Significance of Autoantibody Detection in the Diagnosis of Facial Dermatitis

Xiaofang Zhou[a], Xiangfen Deng[b], Hongzhi Gu[c], Yan Xiao[d], Ling Li[e], Zhiqiang Song[f], Zhifang Zhai[g] and Huan Wang[h,*]

Department of Dermatology, First Affiliated Hospital of Army Military Medical University, 400038, Chongqing, China

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Abstract: To explore the significance of autoantibody detection in the diagnosis and differential diagnosis of facial dermatitis, the results of autoantibody detection in 57 patients with "facial dermatitis" who were first diagnosed in our outpatient department from July 2019 to March 2021 were retrospectively analyzed in this paper. It is found that autoantibody detection is of great significance in the diagnosis and differential diagnosis of facial dermatitis in patients with facial dermatitis, which can avoid missed diagnosis and contribute to the early diagnosis of connective tissue disease.

1 INTRODUCTION

Facial dermatitis is the most common disease in dermatology. It has a variety of clinical manifestations, a long course of disease and many complicated pathogenic factors. These features have a certain impact on the diagnosis and follow-up treatment of patients. In severe cases, facial dermatitis may affect life and work. Because the causes of facial dermatitis are complex. They may related with patients' living environment, such as ultraviolet light, and their use of cosmetics, medicine, their anxiety and depression. Besides, it may also occur on the basis of other diseases, leading to misdiagnosis. For example, it is reported that of systemic lupus erythematosus (sle) may initially misdiagnosed as facial dermatitis (Chen, Tu, Yan, et al. 2018, Li, Zhi 2010).

Therefore, facial dermatitis is clinically suspected to be related to autoimmunity, and autoantibody testing is conducted to further confirm or exclude such etiology. This paper reviewed the results of autoantibody detection in 57 patients with facial dermatitis, and discussed the significance of autoantibody in the diagnosis and differential diagnosis of facial dermatitis, so as to avoid missed diagnosis and contribute to the early diagnosis of connective tissue disease.

2 BACKGROUND REVIEW

Facial dermatitis mainly refers to skin inflammation that occurs on the face and is characterized by pruritic, recurrent and chronic tendency, There are various manifestations, including facial seborrheic dermatitis, facial atopic dermatitis, facial contact dermatitis, hormone-dependent dermatitis, psoriasis, acne, rose acne, lichen planus, lupus erythematosus, etc. The pathogenesis involves many factors such as autoimmunity, allergy, infection and vascular reactivity (Song, Hao 2017). Qu Yan et al. found that

[a] https://orcid.org/0000-0001-9459-6543
[b] https://orcid.org/0000-0001-8221-8924
[c] https://orcid.org/0000-0002-3141-894X
[d] https://orcid.org/0000-0003-2457-6066
[e] https://orcid.org/0000-0003-2174-1177
[f] https://orcid.org/0000-0002-4895-5522
[g] https://orcid.org/0000-0003-0636-4588
[h] https://orcid.org/0000-0001-9459-6543

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contact dermatitis and hormone-dependent dermatitis are the most common types of facial dermatitis in the clinical and pathogenic analysis of patients with facial dermatitis. Skin patch test and prick test are effective methods to find allergens. For contact facial dermatitis, aromatic compounds are the main allergens in the patch test. The highest positive rate of prick test is dust mites and dust mites (Qu, Meng, Yang, et al. 2016).

In addition to these pathogenic factors, facial dermatitis may also be related to autoimmune itself. So conducting autoantibody testing can further confirm or rule out such causes to avoid missed diagnosis and to help early diagnosis of connective tissue diseases.

ANA is a general term for autoantibodies against all antigen components in cells. As an important biological marker of autoimmune diseases, It is commonly seen in patients with systemic (non-organ-specific) autoimmune diseases such as mixed connective tissue disease (MCTD), systemic lupus erythematosus (SLE), sjogren's syndrome (SS), systemic sclerosis disease (SSc), polymyositis (PM) (Chinese Journal of Laboratory Medicine 2018). High titer of anti-U1-NRNP antibody has diagnostic significance for MCTD. Anti-sm antibody is a highly specific serological marker of SLE. Positive anti-SSA antibody and/or anti-SSB antibody are serological criteria for SS diagnosis. Anti-scl-70 antibody is a serological marker in SSc classification criteria, which is associated with poor prognosis, pulmonary fibrosis and heart disease. Anti-centromeric protein (CENP) antibody is a specific serologic marker of localized SSc, suggesting a good prognosis. Ama-a2 with high titer is the characteristic autoantibody of PBC, and the positive rate of anti-JO-1 antibody in PM patients is about 25%-30% (Chinese Journal of Rheumatology 2014). Li Dongjiao et al. also proposed that the combined detection of ANA and anti-ENA antibody has more clinical application value in the early diagnosis of autoimmune diseases than ANA primary screening alone (Li, Guan, Xie, et al. 2020).

Therefore, in this study, ANA and specific autoantibodies against target antigens were detected in patients with clinically suspected autoimmune diseases.

3 DATA AND METHODS

3.1 Clinical Data

From July 2019 to March 2021, in the dermatology department of our hospital, a total of 57 patients were initially diagnosed with facial dermatitis at their first outpatient visit, including 3 males and 54 females. Among them, 11 patients were less than 20 years old, 17 patients were 21 to 30 years old, 9 patients were 31 to 40 years old, 11 patients were 41 to 50 years old, and 9 patients were more than 50 years old. Inclusion criteria: ①The first diagnosis is supposed to be facial dermatitis; ② The clinical data is complete; ③ Patients with incomplete clinical data are excluded.

3.2 Method

3.2.1 Indirect Immunofluorescence (IIF) Detection of ANA in Serum Samples

ANA in serum samples was detected by antinuclear antibody IgG detection kit (indirect immunofluorescence method, Oumeng Medical Laboratory Diagnosis Co., Ltd.).

Operation method: First, centrifuge venous blood samples to be tested, dilute the serum to be tested into 1:100 when conducting qualitative testing and dilute the sample by multiple with PBS Tween buffer to determine the antibody titer; Second, add 25ul of the diluted sample drop bu drop on the reaction zone of the Hep-2 cell matrix slide; Third, place the slide covered with bio-flake face down, cover it in the groove of the sample plate, and incubate at room with temperature of 18℃ to 25℃ for 30 minutes; Then, use a beaker to hold PBS Tween buffer and use it to rinse the slide like running water, and immediately immerse it in a beaker containing PBS Tween buffer for at least 5 minutes; Next, remove the slide from the washing cup, wipe off the moisture on the back and edge of the slide with absorbent paper, and add 20ul goat anti-human IgG dropwise labeled FITC in the reaction area of the clean sample plate, and incubate at room with temperature of 18°C to 25°C for 30 minutes; Then use a beaker to hold PBS Tween buffer and use it to rinse the slide like running water, and immediately immerse it in a beaker containing PBS Tween buffer for at least 5 minutes; And last, remove the slide from the washing cup, wipe off the moisture on the back and edge of the slide with absorbent paper, and add 10ul mounting medium dropwise to mount the slide.

Reading the slide: Observe the stained image of cellsunder a fluorescence microscope (OLYMPUS BX53, 40×objective).

Judgment of results: qualitative and antibody titer results are judged according to the specific fluorescence model. Positive: the nucleus shows a specific fluorescence model. Negative: the nucleus does not show specific fluorescence.

The titer is defined as the highest dilution factor that can be observed for a specific fluorescence reaction compared with the reaction phase with the negative serum diluted by the same multiple Ratio.

3.2.2 Western Blotting Method to Detect Anti-ENA Antibody Profile in Serum Samples

The anti-ENA antibody spectrum in serum samples was detected using the anti-nuclear antibody spectrum IgG detection kit (Western blot method, Oumeng Medical Laboratory Diagnosis Co., Ltd.), including uracil 1-low molecular weight ribonucleoprotein (U1-nRNP), Sm, Sjogren's syndrome A and B (SS-A, SS-B), 11-16 peptide complex antigen (PM-Scl), cytoplasmic histoacyl-tRNA synthetase (Jo-1), Value-added cell nuclear antigen (PCNA), histones, mitochondrial M2 (AMA-M2), nucleosomes, centromere protein B (CENP B), ribosomal p protein, dsDNA, DNA topoisomerase I (Scl-70) .

Operation method: First, dilute the serum to be tested with sample buffer in the ratio of 1:101, take out the required membrane strip, put it into the incubation tank with the numbered side of the membrane strip facing up, add 1.5ml samples to the incubation tank and aspirate the liquid in the incubation tank after 5 minutes of incubation on a rocking bed at room temperature; Then, add 1.5 ml of the diluted serum sample to the incubation tank, incubate for 30 minutes at room temperature (18°C-25°C) on a rocking bed, aspirate the liquid in the tank, and wash the membrane strips 3 times with 1.5ml of washing buffer on the rocking bed, 5 minutes each time, and add 1.5ml anti-human IgG labeled by the diluted alkaline phosphatase to the incubation tank and incubate at room temperature (18°C-25°C) on a rocking bed for 30 minutes; And then aspirate the liquid in the tank, wash the membrane strips 3 times with 1.5ml of washing buffer on the rocking bed , each time for 5 minutes, and add 1.5ml substrate solution to the incubation tank, incubate at room temperature (18℃-25℃) for 10 minutes on a rocking bed, then aspirate the liquid in the tank, and wash the membrane strip in distilled water 3 times, 1minute for each time, and last put the test film strip in the result judgment template, and judge the result after air-drying.

The result is judged according to the coloring intensity of the antigen band and the coloring intensity of the quality control band. Positive: the coloring of the antigen band is medium to strong or the same as the intensity of the quality control band. Negative: a white band appears on the membrane strip where the antigen is coated.

4 RESULTS

Among 57 patients, 14 patients were positive for ANA, with a positive rate of 24.56%. Among them, 11 patients had nuclear granular karyotype and 7 patients, 3 patients and 1 patients with titers of 1:100, 1:320, and 1:1000, respectively. There are 2 cases with cytoplasmic granular karyotype, with a titer of 1:320; 1 case with nuclear homogeneous karyotype, with a titer of 1:100. Results of serum ANA and anti-ENA antibodies in 57 patients with facial dermatitis are shown in the table below. Among the 14 patients with ANA positive, 8 were positive for anti-SS-A antibody, 4 were positive for anti-PM-Scl antibody and anti-histone antibody, 2 were each positive for anti-U1-nRNP antibody and anti-SS-B, and anti-Sm Antibody, anti-AMA-M2 antibody, anti-ribosomal protein p antibody and anti-nucleosome antibody were positive in 1 case each. The final diagnosis was 1 case of SLE, 2 cases of DLE, and 2 cases of undifferentiated connective tissue disease.

Table 1: Results of serum ANA and anti-ENA antibodies in 57 patients with facial dermatitis.

Test items	ANA positive（n=14）	ANA negative（n=43）
Anti-SS-A	8（57.14）	1（2.33）
Anti-PM-Scl	4（28.57）	7（16.28）
Anti-histone	4（28.57）	3（6.98）
Anti-U1-nRNP	2（14.29）	3（6.98）
Anti-SS-B	2（14.29）	0
Anti-Sm	1（7.14）	0
Anti-AMA-M2	1（7.14）	7（16.28）
Anti-ribosomal protein p	1（7.14）	1（2.33）
Anti-nucleosome	1（7.14）	0
Anti-PCNA	0	3（6.98）
Anti-Jo-1	0	1（2.33）
Anti-centromere	0	1（2.33）

Among the 43 patients with negative ANA, 7 were positive for anti-PM-Scl antibody, 7 were positive for anti-AMA-M2, 3 were respectively positive for anti-U1-nRNP antibody, anti-PCNA antibody, and anti-histone antibody, and anti-SS-A antibody, anti-Jo-1 antibody, anti-ribosomal protein p antibody and anti-centromere antibody were positive in 1 case each. Although some of the 43 ANA-negative patients are positive for special autoantibodies, these patients have not yet been diagnosed with autoimmune diseases.

5 CONCLUSIONS

This article retrospectively analyzed the autoantibody test results of 57 patients with facial dermatitis. Of the 57 patients with facial dermatitis, 14 were positive for ANA, with a positive rate of 24.56%. Among the 14 patients with positive ANA, 1 case was diagnosed with SLE, 2 cases was diagnosed with DLE and 2 cases of undifferentiated connective tissue disease; Among the 43 cases of ANA negative, although some specific autoantibodies are positive, these patients have not yet been diagnosed with autoimmune diseases.

In this study, 57 patients with facial dermatitis in the outpatient department were tested by ANA and ENA. 14 cases (24.56%) were positive for ANA. Among them, 1 case was diagnosed as SLE, 2 cases were DLE, 1 case was connective tissue disease, and 1 case of undifferentiated connective tissue disease. This also shows that in this part of patients with facial dermatitis, some of them are the early atypical manifestations of autoimmune diseases. Although some of the 43 ANA-negative patients are positive for specific autoantibodies, these patients are currently not diagnosed with the above-mentioned related autoimmune diseases.

In this study, among the patients with positive autoantibodies, although the results of ANA detected by indirect immunofluorescence were not consistent with the anti-ENA antibody spectrum detected by western blotting, ANA positive patients may still suffer from mixed connective tissue disease (Zhou, Wang, Yang, et al, 2012), systemic lupus erythematosus and other autoimmune diseases (Chen, Chen, Zhang, et al, 2014). Zhang Heng et al. also pointed out in their research reports that for patients with suspected autoimmune diseases, the test results of ANA and ENA may not be completely consistent, and the simultaneous detection of ANA and ENA can reduce the rate of missed diagnosis and play a guiding role in the diagnosis of autoimmune diseases (Zhang, Wu, Tian, et al, 2018).

In conclusion, some of the patients clinically diagnosed with facial dermatitis can detect positive autoantibodies, and some positive antibodies are associated with autoimmune diseases to a certain extent. The detection of autoantibodies in patients with facial dermatitis is of great significance for the diagnosis and differential diagnosis of facial dermatitis, and is helpful for the early diagnosis of autoimmune diseases and avoiding missed diagnosis.

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