, tearing
2	7	F	Itching, Redness
3	5	M	Redness
4	3	F	Pain, blurred vision
5	4	F	Burning, Redness
6	2	F	Itching
7	5.5	M	Recurrent chalazia, Redness
8	3.5	M	Blurred vision, tearing
9	7.5	M	Tearing, Redness
10	4.5	M	Pain
11	2.5	M	Itching, Redness
12	3.5	F	Redness, tearing
13	4.2	M	Itching, Redness
14	4.5	F	Redness, Itching, tearing
15	5.5	M	Burning, Redness
16	7	F	Recurrent chalazia, Redness
17	6.5	M	Redness, Itching
18	3.5	F	Recurrent chalazia, Redness
19	2.5	M	Burning, Redness
20	4	M	Redness, Itching, tearing

According to the table chart above the most common symptoms are itching and redness which are common for othe inflammatory diseases of blepharon. The reason why I am trying to mention the symptoms is that there is no specific symptom to diagnose accurately Blepharodemadecosis and it pushes medical workers to use microscopical and microbiological methods, besides biomicroscopy of Anterior Chamber (AC) or another observation. Basing on the microscopical researches, there were found Human Demodex mites (Demodex folliculorum and Demodex brevis) via using Fluorescein. In treatment, massage of eyelids was provided via olive oil, Tetracyline or Erythromycine ointments for lubrication the eyes 2 times a day and Erythromycin tablets 30-50 mg/kg/day 2 times a day were prescribed. 18 of 20 patients was completely recovered from blepharodemadicosis, while 2 of them has recurrent form. In 2 weeks

the symptoms like itching, burning and redness were lost, when for blurred vision other medicaments were prescribed in order to balance the vision.

To compare with, Zhang, Nuan M.D.; Liu, Yan M.D.; et al. conducted another survey in South China among children aged 3-14 years old, they got result, where *Demodex* mites were detected in 189 of 1,575 (12.0%) children, including *Demodex folliculorum* (*D. folliculorum*) in 180 (11.4%), *Demodex brevis* (*D. brevis*) in 11 (0.7%), and both mites in 2 (0.1%). The median number of *D. folliculorum* mites was 1 (interquartile range [IQR], 1–2) and that of *D. brevis* was 1 (IQR, 1–1). Children with *Demodex* infestation did not exhibit more ocular discomfort than those without (21.2% vs. 23.1%; P=0.56). However, lash abnormalities, including trichiasis, cylindrical dandruff, or scaly discharge at the lash root, were more prevalent in children with *Demodex* infestation (24.9% vs. 12.8%; P<0.001) and in the 7 to 14-year subgroup (33.7% vs. 12.8%; P<0.001). Multiple logistic regression revealed that autumn–winter was associated with a higher detection rate of *Demodex* infestation (all P<0.05). In the 3-6-year subgroup, children residing in rural regions exhibited a higher prevalence of *Demodex* infestation (P=0.03)[4]. Moreover, according to the survey conducted by another group of scientists, there were mentioned that in pathogenesis of demodicosis, co-infection was also occurred with a bit severe sypmtoms counted above. For example, Demodex spp. infection is known for its coincidence with bacterial and fungal infections, as it can facilitate the transmission of other microbes to adjacent tissues or other people. Examples of co-infecting organisms and associated manifestations are summarized in Table 2.

Co-infecting organisms associated with demodicosis. ***Table 2***

Microorganism	Symptoms
Staphylococcus spp. (S. aureus, S. epidermidis)	blepharitis, conjunctivitis, cutaneous diseases
Streptococcus spp.	blepharitis
Bacillus oleronius	blepharitis, rosacea
Propionibacterium acnes (Cutibacterium acnes)	blepharitis, acne
Corynebacterium spp.	blepharitis
Funghi: - Microsporum canis (spores) - Trichophyton spp.	cutaneous diseases, dermatophytosis, dermatological disorders, pityriasis folliculorum

The studies of Liang et al., 2021 emphasize the participation of other microorganisms in eye infestations, especially bacteria, classifying them as co-pathogens of Demodex sp. such as Acinetobacter calcoaceticus, Novosphingobium, and the Anoxybacillus and Pseudomonas genera. It has been shown that in patients with demodicosis, the combination of anti-degenerative and antibacterial therapy often gave better results[5].

CONCLUSION

To conclude with, Human Demadecosis of Ocular surface in children with its various presentations poses a major challenge, especially with no specific symptom which makes this illness appearing like other inflammatory blepharitis.

Spreading awareness regarding this disease with its various clinical sypmtoms and just using light microscopy in diagnosing, may help in facilitating early presentation and treating with clear mind.

For future perspectives of this disease treatment, there could be found another possible ways of diagnostics that could save time and treat with high accuracy.

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