# PSORIATIC ARTHRITIS "SINE PSORIASIS" – A RARE FORM OF DISEASE THAT RAISES POSITIVE AND DIFFERENTIAL DIAGNOSIS PROBLEMS

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**Abstract**

Psoriatic arthritis is part of the big group of spondylarthropaties, presenting numerous clinical forms and having both musculoskeletal and extraarticular manifestations. Usually, the disease diagnosis is set after the presence of clinical signs of skin psoriasis. In that case, the diagnosis is made quite easily. The condition puts a lot of problems regarding differential diagnosis especially in the situation when it precedes the onset of skin lesions. Regarding the presented case, a correct diagnosis of psoriatic arthritis "sine psoriasis" was made after about 20 years of disease evolution, at which time the specific nail lesions of psoriasis appeared.

**Keywords:** psoriatic arthritis, skin psoriasis, sine syndromes

## INTRODUCTION

Psoriatic arthritis (PsA) is a chronic progressive inflammatory disease that is part of the spondylarthropaties family, thus having a lot of clinical features of these conditions. PsA is usually associated with skin psoriasis and follows these manifestations. Arthritis is erosive, destructive, being a rapidly progressive and disabling condition for the patient. The disease can manifest through five clinical forms, having both peripheral manifestations of oligo or polyarticular type, as well as axial manifestations. Also, in PsA can be frequently highlighted clinical features of enthesitis and dactylitis. Psoriatic arthritis and psoriatic skin disease are certainly two conditions in a tight connection. In the situation in which the articular manifestations precede the skin lesions, both the diagnosis and the correct treatment represent a challenge for the doctor.

## CASE REPORT

This paper presents the case of a male patient from urban area who, in 1996 (at the age of 36) has been admitted for the first time in our clinic accusing pain and swelling of the bilateral ankles and forefeet. The patient has no significant previous personal medical history. However, the patient has a significant family history - mother with cutaneous psoriasis.

The clinical examination revealed painful swelling in ankles and biologically, an inflammatory syndrome was detected (erythrocyte sedimentation rate – ESR = 70 mm/h, C-reactive protein – CRP= 32 mg/dl) and a normal uric acid level. Raising various assumptions of differential diagnosis, the patient was tested for rheumatoid arthritis and for the group of spondylarthropaties. Thus, the patient has a negative rheumatoid factor and negative anti-citrullinated peptide antibodies. Also, the antigen HLA-B27 and antinuclear antibodies were absent. Serology for *Yersinia, Campylobacter, Salmonella, Shigella*, and *Chlamydia trachomatis* was also negative. Liver antigens for viral B and C hepatitis was not detected. X-rays were performed to exclude other conditions. Thus, chest radiography was normal, hands and feet X-rays with no changes and pelvis X-ray for sacroiliac joints did not show any modifications.

In 1996, after the first complete clinical-biological evaluation the diagnosis of undifferentiated spondylarthritis was sustained and treatment with sulfasalazine 2 g/day was started in combination with a nonsteroidal anti-inflammatory drug (NSAID)

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- Diclofenac 150 mg/day as needed. The evolution was favorable with the improvement of the symptomatology after 6 months objectified both clinically and by reducing the inflammatory markers.

Unfortunately, the patient is not compliant and returns to our clinic only in 2009 (after 13 years of disease evolution), being without treatment for about 10 years. Clinically the patient had a severe condition with arthritis in the fists, small joints of the hands, knees, ankles, small joints of the feet, dactylitis of bilateral toes, but with no modifications of teguments or nails. A normochromic normocytic anemia (Hb = 10.5 g/dl) and raised ESR and CRP levels (ESR = 95 mm/h, CRP = 70 mg/l) were highlighted. The immunological profile was also negative. Radiography of the hands showed: microgeodes of bilateral distal interphalangeal joints, minimal joint spaces narrowing at the level of proximal and distal interphalangeal joints. Radiography of the feet showed: severe changes of arthritis of the tarsal-metatarsal joints, and interphalangeal joints with narrowed joint spaces, aspect of „pencil-in-cup“, periostitis of diaphysis of V left metatarsal, cuneiform erosions of the bilateral V metatarsals bones.

In 2009, using CASPAR classification criteria of 2006, the diagnosis of psoriatic arthritis “sine psoriasis” was sustained. Thus, the patient fulfilled the following diagnostic criteria: (peripheral) inflammatory musculoskeletal impairment plus family history of psoriasis in first degree relatives, negative rheumatoid factor, dactylitis and radiological signs of new juxtaarticular bone formation (4 points). In this situation, the patient began treatment with Methotrexate 20mg/week. The evaluation after 6 months showed a relatively favorable evolution with the significant improvement of the articular manifestations, the decrease of the inflammatory markers, the normalization of the hemoglobin level, the normal liver and renal functional tests.

This time also the patient was noncompliant, returning to evaluation in our clinic after 7 years (in 2016) and having discontinued treatment since 2010. Also, in 2016 the patient was chronically consuming of ethanol and tobacco - 30 packs / year. Clinically, the patient was in a bad condition presenting: deformed ankle and feet arthritis, anterior thoracic vascular stars, palmar erythema, jaundice teguments, hyperkeratosis nailfold, feet onychodystrophy. The dermatological consult revealed psoriatic onychopathy. Figure 1 shows the clinical and radiological aspect of our patient‘s hands and feet.

Biologically, the patient presented with an important inflammatory syndrome, pancytopenia, hepatocytolysis and cholestasis syndrome and positive an-

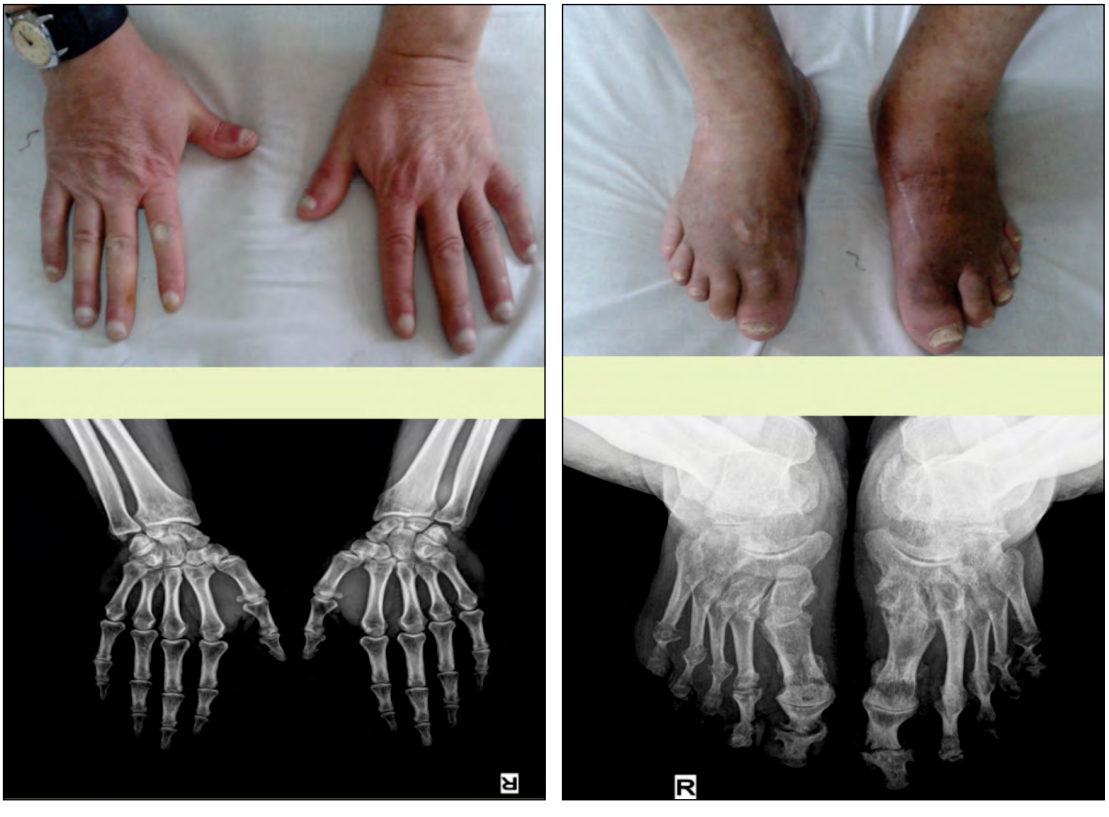

***FIGURE 1.*** *Clinical and radiological aspect of patient‘s hands and feet*

ti-hepatitis C antibodies. Gastroenterological consultation mentioned the diagnosis of toxic and postviral C hepatic cirrhosis parenchymatically decompensated.

In this new situation, in the face of a totally misunderstanding patient, chronic ethanol consumer and with decompensated liver cirrhosis, the only treatment option was the administration of hepatoprotectors, the psychiatric counseling of the patient and the reassessment of the therapeutic approach after the compensation of the liver disease.

## DISCUSSIONS

This paper presents the case of a young man in whom the nail lesions of psoriasis appeared after 20 years of evolution of the joint disease. The patient was initially diagnosed as having undifferentiated spondylarthritis, and later, following radiological evidence of the disease, the final diagnosis of psoriatic arthritis "sine psoriasis" was made. Unfortunately, due to the patient's non-compliance regarding the treatment, the disease evolved through major joint damage and was associated with a marked degree of disability.

PsA is a progressive and destructive inflammatory disease, having three different clinical forms: established psoriatic arthritis, psoriatic arthritis "sine psoriasis" and early psoriatic arthritis. Each form of the disease is characterized by a certain joint pattern involvement, being associated with the presence or absence of skin or nail psoriasis lesions (1).

The etiology of the disease is still unknown, studies talking about a host with a genetic predisposition and some triggering environmental factors. Is described the concept of „psoriatic disease" - a condition characterized by affecting several different anatomical sites in the same patient: skin, joints / entheses, intestine (2). In pathology, activated T-lymphocytes from the intestinal lymphoid tissue (GALT) that migrate to inflammatory skin or joint sites are involved (2). Also, the particular genetic background (HLA) and environmental factors influence the clinical expression of this multisystemic disorder (2,3).

Psoriatic arthritis and skin psoriasis are certainly two conditions that are interrelated, having genetic correlations proven by epidemiological and immunological studies (4). Thus, genes such as HLA B-13, HLA B-17, HLA B-57, HLA Cw6 are positively associated with cutaneous psoriasis. HLA-Cw * 0602 is present in 100% of cases of guttate psoriasis, psoriatic arthritis and early onset of psoriasis. HLA B-27 is associated with axial involvement, and HLA B-38 and HLA B-39 with a peripheral polyarticular involvement (5). Moreover, HLA Cw6 is associated with the family history of psoriasis, the presence of dactylitis and the impairment of distal interphalangeal joints (4,5).

The clinical expression of the articular and skin involvement of this disease has a great variability. The diagnosis relies mainly on clinical evaluation. In 1973, Moll and Wright proposed diagnostic criteria that have been widely used (6). Five clinical models have been developed that can be combined or evolved from one to the other (6). However, they have been shown to discriminate poorly between psoriatic and rheumatoid arthritis (7).

In 2006, the Classification Criteria for Psoriatic Arthritis (CASPAR) was published, having a sensitivity of 91.4% and a specificity of 98.7% (8). These criteria identified the disease if the patient had at least 3 points from the following clinical manifestations: current psoriasis, a personal history of psoriasis, a family history of psoriasis, dactylitis, juxta-articular new bone formation, negative RF and psoriatic nail lesions.

In 2007, Scarpa et al. proposed 3 forms of clinical presentation of PsA. Defined psoriatic arthritis - in patients with obvious skin / nail psoriatic lesions; it can fit into one of the five classical clinical forms, which may overlap or change (the oligoarticular form can become a polyarticular one). Psoriatic arthritis "sine psoriasis" - in patients without cutaneous psoriasis (but with a family history of psoriasis). Early psoriatic arthritis - recent onset (< 12 weeks) of joint involvement in patients with obvious cutaneous psoriasis or in „sine psoriasis" forms (1).

Although PsA is primarily found in those patients with skin psoriasis, arthritis can precede skin and/or nail disease in 20% of the cases (9). The CASPAR criteria do not require the presence of psoriasis skin disease. The diagnosis remains unclear until the appearance of skin/nail manifestations. However, according to the CASPAR classification criteria, we can define psoriatic arthritis "sine psoriasis" in the case of patients with articular clinical manifestations and with a family history of psoriasis in first or second-degree relatives (5,8).

Regarding the clinical manifestations of psoriatic arthritis "sine psoriasis", in 2009, Olivieri et al. published the results of a study that included 20 patients followed over a 12-month period (10). The study in-

cluded 16 men and 4 women with a mean age of 44.1 years and an average disease duration of 5.3 years. Inclusion criteria were: symptoms and signs suggestive of PsA and psoriasis in first-degree relatives, absence of another inflammatory rheumatic disease. The main clinical manifestations highlighted were: 5 patients - peripheral arthritis, enthesitis, tenosynovitis, 2 patients - peripheral arthritis, tenosynovitis, axial impairment, 4 patients - peripheral arthritis and tenosynovitis, 4 patients - peripheral enthesitis and tenosynovitis, 1 patient - peripheral arthritis and enthesitis, 3 patients - peripheral arthritis and 1 patient with enthesitis. The authors concluded that the clinical spectrum of psoriatic arthritis "sine psoriasis" is as wide as that of the defined PsA and highlighted a low sensitivity of the Amor and ESSG classification criteria.

The study published by Scarpa aimed to characterize the clinical pattern of psoriatic arthritis "sine psoriasis". Included were 57 patients: 31 women, 26 men with undifferentiated spondyloarthropathy defined according to ESSG criteria followed over a 9-month period. Of these, 21 patients had a positive family history for cutaneous psoriasis. The prevalence of the following variables was evaluated: low lumbar pain, entesopathy, dactylitis, distal interphalangeal and axial impairment, discitis. The findings highlighted that dactillitis and arthritis of the distal interphalangeal joints are significantly more common in patients with a family history of psoriasis (5). Also, the authors observed a higher frequency of HLA B27 in patients without a family history of psoriasis ($p = 0.019$) and a higher frequency of HLA Cw6 in patients with a positive family history of psoriasis ($p = 0.015$), data with statistical significance. In conclusion, the authors argued that psoriatic arthritis "sine psoriasis" involves distal interphalangeal arthritis, and/or dactylitis, the presence of HLA Cw6 and a family history of skin psoriasis.

The early recognition of the disease leads to better outcomes. Chandran's study on a group of 107 patients with early disease (evolution below 2.5 years) showed that CASPAR criteria may be useful in classifying early forms of the disease (11). The diagnosis of early PsA should be considered in patients with peripheral arthritis (especially oligoarticular and distal interphalangeal disease), peripheral enthesitis, tenosynovitis, dactylitis and/or inflammatory pain in the spine and cutaneous psoriasis or family history of psoriasis (12).

The main differential diagnosis is made with rheumatoid arthritis. Differentiating between psoriatic arthritis "sine psoriasis" and rheumatoid arthritis is difficult especially in the early stages, requiring new paraclinical investigations. Thus, the dermatologists tried to demonstrate the differences of the dermoscopic aspect of the vascularization of the nailfold and of the tegument at the level of the elbow in these 2 conditions (13). The group with psoriasis arthritis "sine psoriasis" included 15 patients. The nailfold with reddish background with or without pointed and rare vessels was highlighted, and at the level of the elbow - reddish vessels, diffused punctate distributed. 12 cases with rheumatoid arthritis were included. Nailfold was observed with short/punctate parallel linear vessels or purple, branched, irregular vessels, and at the elbow 3 aspects: irregular, violet vessels; avascular appearance or rare, punctate, purple vessels. The control group included 12 cases. The nailfold did not present any of the aforementioned aspects, while the elbow presented an aspect similar to rheumatoid arthritis. In conclusion, the utility of dermoscopy for the early diagnosis of psoriatic arthritis "sine psoriasis" has been proposed. The study, although conducted on a small number of patients, may open new perspectives in the use of this technique for an early diagnosis.

Another study recently published in 2018 focused on the role of dermoscopy associated with ultrasound in differentiating early psoriatic arthritis from early seronegative rheumatoid arthritis (14). 73 subjects were included in the study, of which 25 with rheumatoid arthritis with positive RF, 23 with rheumatoid arthritis with negative RF and 25 with PsA. One quarter of those diagnosed with rheumatoid arthritis with negative RF, but who also showed cutaneous psoriasis changes at the level of the nailfold and of the skin at dermoscopic evaluation, were diagnosed with psoriatic arthritis "sine psoriasis". The presence of at least one extra-synovial manifestation of the hand at ultrasonography and the nail punctiform hemorrhages at dermoscopy was significantly associated with psoriatic arthritis "sine psoriasis", having a sensitivity of 68.0% and 96.0% and a specificity of 88.1% and 83.3% for ultrasonography and dermoscopy. So, using ultrasonography and dermoscopy together, the specificity for the diagnosis of psoriatic arthritis "sine psoriasis" increases to 90.5%.

## CONCLUSIONS

We have presented the case of a young man in whom the joint disease began 20 years before the

onset of nail lesions of psoriasis, which made the final and correct diagnosis difficult. Due to the patient's non-compliance with the treatment, the disease had a destructive and disabling evolution, being associated with a poor quality of life of the subject. As we well know, in 20% of patients with PsA the articular manifestations can be highlighted before the appearance of the skin lesion. Arthritis can precede the skin lesion by more than 10 years. In the past, using the old classification criteria, patients with psoriasis arthritis "sine psoriasis" were diagnosed as undifferentiated spondyloarthritis. Currently, the family history of psoriasis in relatives of the first or second degree, dactylitis, distal interphalangeal arthritis and the particular genetic field HLA Cw6 are the indicators for the correct diagnosis of psoriatic arthritis "sine psoriasis". The CASPAR classification criteria can support the diagnosis of psoriatic arthritis "sine psoriasis" in patients with characteristic articular manifestations and a family history of skin psoriasis. Because differential diagnosis is sometimes difficult to achieve, new methods of differentiation between psoriatic arthritis "sine psoriasis" and rheumatoid arthritis with negative RF must be considered - dermatoscopy being able to be one of the useful tools.

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