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Psychodermatology of acne: Dermatologist's guide to inner side of acne and management approach

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Abstract

Acne vulgaris (AV) is a skin disease that is commonly seen and causes scar formation especially when left untreated. It can cause serious psychological comorbidities due to the intense involvement of appeared areas such as face and also being common in adolescence in which the body perception is not yet well established. Although psychiatric comorbidities frequently accompany AV patients in dermatology, they almost never directed to dermatology-psychiatry liaison clinics. Depression, anxiety, stress, decreased self-esteem, suicidal thoughts and even suicide attempts are too frequent to ignore in these patients, and many studies have been conducted on the positive or controversial effects of acne treatments. For this reason, serious responsibilities fall to dermatologists. They should not treat AV lesions only, but also to determine the AV patients' psychological conditions and to direct them to get help when necessary.

KEYWORDS

acne vulgaris, anxiety, depression, psychodermatology, stress

1 | INTRODUCTION

Acne Vulgaris (AV) is a chronic inflammatory disease of the pilosebaceous unit that is common in both young and adult, and can result in scar formation when left untreated. Many lesions such as, comedones, papules, pustules, nodules, and cysts can be seen together in patients, as well as causing scarring and pigmentation changes. AV may be associated with much physiological and psychological comorbidity in patients.¹

Quality of life is also frequently affected in AV. In these patients, to reveal one's social life and psychological state, many different indexes have been developed such as "Cardiff Acne Disability Index", "Acne Quality of Life", "Assessment of the Psychological and Social Effects of Acne".² In studies conducted with these indexes, it has been shown that the quality of life decreases in AV patients, especially in women, patients under 18 years of age, who had facial involvement, scarring and severe disease.³ However, regardless of these situations, it has been shown in many studies that the quality of life in AV patients has decreased.²

1.1 | Prevalence

In "The Global Burden of Disease" study conducted between 1990 and 2010, which investigated the most common diseases causing disability, AV was identified as the eighth most common disease in the world.⁴ Considering all ages, its prevalence is 9.38%. This rate was found to be 8.96% in men and 9.81% in women.⁴ Considering the studies conducted with school children and adolescents in different countries, a very high prevalence was reported between 47.3% to 96%.⁵ Although it can be seen at almost any age, it is more common in the age range of 12 to 24, and moderate to severe AV is seen in 15% to 20% of cases in this age range.⁶ Compared to the years spent with the disease, AV has been accepted as the skin disease that constitutes the longest period after eczema.⁴

2 | PSYCHOPHYSIOLOGY

AV patients can face many conditions such as anxiety, depression, anger, weak body perception, loss of self-confidence, social isolation, and activation restriction, because they are often at a sexually critical

social age and the presence of lesions in visible areas such as the face.^{7,8}

Exposomes are the sum of both environmental and intrinsic factors that a person is exposed to from the mother's womb to death.⁹ Intrinsic factors are one's own characteristics and are personal. These factors may be the physiology, age, body morphology, and genetics of the person. Gender and stress related hormones are also included in these. Acne exposomes are defined as the sum of all environmental factors that affect the formation, severity, and duration of AV. However, it would not be wrong to add internal factors to these factors. Psychosocial and lifestyle related factors such as stress, emotions and insomnia, and modern lifestyle are known to be effective in inflammatory diseases. Food among exposomes, air pollution, stress, heavy skin cleansing, climate, sun and insomnia have been associated with AV.¹⁰ However, since the relationship between exposomes and AV is mostly uncontrolled case series and anecdotal observations, more evidence is needed. One of the most investigated among these exposomes with AV is stress.

3 | ACNE AND STRESS

Stress is a factor that threatens the physical, social and mental balance of the person.¹¹ Exposure to stress is perceived by the central nervous system and activates the hypothalamic-pituitary-adrenal [HPA] system. Several neurotransmitters are released and the autonomic nervous system is activated, causing peripheral responses in a number of organs, including the skin. Some immune cells, hormones and neurotransmitters in the skin are activated. Immune cells cause a number of pro-inflammatory or anti-inflammatory responses on the skin.¹¹ In addition, the release of corticotropin-releasing hormone, glucocorticoids and adrenal androgens increases.¹² This situation increases the conversion of androgen precursors to testosterone and decreases the permeability of the skin while increasing the sebaceous hyperplasia.¹³ It also decreases the body's antimicrobial resistance. It accelerates the formation of AV in this way (Figure 1).^{12,14}

Stress is known to increase eating, especially for women, to relax. On the other hand, changes in obesity increase the insulin synthesis and cause tendency to differentiation of sebocytes, toll-like expression, and inflammation and hence acne by increasing the level of leptin.¹⁵ Acne excorie caused by excoriations and tearing the lesions is more common in stressed individuals.

Brain - derived neurotrophic factor (BDNF) signals are thought to be related to factors such as stress. In a study on BDNF signals in patients with AV, BDNF levels in the blood were found to be significantly lower than the control group. The authors attributed this result to that stress can have an effect on both the aggravation and pathogenesis of AV disease.⁸

Most of the patients state that AV lesions increase during their stressful periods. In a study conducted with 4676 patients, 55% of patients reported that the disease exacerbated 2 days after the emotional stress episodes.¹⁶ In a study conducted with 1236 diseases in Korea, even if 43% of patients were severe, 7.6% were mild, all of

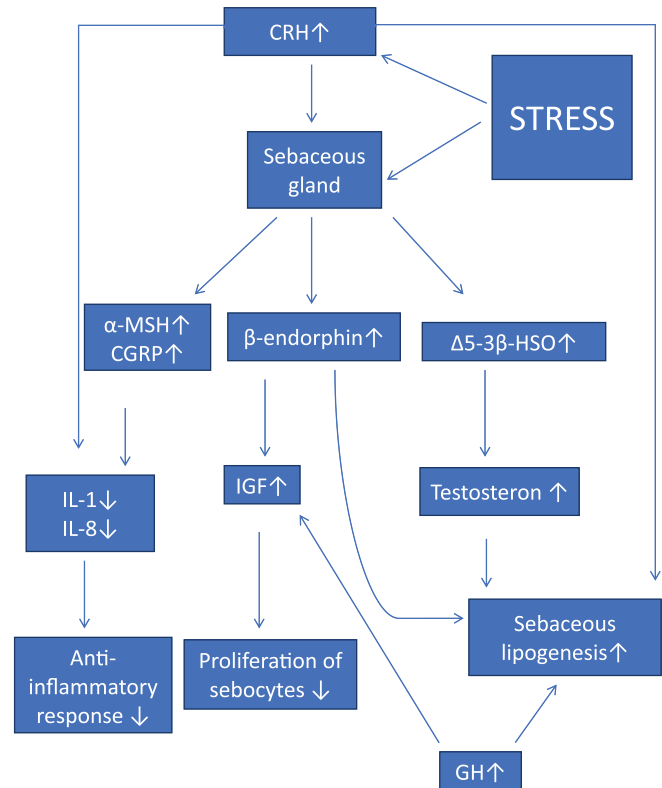


FIGURE 1 Effect of stress on acne formation.^{12,14} Stress contributes to the formation of acne both by increasing corticotropin releasing hormone (CRH) and growth hormone (GH) by directly affecting sebaceous glands. Stress stimulation increases the binding of α -melanocyte-stimulating hormone (α -MSH), calcitonin gene-related peptide (CGRP), β -endorphin receptors, decreases α -MSH and CGRP interleukin (IL) 1 and IL8 levels within the cell, increase of GH and increase of β -endorphin response stimulates Insulin like growth factor (IGF) and sebocyte proliferation decreases. In addition, Testosterone formation increases from dihydrotestosterone with activation of 3β -hydroxysteroid dehydrogenase/ Δ^{5-4} isomerase ($\Delta^5-3\beta$ -HSD) enzyme. Increased β -endorphin, GH, testosterone and CRH increase sebaceous lipogenesis. Acne lesions occur as a result of these conditions

them reported that they felt stress due to AV disease.¹⁷ 82% of the same patient group stated that when they felt emotional stress, their lesions increased.¹⁷ In other studies, 50% to 80% of patients reported that psychological stress increased acne lesions.^{18,19}

The relationship between AV and stress can be considered as a vicious circle of a chicken and egg situation. However, whether there is an increase in AV or the presence of AV stresses the patients out, it cannot be ignored that there is a strong relationship between them.

4 | ACNE AND DEPRESSION

Many studies have been conducted on the relationship between acne and depression. The vast majority of them said that the prevalence of depression increased in acne patients, while a few reported no

association.^{20,21} Depression has been reported in 5.6% to 8.8% of patients with AV.²⁰ Compared to the general population, the rate of depression in AV patients was found to be 2 to 3 times higher.²² Various scales such as Beck depression scale, The Patient Health Questionnaire depression module, Hamilton depression scale are used to measure the depression of the patients. Whether people have depression or the severity of depression can be measured with these scales.²³ In a meta-analysis in which 42 studies were investigated, both adolescents and adult patients were compared with their non-AV peers, the incidence of depression was observed to increase in AV patients.²³ This rate was found as higher in adult patients.²³ The authors attributed this to feeling different from other non-AV adults and considering the acne as a sociocultural puberty problem. However, it is also true that the adults with acne who have admitted to the hospital have more dissatisfaction with their diseases.²³

Considering the gender differences, it has been reported that depression is approximately twice as common in women with AV than men with AV.²⁰ Considering the geographical differences, it was observed that depression and anxiety due to AV were higher in the Middle East than in other regions of the world.²⁴ However, it is also known that depression is more common in the general population in these regions.²⁵

There are claims that systemic isotretinoin used in treatment of AV patients also causes depression. Later, retrospective studies supporting this situation were conducted. However, no relationship was found in prospective studies between isotretinoin and depression and even an improvement in depression scores was observed.²⁶

5 | ACNE AND ANXIETY

The association of AV with anxiety also attracts attention. In the studies conducted, the presence of anxiety in patients with AV was reported at quite variable rates such as 4.35% to 68.3%, but was found higher than the control groups.^{21,27} Scales such as hospital anxiety scale, mental health inventory were used in these studies.

Especially in women, for those the disease started early, those who had the disease for a long time and those who had a severe disease, anxiety was more common, but no significant difference was found between races. In general, anxiety is reported to be more common in female gender and adolescents.²⁸ This may be due to hormonal factors, and being the social acceptance and views are more important. Some studies have shown that anxiety increases in severe AV. In some studies conducted with adolescents, although anxiety is seem to be more in girls, no relationship was found between the severity of the disease and anxiety in both genders.²⁹ In a study conducted in India, the presence and severity of anxiety was not associated with age, gender, marital status, scar formation. However, the authors reported that anxiety was observed when different body perception occurred in individuals.³⁰ They explained this situation as perceiving a small lesion on the face of the person as too large.

In the meta-analysis study conducted by Samuels et al, it was observed that AV patients were more anxious than the control groups

with their peers in both adult and adolescent patients, as in depression. As with depression, anxiety was found to be more common in adults and was associated with AV.^{23,29,30}

6 | ACNE AND LOW SELF ESTEEM

Self-esteem can be explained as the value the person gives to and how treats oneself.³¹ With social media getting more into our lives, people have started to pay more attention to their appearance. This situation may pose a more serious problem especially in adolescents, where AV is also common and who use social media more frequently. Low self-esteem may coexist with conditions such as anxiety and depression. People with low self-esteem are those who have negative feelings towards themselves, are not proud of themselves, feel useless and worthless.

It has been observed that changes in the person's appearance play an important role in AV-related self-esteem. Acne lesions may increase suddenly or change appearance, which may be a difficult situation for patients to cope with. Both adolescents and young adults (18-25 years old) want to prove themselves in many different areas of life, such as the discovery of one's own identity and lifestyle and educational arrangements, and demographic changes.³² A number of changes that may occur on the face during this period can push the person towards social isolation and decrease self-esteem.

In studies conducted with adolescents, both male and female AV patients had lower self-esteem than control groups.³¹ However, in studies conducted with university students, no significant difference was observed in both men and women.³³ It has been observed that self-esteem increases after chemical peeling for both those with AV and rosacea for the purpose of treatment or for cosmetic reasons such as wrinkles, hyperpigmentation.³⁴ The authors attributed the improvement of person's skin and body image with increased self-esteem.³⁴ In a study conducted on patients with AV, it was shown that self-esteem decreased with increasing anxiety and decreasing quality of life, but it was not found different from the control group.³⁵ In a study involving 3775 students aged 18 from Norway, Germany and the United States of America, 25% of female and 13% of men patients with AV stated that they felt worthless. Patients in both genders with AV indicate that they feel less worthless than the control groups, while this is more evident in female patients.³¹

7 | ACNE AND SELF HARM/SUICIDAL THOUGHTS

AV may cause lower self-harm and suicidal tendency in individuals. Although rare, AV can be seen together with mental diseases such as psychosis, which will give suicidal tendency. Also, the presence of scars, the way acne is involved and its severity can contribute to suicidal thoughts.

Extra caution is required in diseases such as AV, psoriasis, atopic dermatitis, malignant melanoma, which can progress with high anxiety and depression.³⁶ When depression or suicidal tendency is suspected

in the routine examinations of the patients, an opinion can be formed about whether a person has suicidal ideation by applying Patient Health Questionnaire-2³⁷ (Table 1).

Table 1: Patient Health Questionnaire-2 questions and scoring conducted to reveal the tendency to depression and suicide in individuals.³⁷

Compared to other face-involved diseases such as rosacea, perioral dermatitis; anxiety, depression, and suicidal ideation were mostly detected in AV patients.³⁸ In a study of 213 AV patients including 13 European countries, 40.6% of the patients stated that they had discomfort related to the disease. In 12.3% of these patients stated that they had suicidal ideation and 4% said that suicidal ideation was related to AV disease.²⁸ Anxiety was seen three times more in those with suicidal thoughts, while the frequency of depression did not increase.³⁹ In a study conducted with school children between the ages of 12-18 years, suicidal ideation was 23.6% in all children; suicide attempt in the last year was 7.8%, while this rate was 34% and 13% in those with AV, respectively. Again, in this study, no relation was found between anxiety and depression and suicide attempt.⁴⁰ Although anxiety and depression are under control, suicidal thoughts related to AV can continue. This situation suggests that AV creates a tendency to suicide in other ways than affective disorder. The feeling of anger, loss of self-esteem and presence of social isolation may also affect suicidal tendencies in those with AV.⁴⁰

Isotretinoin treatment is one of the most successful treatments frequently used in acne patients. There are ongoing debates about whether isotretinoin has an effect on individuals' suicidal tendency. The first suicide case in which isotretinoin was accused was reported in May 2000 in a 17-year-old boy, and then dozens of case reports were published.⁴¹ It has been reported that the cause of death was suicide in 10 of the 12 cases who died while using isotretinoin in the UK in 2019. In a systematic review comparing antibiotic users and isotretinoin users, no difference was found between the two groups in terms of depression and suicide attempt.³⁹ In a French study of 328 018 people, no increased suicide attempt or suicide-related death in those using isotretinoin was seen.⁴² Successful treatment of AV also improves depression, anxiety and quality of life in individuals; therefore, some of the authors

suggest the opposite and suggest that the psychological condition is improved in those receiving isotretinoin treatment. We did not find suicide attempts during treatment period in any of our patients, for whom we prescribed hundreds of isotretinoin treatments. Due to contradictory publications, patients should be questioned for psychiatric disorders before and during treatment in all patients for whom isotretinoin is prescribed. In the presence of depression and anxiety development noticed in the patient, the dose of the drug should be reduced and the patient should be directed to psychiatry.⁴¹

7.1 | AV and other psychiatric diseases

It has been reported that mental illnesses such as psychosis and obsessive compulsive disease can also be associated with acne. In a 17-year-old patient using isotretinoin, the psychotic attack, which could not be attributed to any other cause, resolved 2 weeks after discontinuation of the drug and antipsychotic treatment.⁴³ There are several reports of psychosis associated with isotretinoin use in the literature, but this has not been reported in large series.

No difference was found in terms of alcohol and substance dependence between those who had been followed up for 23 years after birth with AV and those without.⁴³

In a study conducted in Spain, it was found that body dysmorphic syndrome was more common in AV patients. In the study using Body Dysmorphic Disorder Questionnaire, this disorder was more common in female patients and patients with inflammatory lesions. People are particularly concerned about their faces, and this takes at least 2 hours a day.⁴⁴ In a study conducted with patients with severe acne, 13% of cases had obsessive compulsive personality disorder.⁴⁵ In patients with body dysmorphic disorder, looking in the mirror is often seen as a compulsion. Psychogenic excoriations can be seen in 2% of dermatology patients, and one example of this is acne excoriee des jeunes filles patients who excoriate acne lesions. These patients may have comorbidities as obsessive compulsive behavior.⁴⁶

TABLE 1 Patient Health Questionnaire-2³⁷

How often have you been bothered with the followings, over the past 2 weeks?			
I have little interest or pleasure in doing things			
Not at all 0 point	Several days 1 point	More than half the day 2 points	Nearly every day 3 points
I am feeling down, depressed, or hopeless			
Not at all 0 point	Several days 1 point	More than half the day 2 points	Nearly every day 3 points
Total points < 3		Total points ≥ 3 ask the followings	
No need to ask questions on suicidal ideation		Do you ever think about ending your own life?	
Repeat the questionnaire at future visits		Do you have a current plan to commit suicide?	
		If first answer is positive but the second is negative;	
		• Urgently refer to family physician	
		If both answers are positive;	
		• Patient needs immediate support of a psychiatrist, refer to emergency department, better to accompany the patient.	
		If both answers are negative;	
		• Refer the patient to family physician but without emergency	
All of the risk factors, answers and recommendations should be documented in the medical records of the patients			

AV may be associated with eating disorders such as anorexia nervosa and bulimia, which is a serious problem with body image in some patients.⁴⁷ In a 14-year retrospective study, attention deficit and hyperactivity disorder were more common in AV patients compared to other dermatological diseases.⁴⁸

8 | MANAGEMENT APPROACH

Medical treatment in patients with AV improves the appearance and lesions of the person and also provides improvement of comorbidities such as depression and anxiety. Successful treatment of acne lesions can improve the depression and anxiety scores associated with AV without any psychiatric treatment. Posttreatment anxiety scores were found to be lower in patients using doxycycline compared to pretreatment.⁴⁹ There are studies showing that systemic isotretinoin use improves comorbidities such as depression and anxiety in patients.⁵⁰

Studies comparing the results of life quality index after medical treatments in AV before and after treatment were conducted. It has been shown that applying combination of adapalene 0.1%, benzoyl peroxide 2.5% and clindamycin 1.2%, erythromycin 3% and benzoyl peroxide 5%, 5% benzoyl peroxide alone, clindamycin gel alone, adapalene 0.1% and clindamycin 1% once or twice a day provides an improvement of at least 40% in quality of life indices.⁵¹ Systemic use of oral isotretinoin 0.5-1 mg/kg/day, minocycline 100 mg/day, tetracycline 500 mg/day and topical adapalene 2 times a day, oral contraceptive use containing Norethindrone acetate/ethinyl estradiol and low-dose phasic ethinyl estradiol provided a minimum improvement of 40% in quality of life indices.⁵¹ In treatment comparisons, use of isotretinoin 1 mg/kg/day for 16 weeks showed significant changes in quality of life indices compared to placebo.⁵² However, when patients using 1 mg/kg/day systemic isotretinoin and patients using 500 mg tetracycline and topical adapalene twice daily are compared, a significant improvement in quality of life was observed in both groups, but no difference was observed between the two groups.⁵³ In another study comparing oral antibiotics and isotretinoin, isotretinoin improved the quality of life indices significantly.⁵⁴ In a study in which the systemic isotretinoin was compared with the combination of topical antibiotics and retinoids, there was a positive difference in the subjects who received topical treatment in the second and fourth months of the scores.⁵⁵ This may be due to the discomfort caused by the side effects seen while using systemic isotretinoin.

While treating patients with AV, not only pharmacological treatment, but also triggering factors such as stress and reducing the accompanying psychological factors should be planned. In addition to the dermatological findings before the treatment, it is important to make a general evaluation and to question the patients in terms of depression and anxiety. It will also be useful to apply Patient Health Questionnaire-2 in individuals with a predisposition to understand suicidal tendency.

Weight control should be provided in patients with obesity; patients should be directed in this respect and should be directed to healthy nutrition by reducing the foods that can trigger acne.

Achieving weight control in patients who eat healthy and exercise regularly also decreases the stress level, leading to a decrease in acne severity. It can also prevent the excoriations that are more common in stressful people. Providing sleep order and improving its quality is also beneficial for stress control.

It is known that scar formation increases depression and anxiety. Therefore, it is very important to start treating the patient before the scar formation. Considering both the clinical and psychological status of the patient, appropriate treatment should be selected and lesion removal should be avoided. In addition, it is important to explain to the society that AV is a disease that occurs in adolescence and will not heal on its own.

9 | ROLE OF DERMATOLOGY-PSYCHIATRY LIAISON CLINICS

Psychodermatological diseases include skin diseases with psychosomatic and behavioral aspects. They are examined in two main groups: I. Coexistence of psychiatric diseases with skin diseases II. Skin diseases that are triggered by stress and can coexist with a wide range of psychiatric disorders.⁵⁶ Acne excorie is included in the second group of diseases.⁵⁶ However, even if there are no excoriations, standard AV patients should also be considered as psychodermatological patients.

Dermatology-Psychiatry Liaison clinics are clinics in which dermatology and psychiatry work together, which deal with psychodermatological diseases and other dermatological diseases that may have psychological effects. Patients with diseases such as psoriasis, urticaria, prurigo, chronic itching are often directed to these clinics and AV, which is often associated with psychiatric disorders, is ignored.⁵⁷ It is noteworthy that patients with acne excorie, which is considered a psychocutaneous disease rather than standard acne patients, are intense.⁵⁷

Cognitive behavioral therapy is a successful method of treatment in many cases such as somatoform disorders, stress, depression and anxiety. It has been found beneficial both in decreasing depression and anxiety levels and treatment duration in acne excorie patients in a period of 2 months.⁵⁶

The use of psychiatric drugs such as antidepressants is useful in the treatment of conditions such as depression accompanying AV.⁵⁸ Reducing anxiety of people and treating their depressions increase compliance with medical treatment for acne lesions.

Therefore, in AV patients, for whom the relationship with anxiety and depression is well known, these situations should be revealed with standard questionnaires and one should not hesitate to refer to Dermatology-Psychiatry Liaison clinics if necessary.

10 | CONCLUSION

Physicians usually conduct psychological assessment if the person has a remarkable psychological impact or if the disease is considered too

severe. However, there may be serious differences between how the patient perceives the illness and how the physician perceives the patient. For this reason, it is important to listen to the patients without judgment, to examine the disease as a whole and to examine it in all aspects as much as possible. Acne is one of the most common skin diseases, and patients have frequent and serious association of depression, anxiety, decreased self-esteem, suicidal ideation and even suicide attempts. Dermatologists are primarily responsible for these patients to receive the necessary support.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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