Association of Demodex Folliculorum in Acne/Rosacea and Folliculitis and the Efficacy of Combined Therapy (Metronidazole and Benzyl Benzoate)

Liana Manolache*

Cetatea Histria Polyclinic, Dermatology, Bucharest, Romania

Abstract: *Purpose*: The aim of the study was the evaluation of the role of Demodex infestation in acne/rosacea, folliculitis, perioral dermatitis.

Patients and Method: One hundred and forty-eight outpatients were enrolled and the direct microscopic examination of the lesions was done.

Results: 83% of patients were women. The mean age was 31.21 years (SD=14.2). 84% of patients had positive results for Demodex folliculorum. The presence of pets could be a risk for infestation, but 33% of patients had no contact with animals. Oral metronidazole for 10 days and a month of topical benzyl benzoate mixture (6.5%-12.5%) added with a metronidazole mixture had significant favorable effects. The treatment was repeated for another month. Negative microscopic exams were obtained after two months. There was a low risk of recurrence or re-infection.

Conclusion: Demodex folliculorum infestation has to be considered in resistant acne/folliculitis, in lower face and cervical acne lesions or in rosacea. It is important to clean the parasitic infection for a better effect of classical therapy of acne.

Keywords: Demodex, metronidazole, benzyl benzoate, acne, rosacea, folliculitis.

INTRODUCTION

Demodex mites (demodex folliculorum and demodex brevi) are common, spread in the pilosebaceous unit, especially on the human face. Their potential role is often underestimated or ignored [1-3]. Demodex mite is feeding with sebum [4]. A report from 1976 describes different habitats for the two types of Demodex (D. folliculorum in the hair follicles and D. brevis in the sebaceous glands). D. folliculorum was found aggregated and plugging the follicular orifices and D. brevis was usually solitary [5].

The highly infected sites by these mites are: forehead, area around the orbit, nose and mouth or chin. A survey in China mentioned a prevalence of Demodex infestation of 21, 2% of 565 urban and rural residents. Farmers and service employees showed a higher prevalence than other occupations [6].

Infection of the skin with D. folliculorum seems to appear more frequent among females, elderly people [6, 7], people with oily skin [6] or people with acne [6, 8].

METHOD AND PATIENTS

The study was conducted between June 2010 and June 2011 in Cetatea Histria Polyclinic in Bucharest. The polyclinic is attended by out-patients (both children and adults) from a large area of the city (around 500.000 inhabitants) and surroundings.

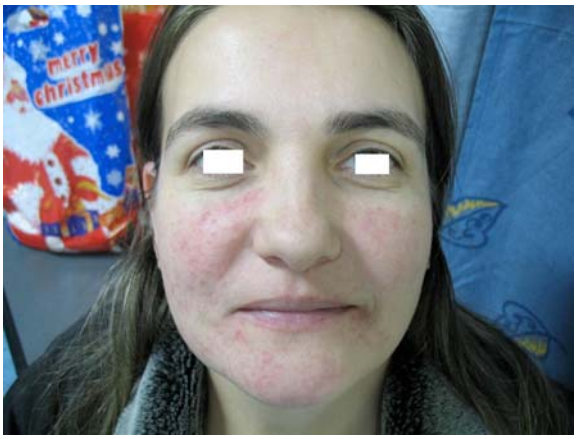

Figure 1: rosacea with demodex.

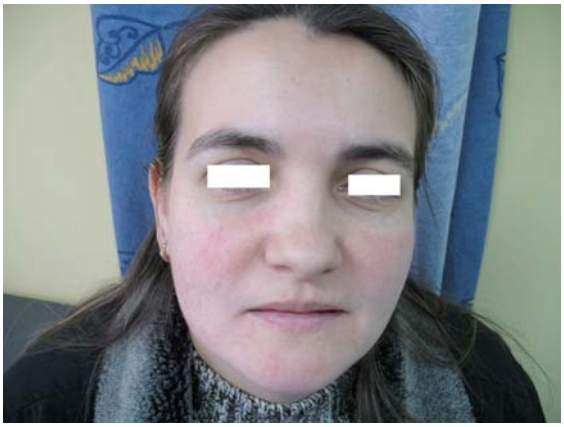

Figure 2: rosacea with demodex after six weeks of therapy.

*Address correspondence to this author at the Cetatea Histria Polyclinic, Dermatology, Bucharest, Romania; Tel: +40723227427; Fax: +40214135379; E-mail: lianamanolache@yahoo.com

E-ISSN: 2310-998X/14

There were included 148 patients with rosacea (papulo-pustular form) (Figures **1**, **2**), perioral dermatitis (Figure **3**), demodecidosis (Figures **4**, **5**), recurrent folliculitis with no result of oral antibiotics, recent episodes of acne in persons who had no acne before, some of them treated topically for a short time (a few weeks) with no improvement, resistant acne to usual therapy (at least 4 months of treatment), acne with lesions mostly in the lower part of the face and neck (Figure **6**).

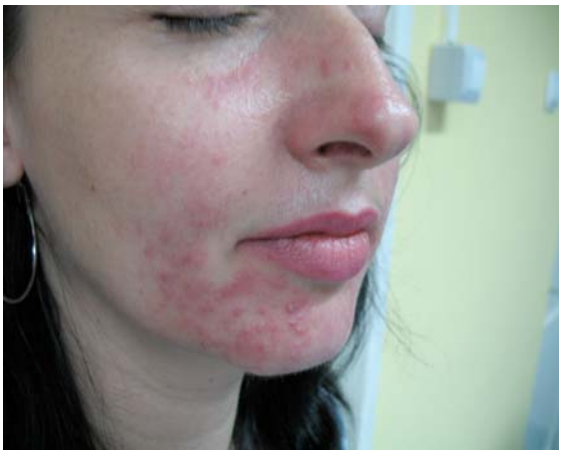

Figure 3: Perioral dermatitis with demodex.

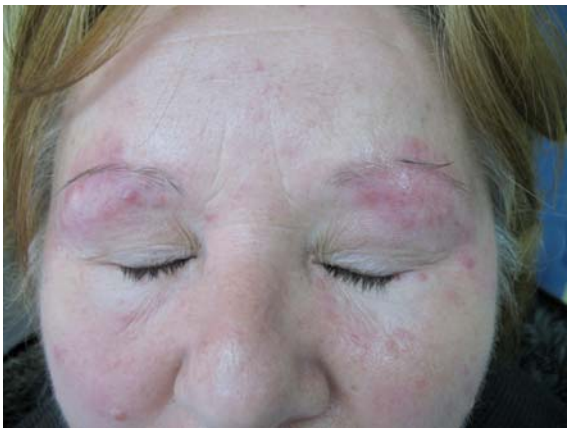

Figure 4: Demodecidosis.

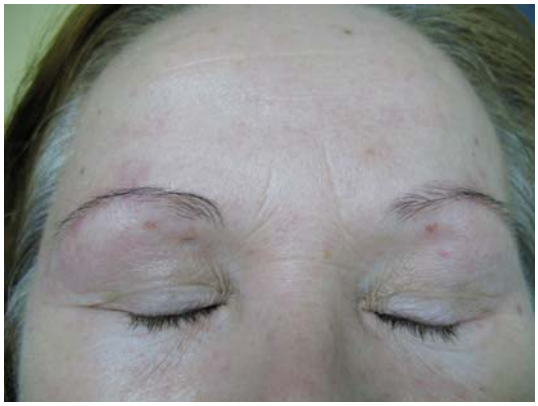

Figure 5: Demodecidosis after 6 weeks of therapy.

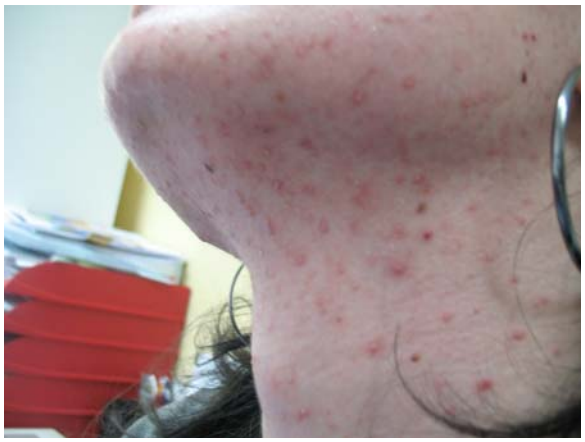

Figure 6: Acne of the lower part of face and neck, demodex present.

Direct microscopic examination was requested. There were also done additional bacterial cultures of the pustules and Helicobacter pylori antigen.

We started the treatment with oral metronidazole (250mg, 3 times per day for 10 days or 250mg, 2 times per day for 15 days). As topical therapy we added a combination of mixtures. First mixture was with benzyl benzoate (6.5%, 10% or 12.5%), for maximum 2 hours application. Then, there was an application of a mixture with metronidazole (2%) +/- clindamycin (2%) for the whole night. Clindamycin was added in the mixture only in patients who had other bacteria associated in the pustules (as appeared on antibiogram). The topical treatment was used for a month. If it was necessary, we have extended the same procedure for the next month. Most of the patients have come for the first control after a month. Thirty-eight patients (25%) have not come in the next two months. Some of them had another visit over a period of time with other skin problems.

We have to mention that oral Ivermectin is not approved yet in Romania for human usage, only for veterinary one, so, we could not take it in consideration.

RESULTS

In the clinical observation were included 123 women (83.1%) and 25 men (16.9%). The mean age of the group was 31.21 years (SD= 14.2), age ranged from 14 to 80 years old. Data regarding clinical and epidemiological aspects are presented in Table **1**. The acne patients (91cases) were as follows: recent lesions of acne (forehead, cheeks-49 patients, lower part of the face and neck-20 patients) in patients with no history of acne and with a self-administered topical treatment (a

Table 1: General Data about the Group

	Females	Males	Total
a. Age distribution			
1. 14-19 years old	18	3	14.2%
2. 20-29 years old	52	9	41.2%
3. 30-39 years old	28	5	22.3%
4. 40-49 years old	11	4	10.1%
5. 50- 59 years old	7	2	6.1%
6. > 60 years old	7	2	6.1%
b. Types of lesions			
1. rosacea (topical steroid induced)	23(9)	6 (2)	
2. folliculitis	3	5	
3. demodecidosis	3	0	
4. perioral dermatitis	15	2	
5. acne	79	12	
socio-professional data			
- pupil/student	44	7	34.5%
- high level	23	6	19.6%
- average level	40	9	33.1%
- low/housewife/ unemployed/retired	16	3	12.8%

few weeks) with no improvement, resistant acne at usual therapy (at least 4 months of treatment-7 patients) or acne episodes, long time after an oral isotretinoinum therapy (at least 1 year after – 13 patients).

In 124 patients (84%), Demodex folliculorum was found in direct microscopy examination. The rest did not make the examination and wanted a treatment without a confirmation. In a few cases there were some associations in the bacterial cultures of the pustules: 4 cases - Enterobacter, 3 cases -Staphylococcus aureus, 1 case- Proteus, 1 case - E.coli. In 5 cases there was also an infection with Helicobacter pylori. A lot of patients had pets at home (40 had dogs, 15 had cats, 3 had dogs and cats, 4 had guinea pigs). But, 49 patients (33%) had mentioned no contact with animals at all. The others could not deny the contact with pets (relatives, at job, etc).

In a month, from the patients coming for a control visit, only one got no improvement, the others had significant clinical changes. Less than 20% improved in 2-3 months. Besides the clearance of lesions, about 40% of patients had repeated the direct microscopic examination for Demodex. In 2-3 months they got a negative parasitologic exam. Only a few (5 cases) had positive results in 2 months, with absence of the parasite in 4 months, after an extension of topical treatment. Five patients had a recurrence in 3-6 months. One patient had a re-infestation after 1 year. 25% of patients did not come for a control in the next two months.

DISCUSSION AND CONCLUSION

The studies are showing that Demodex prevalence increases with age and Demodex appears in nearly all human adults [8]. There were papers on homogenous populations such as students and they revealed at least 30% rate of infection, with a higher prevalence for the students sharing washing materials with family members or living in a humid environment [9, 10]. Students aged over 18 years had 22.1 times higher odds of Demodex infestation compared to those under 16 years. Students aged 16-18 years also had 2.1 times higher odds compared to those aged 13-15 years [11]. Even higher scores are shown in a study on 2200 medical students, with a prevalence of Demodex in 51%, with the same tendency of increasing with age [12]. In their results, the males are more affected than females [12], contrary to other publications or our results [6, 7]. In Brasil, from 100 studied individuals, 72 had Demodex (51% D. folliculorum, 2% D. brevis and 19% both species) [13]. It seems to be a high prevalence of Demodex also among workers in hospitals (almost 75%) [14], in rural residents [6] and people sharing public toiletries [6]. In couples, only in 20% of cases there are both partners infested [6].

Sebaceous hyperplasia with oily or mixed skin seems to favor Demodex proliferation [8]. The prevalence was two times higher in oily skin than in dry skin (47% vs. 26%) [10]. For the mixed skin the prevalence was 34% [10].

Demodex mites could be examined through potassium hydroxide examination, skin biopsy or dermatoscopy [15, 16]. The new tool of dermatoscopy shows a specific picture consisting of Demodex "tails" and Demodex follicular openings. In patients with an inflammatory variant of demodecidosis, reticular horizontal dilated blood vessels were also visualized [16].

Demodex mites could be involved in pityriasis folliculorum, rosacea-like demodicosis, perioral dermatitis- like, folliculitis, acne vulgaris, seborrhoeic dermatitis, blepharitis, facial pruritus, demodecidosis gravis [8, 15, 17].

It was suggested that demodecidosis could be primary or secondary. The primary one is due to D. folliculorum causing an erythemato-squamos eruption in the facial T-zone. The eruption is itchy and has seasonal exacerbations. The secondary type is usually caused by D. brevis and appears as symmetrical malar papulopustular eruption, covering 30-40% of the face [18].

Students with a facial skin disease had 3.0 times higher odds of being infested with Demodex compared to those without cutaneous lesions [11]. Demodex acari were found in 42% of follicles with inflammation, but in just 10% of the ones without inflammation, Demodex being associated with histologic folliculitis (spongiosis and lympoid inflammation), even minor one [19, 20].

First mention of the association rosacea–demodex folliculorum was in 1952 [21]. Most of the reports are discussing the potential role of demodex in the pathogenesis of rosacea [22-25]. The prevalence of Demodex mites is much higher in subjects with previous history of blushes, facial pruritus, acne or rosacea [8, 10, 14]. The infestation varies from 38% up to 90% (controls from 10% to 27%) [26-30]. The prevalence was also higher in patients with rosacea comparing with allergic diseases, and especially for those over 20 years old [3]. Another study found higher rates of demodex prevalence in rosacea (38%) comparing with discoid lupus (21%) or actinic lichen planus (10%) [27].

The highly infested site was the cheek [31-33], than the area around the orbit, nose, chin and lastly area around the mouth [31]. Another study found forehead and than cheeks as most infested areas, with higher prevalence in males than in females [29]. A statistically significant increase in mites was found in all subgroups of rosacea, being most marked in those with steroid-induced rosacea [33].

Demodex folliculorum represents a significant cofactor that may contribute to the transition of the disease from a vascular to an inflammatory, papulopustular stage [22, 34]. This increased mite density may play a role in the pathophysiology of rosacea by triggering inflammatory or specific immune reactions, mechanically blocking the follicles, or acting as a vector for bacteria [35]. Antigenic proteins related to a bacterium (B. oleronius), isolated from a D. folliculorum mite, have the potential to stimulate an inflammatory response in patients with papulopustular rosacea [36]. Hair follicle infestation was associated with intense perifollicular infiltrate [29] of predominantly (90-95%) CD4 helper/inducer T cells [30]. There was observed an increased number of macrophages and Langerhans cells only in those subjects with a positive D. folliculorum finding. Immunohistochemical findings suggest that a delayed hypersensitivity reaction, possibly triggered by antigens of follicular origin, probably related to D. folliculorum, may occur, stimulating progression of the affection to the papulopustular stage [30]. Other mechanisms proposed for Demodex could result from mechanical blockage of follicles or by acting as vectors for microorganisms [33].

As for perioral dermatitis, the presence of Demodex varies from 27% [26] up to 58% [37]. Another observation refers to perioral dermatitis in patients who received previous topical steroid therapy. They had a significantly higher mite density, increasing with the length of treatment with topical steroids, suggesting the presence of Demodex as a secondary phenomenon due to steroids [38].

There are studies concluding that acne vulgaris is associated with Demodex infestation [8]. This indicates that when regular treatments for acne vulgaris are ineffective, examination of Demodex mites and necessary acaricidal therapies should be considered [8].

As regarding children, Demodex infestation is rare, mostly in those with leukemia or HIV-infection [39-41].

Papulovesicular rosacealike lesions and spiny blepharitis often respond to agents that reduce Demodex numbers [1]. The recommended treatment includes: systemic metronidazole [2], topical metronidazole [2], crotamiton [2, 43, 44], gamma benzene hexachloride [2], oral ivermectin [42-44], permethrin cream 5% [42, 43], hexachlorocyclohexane 0.25% [37]. There is one mention of the acaricidal activity of topical benzyl benzoate (BB) 10% [46]. There is a study of the *in vitro* effect of sodium dodecylbenzene sulfonate that

reports the killing of Demodex, being highly effective as treatment [47]. Another substance that seems to be safe and effective on Demodex is di-n-butyl phthalate-OP emulsion [48]. Freshly prepared camphor oil with or without glycerol dilutions gave complete cure with concentrations of 100%, 75% and 50% [49, 50]. Incomplete cure but marked drop in infestation density was achieved with diluted camphor oil at concentrations of 25-20%. Camphor oil application proved to be safe with no side effects [49].

The dosage used for oral ivermectin was 200 microg/kg [45]. Metronidazole was given orally for 500 mg daily for 15 days [50]. There is a study comparing the oral ivermectin to the combined therapy (ivermectin-metronidazole), showing a superior efficacy in decreasing the D. folliculorum count to the normal level in rosacea and in anterior blepharitis, but the same effect in in acne and perioral dermatitis lesions [44].

5% permethrine cream was applied twice daily for 15 to 30 days [51]. The treatment for permethrine cream was 7 weeks for rosacea and 5 weeks for perioral dermatitis [37]. There is a study showing that the effect of permethrin 5% cream on Demodex was superior to that of metronidazole 0.75% gel. The effect was mostly on erythema and papules and less on pustules [52, 53].

Our study could answer to the some of the questions of “what to do with resistant acne or folliculitis” and “what to do to neck acne lesions”. As Zhao *et al*. [8] concluded, we have to take in consideration first the cure of Demodex and then the classical individual approach of acne. The simple treatment with benzyl benzoate (BB), together with oral metronidazole is very efficient and there is only one mention of BB use in the literature. We consider that we have to keep in mind this possible Demodex infestation, especially for lesions located perioral, on the neck or in the inferior part of the face.

REFERENCES

[1] Elston DM. Demodex mites: facts and controversies. Clin Dermatol 2010; 28: 502-4. http://dx.doi.org/10.1016/j.clindermatol.2010.03.006

[2] Hsu CK, Hsu MM, Lee JY. Demodicosis: a clinicopathological study. J Am Acad Dermatol 2009; 60: 453-62. http://dx.doi.org/10.1016/j.jaad.2008.10.058

[3] Aycan OM, Otlu GH, Karaman U, Daldal N, Atambay M. Frequency of the appearance of Demodex sp. in various patient and age groups. Turkiye Parazitol Derg 2007; 31: 115-8.

[4] Saint-Léger D. Normal and pathologic sebaceous function. Research in a shallow milieu? Pathol Biol (Paris) 2003; 51: 275-8. http://dx.doi.org/10.1016/S0369-8114(03)00074-9

[5] Nutting WB, Green AC. Pathogenesis associated with hair follicle mites (Demodex spp.) in Australian Aborigines. Br J Dermatol 1976; 94: 307-12. http://dx.doi.org/10.1111/j.1365-2133.1976.tb04388.x

[6] Cui JH, Wang C. Facial Demodex infestation among urban and rural residents in Shangqiu City of Henan Province. Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi 2012; 30: 283-5.

[7] Wesołowska M, Baran W, Szepietowski J, Hirschberg L, Jankowski S. Demodicidosis in humans as a current problem in dermatology. Wiad Parazytol 2005; 51: 253-6.

[8] Zhao YE, Hu L, Wu LP, Ma JX. A meta-analysis of association between acne vulgaris and Demodex infestation. J Zhejiang Univ Sci B 2012; 13: 192-202. http://dx.doi.org/10.1631/jzus.B1100285

[9] Wang GY, Zhang YS. Investigation of Demodex infection among medical students. Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi 2006; 24: 156-7.

[10] Cao YS, You QX, Wang L, *et al*. Facial Demodex infection among college students in Tangshan. Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi 2009; 27: 271-3.

[11] Zhao YE, Guo N, Xun M, Xu JR, Wang M, Wang DL. Sociodemographic characteristics and risk factor analysis of Demodex infestation (Acari: Demodicidae). J Zhejiang Univ Sci B 2011; 12: 998-1007. http://dx.doi.org/10.1631/jzus.B1100079

[12] Hu Q, Wang Y. Investigation on the prevalence of human Demodex among 2,248 medical students in inner Mongolia. Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi 2001; 19: 239-40.

[13] Madeira NG, Sogayar MI. The prevalence of Demodex folliculorum and Demodex brevis in a population sample from Botucatu, São Paulo, Brazil. Rev Soc Bras Med Trop 1993; 26: 221-4. http://dx.doi.org/10.1590/S0037-86821993000400004

[14] Firat PY, Geçıt I, Depecık F, *et al*. Demodex spp. Positivity among Laboratory Staff, Kitchen Staff, Cleaning Workers and Nurses working in a State Hospital. Turkiye Parazitol Derg 2010; 34: 164-7. http://dx.doi.org/10.5152/tpd.2010.05

[15] Hsu CK, Hsu MM, Lee JY. Demodicosis: a clinicopathological study. J Am Acad Dermatol 2009; 60: 453-62. http://dx.doi.org/10.1016/j.jaad.2008.10.058

[16] Segal R, Mimouni D, Feuerman H, Pagovitz O, David M. Dermoscopy as a diagnostic tool in demodicidosis. Int J Dermatol 2010; 49: 1018-23. http://dx.doi.org/10.1111/j.1365-4632.2010.04495.x

[17] Karaman U, Celik T, Calik S, Sener S, Aydin NE, Daldal UN. Demodex spp. in hairy skin biopsy specimens. Turkiye Parazitol Derg 2008; 32: 343-5.

[18] Akilov OE, Butov YS, Mumcuoglu KY. A clinico-pathological approach to the classification of human demodicosis. J Dtsch Dermatol Ges 2005; 3: 607-14. http://dx.doi.org/10.1111/j.1610-0387.2005.05725.x

[19] Vollmer RT. Demodex-associated folliculitis. Am J Dermatopathol 1996; 18: 589-91. http://dx.doi.org/10.1097/00000372-199612000-00006

[20] Elston DM. Demodex mites: facts and controversies. Clin Dermatol 2010; 28: 502-4. http://dx.doi.org/10.1016/j.clindermatol.2010.03.006

[21] Brodie RC. Rosacea: the role of demodex folliculorum. Aust J Dermatol 1952; 1: 149-52. http://dx.doi.org/10.1111/j.1440-0960.1952.tb01419.x

[22] Lazaridou E, Giannopoulou C, Fotiadou C, Vakirlis E, Trigoni A, Ioannides D. The potential role of microorganisms in the development of rosacea. J Dtsch Dermatol Ges 2011; 9: 21-5. http://dx.doi.org/10.1111/j.1610-0387.2010.07513.x

[23] Zhao YE, Wu LP, Peng Y, Cheng H. Retrospective analysis of the association between Demodex infestation and rosacea. Arch Dermatol 2010; 146: 896-902.

[24] Preisz K, Kárpáti S. Rosacea: pathogenesis, clinical forms and therapy. Orv Hetil 2010; 151: 1209-14. http://dx.doi.org/10.1556/OH.2010.28885

[25] Mc Aleer MA, Lacey N, Powell FC. The pathophysiology of rosacea. G Ital Dermatol Venereol 2009; 144: 663-71.

[26] Raszeja-Kotelba B, Jenerowicz D, Izdebska JN, Bowszyc-Dmochowska M, Tomczak M, Dembińska M. Some aspects of the skin infestation by Demodex folliculorum. Wiad Parazytol 2004; 50: 41-54.

[27] Moravvej H, Dehghan-Mangabadi M, Abbasian MR, Meshkat-Razavi G. Association of rosacea with demodicosis. Arch Iran Med 2007; 10: 199-203.

[28] Sibenge S, Gawkrodger DJ. Rosacea: a study of clinical patterns, blood flow, and the role of Demodex folliculorum. J Am Acad Dermatol 1992; 26: 590-3. http://dx.doi.org/10.1016/0190-9622(92)70086-U

[29] Roihu T, Kariniemi AL. Demodex mites in acne rosacea. J Cutan Pathol 1998; 25: 550-2. http://dx.doi.org/10.1111/j.1600-0560.1998.tb01739.x

[30] Georgala S, Katoulis AC, Kylafis GD, Koumantaki-Mathioudaki E, Georgala C, Aroni K. Increased density of Demodex folliculorum and evidence of delayed hypersensitivity reaction in subjects with papulopustular rosacea. J Eur Acad Dermatol Venereol 2001; 15: 441-4. http://dx.doi.org/10.1046/j.1468-3083.2001.00331.x

[31] El-Shazly AM, Ghaneum BM, Morsy TA, Aaty HE. The pathogenesis of Demodex folliculorum (hair follicular mites) in females with and without rosacea. J Egypt Soc Parasitol 2001; 31: 867-75.

[32] Erbağci Z, Ozgöztaşi O. The significance of Demodex folliculorum density in rosacea. Int J Dermatol 1998; 37: 421-5. http://dx.doi.org/10.1046/j.1365-4362.1998.00218.x

[33] Bonnar E, Eustace P, Powell FC. The Demodex mite population in rosacea. J Am Acad Dermatol 1993; 28: 443-8. http://dx.doi.org/10.1016/0190-9622(93)70065-2

[34] Forton F, Seys B. Density of Demodex folliculorum in rosacea: a case-control study using standardized skin-surface biopsy. Br J Dermatol 1993; 128: 650-9. http://dx.doi.org/10.1111/j.1365-2133.1993.tb00261.x

[35] Powell FC. Rosacea and the pilosebaceous follicle. Cutis 2004; 74(Suppl): 32-4.

[36] Lacey N, Delaney S, Kavanagh K, Powell FC. Mite-related bacterial antigens stimulate inflammatory cells in rosacea. Br J Dermatol 2007; 157: 474-81. http://dx.doi.org/10.1111/j.1365-2133.2007.08028.x

[37] Rufli T, Mumcuoglu Y, Cajacob A, Büchner S. Demodex folliculorum: aetiopathogenesis and therapy of rosacea and perioral dermatitis (author's transl). Dermatologica 1981; 162: 12-26. http://dx.doi.org/10.1159/000250229

[38] Dolenc-Voljc M, Pohar M, Lunder T. Density of Demodex folliculorum in perioral dermatitis. Acta Derm Venereol 2005; 85: 211-5. http://dx.doi.org/10.1080/00015550510030069

[39] Patrizi A, Neri I, Chieregato C, Misciali M. Demodicidosis in immunocompetent young children: report of eight cases. Dermatology 1997; 195: 239-42. http://dx.doi.org/10.1159/000245951

[40] Barrio J, Lecona M, Hernanz JM, *et al*. Rosacea-like demodicosis in an HIV-positive child. Dermatology 1996; 192: 143-5. http://dx.doi.org/10.1159/000246341

[41] Benessahraoui M, Paratte F, Plouvier E, Humbert P, Aubin F. Demodicidosis in a child with xantholeukaemia associated with type 1 neurofibromatosis. Eur J Dermatol 2003; 13: 311-2.

[42] Allen KJ, Davis CL, Billings SD, Mousdicas N. Recalcitrant papulopustular rosacea in an immunocompetent patient responding to combination therapy with oral ivermectin and topical permethrin. Cutis 2007; 80: 149-51.

[43] Rebora A. The management of rosacea. Am J Clin Dermatol 2002; 3: 489-96. http://dx.doi.org/10.2165/00128071-200203070-00005

[44] Salem DA, El-Shazly A, Nabih N, El-Bayoumy Y, Saleh S. Evaluation of the efficacy of oral ivermectin in comparison with ivermectin-metronidazole combined therapy in the treatment of ocular and skin lesions of Demodex folliculorum. Int J Infect Dis 2013; 17: e343-7. http://dx.doi.org/10.1016/j.ijid.2012.11.022

[45] Abd-El-Al AM, Bayoumy AM, Abou Salem EA. A study on Demodex folliculorum in rosacea. J Egypt Soc Parasitol 1997; 27: 183-95.

[46] Forton F, Seys B, Marchal JL, Song AM. Demodex folliculorum and topical treatment: acaricidal action evaluated by standardized skin surface biopsy. Br J Dermatol 1998; 138: 461-6. http://dx.doi.org/10.1046/j.1365-2133.1998.02125.x

[47] Zang Y, Wu DJ, Song JB. Experimental and clinical studies on the effect of sodium dodecylbenzene sulfonate in *in vitro* killing Demodex and in treating demodicidosis. Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi 2005; 23: 221-4.

[48] Xia H, Hu SF, Ma WJ, Ge JH. Studies of di-n-butyl phthalate-OP emulsion in the treatment of demodicidosis. Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi 2004; 22: 248-9.

[49] Morsy TA, Morsy GH, Sanad EM. Eucalyptus globulus (camphor oil) in the treatment of human demodicidosis. J Egypt Soc Parasitol 2002; 32: 797-803.

[50] El-Shazly AM, Hassan AA, Soliman M, Morsy GH, Morsy TA. Treatment of human Demodex folliculorum by camphor oil and metronidazole. J Egypt Soc Parasitol 2004; 34: 107-16.

[51] Karincaoglu Y, Bayram N, Aycan O, Esrefoglu M. The clinical importance of demodex folliculorum presenting with nonspecific facial signs and symptoms. J Dermatol 2004; 31: 618-26.

[52] Koçak M, Yağli S, Vahapoğlu G, Ekşioğlu M. Permethrin 5% cream versus metronidazole 0.75% gel for the treatment of papulopustular rosacea. A randomized double-blind placebo-controlled study. Dermatology 2002; 205: 265-70. http://dx.doi.org/10.1159/000065849

[53] Swenor ME. Is permethrin 5% cream effective for rosacea? J Fam Pract 2003; 52: 183-4.

Received on 13-11-2013 Accepted on 13-12-2013 Published on 05-03-2014

DOI: http://dx.doi.org/10.12970/2310-998X.2014.02.01.3