CASE AND RESEARCH LETTER

Variability of Mucocutaneous Signs Within the Spectrum of Reactive Arthritis Syndrome

Variabilidad en las manifestaciones mucocutáneas dentro del espectro del síndrome de artritis reactiva

To the Editor,

The concept of reactive arthritis (ReA) defines a subset of peripheral spondyloarthitis following an infectious process, often occurring at Gl or genitourinary tract level. It is often found in young adults with an HLA-B27 positive genotype. Associated mucocutaneous clinical signs are seen in over 50% of the patients and include circinate balanitis, oral aphthae, ulcerative vulvitis, and psoriasiform nail changes. However, in rare instances, this process presents with the full spectrum of symptoms, thus complicating the diagnostic process.

Patients diagnosed with ReA syndrome admitted to a tertiary-level dermatology unit were reviewed from 2007 through 2022. The clinical, pathological, analytical, and evolutionary characteristics of patients who met the diagnostic criteria (established in the Fourth International Workshop on Reactive Arthritis in 1999) with cutaneous-mucosal clinical signs were recorded. Additionally, patients who – even without a definitive diagnosis of ReA due to the absence of clear arthritis – presented with typical dermatological signs associated with an infectious event, were also included. Therefore, our case series is representative of the wide clinical and temporal variability of this condition and the diagnostic challenges it can pose (Table 1).

Regarding the mucosal signs reported in our series, circinate balanitis was found in 5 patients (71.4%) (Fig. 1; case #1), while 3 out of 7 patients (42.8%) had recurrent oral aphthae. One patient exhibited nail dystrophy associated with typical keratoderma blennorrhagicum (14.2%), with histopathological findings of psoriasiform epidermal hyperplasia, spongiotic pustules, neutrophilic exocytosis, and a perivascular lymphohistiocytic inflammatory cell infiltrate on the superficial dermis. Case #3 presented with multiple psoriasiform plaques on the forearms associated with dactylitis (Fig. 2; case #3). Dactylitis was present in 2 out of 7 patients, along with joint symptoms. Three patients (42.8%) had conjunctivitis along the course of the disease.

The diagnosis of ReA is primarily clinical, based on the patient’s past medical history and a thorough physical examination. There is no consensus on the diagnostic criteria for ReA. Additionally, atypical, or incomplete forms of the disease have been described in numerous cases. In our series, the characteristic triad of urethritis, arthritis, and conjunctivitis was seen in 3 patients only (42.8%). Also, joint symptoms did not always precede or accompany mucocutaneous symptoms. Additionally, in more than 10% of the cases, the infection can be subclinical and go completely unnoticed. We should mention that, based on the typical

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dermatological signs, the initial diagnosis could be achieved or guided in 5 out of 7 cases, meaning that dermatologists should become familiar with associated mucocutaneous clinical signs.

All our patients were men aged between 31 and 67 years. Urogenital infection-related ReA is more common in men, while GI tract-related infections affect both sexes equally. In our cases, we detected an absolute predominance in middle-aged men. Some authors attribute this high percentage to the high rate of asymptomatic infections among women, making it difficult to detect the past medical history that would lead to diagnosis.

It is advised to determine acute-phase reactants (CRP, ESR), detect HLA-B27, perform serological tests for HIV, and try to identify the culprit agent via cultures, CRP, or serology according to the clinical signs reported. Depending on different geographical regions, age, gender, and various microbial agents have been included in this screening as well. In our series, the most widely involved microorganism was Chlamydia trachomatis. In over 10% of the cases, the predisposing infection can be subclinical and go unnoticed.

A total of 85.71% of the cases were HLA-B27 positive. These patients represent between 60% and 85% of all cases of ReA, while this haplotype is found in the overall population with a prevalence of 10%. Although the determination of HLA-B27 is not a diagnostic criterion, it can provide guidance in the overall clinical picture and is associated with a larger number of extra-articular signs. Consistent with these findings, in our series, the patient who had the fewest skin symptoms was HLA-B27 negative. Additionally, HLA-B27 positive patients tend to have more chronic disease progressions, extra-articular signs are usually more common, and they have a worse prognosis. Cutaneous-mucosal signs are more common in HLA-B27 positive patients and often occur 1–4 weeks after the infectious process has begun. Still, there is great variability in their chronology, with some signs appearing even months or years after the triggering infectious episode.

On the other hand, 57.1% of the patients were also HIV-positive. This syndrome has been described in up to 10% of the people living with HIV. Also, it has been reported that in HLA-B27 positive patients, HIV infection triples the risk of developing the disease. This group of the patients tends to have a more aggressive and refractory course of ReA, which is why most authors recommend its determination.

Regarding cases that could be classified as atypical, one of our patients did not exhibit any joint symptoms, which raises doubts on the diagnosis of ReA. The observation of isolated characteristic dermatological signs could be the result of either an isolated skin process with possible shared pathogenic mechanisms with ReA, or an actual ReA with low/absent joint expressivity (Table 1).

In conclusion, there is significant heterogeneity in this disease with highly variable clinical signs in terms of number, presentation, and symptom severity, which stresses the importance of a thorough medical history and physical examination, especially of the skin, in cases with incomplete, or atypical forms.
Conflicts of interest

None declared.

References


A. Ciudad*, M. Rivera, R.M. Pujol, G. Martín-Ezquerra

Department of Dermatology, Hospital del Mar, Passeig Marítim 25-29, 08003 Barcelona, Spain

*Corresponding author.

E-mail address: andrea.ciudad.moro@psmar.cat (A. Ciudad).