

Ultrasound as a tool for the early diagnosis of psoriatic arthritis

Abstract

Psoriasis is a common chronic, immune-mediated, systemic inflammatory disease, with a special predilection for the skin and joints. Approximately one third of patients with psoriasis will have associated psoriatic arthritis and it usually begins with the skin lesions, evolving to articular manifestations. Since psoriatic arthritis could present with permanent articular damage with chronic pain and disability, it is important to seek for early diagnosis. We will talk about our recent experience with rheumatological ultrasound, studying a small and selected group of patients, along with an important literature review.

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Introduction

Psoriasis is a chronic, immune-mediated, systemic inflammatory disease, with a special predilection for the skin and joints. It affects around 2 to 3% of the general population and causes a profound impact on quality of life, especially when present in its severe forms.¹⁻¹⁰ Classic studies indicate that approximately one third of patients with psoriasis will have associated psoriatic arthritis (PsA). And, in 70% of cases, joint disease follows cutaneous involvement, placing the dermatologist in a prominent position to suspect this diagnosis. It is essential to emphasize that psoriatic arthritis, due to its inflammatory, chronic and erosive nature, is characterized by the possibility of inducing permanent damage to the joint. Therefore, early diagnosis is essential to improve outcomes.¹¹⁻¹³

Methods

We designed a case-control study in search of a better understanding of the intestinal microbiome of Brazilian patients with severe psoriatic disease, when compared to control individuals without psoriatic disease. For this purpose, 30 patients with psoriatic disease and 30 individuals without psoriasis and without psoriatic arthritis were gathered, selected as controls, from the same geographic unit. All of them, using fecal samples, performed high-throughput DNA sequencing of the 16S rRNA gene, V3/V4 regions. Based on this study, a new analysis was carried out, focused on the group of

patients with psoriatic disease, seeking to evaluate the microbiome in patients with and without psoriatic arthritis.

For the study that originated this statement, which aimed to evaluate the microbiome of patients with and without joint disease, it was essential to ensure that patients had joint disease. The opposite is also true. It was necessary to ensure that individuals labeled as having psoriasis vulgaris had no stigma of joint disease. For this reason, all 30 patients were evaluated together with a rheumatologist, a specialist from the rheumatology society, with more than 20 years of practice in the specialty. During the clinical examination with the rheumatologist, all 30 patients underwent ultrasound of joints, entheses and nail devices (same doctor performing it, single device, with defined sequential methodology). In parallel, all 30 patients answered the screening questionnaire called PEST and collected peripheral blood for analysis of inflammatory tests: erythrocyte sedimentation rate and quantitative c-reactive protein. Our project was submitted to Brazil Platform, being ethically approved without additional considerations.

Results

Table 1 groups the main findings of patients with psoriatic disease included in the microbiome study, involving patients with and without joint disease.

Table 2 compiles the findings of the 15 patients with psoriatic arthritis.

Table 1 Clinical epidemiological profile of patients included in the samples as cases of severe psoriatic disease, in total and in subgroups, with and without psoriatic arthritis

Cases (n= 30)	Cases (n= 30)	Pso (n=15)	PsA (n=15)	p
Gender:	15 (50%)	9/15 (60%)	6/15 (40%)	
Female (absolute and percentage frequency):				
Average age (years)	48.3 (±12.4)	47.93 (±13.91)	48.67	0.871
+ standard deviation:			(±10.34)	
Average time of disease evolution (years):	14.7 (±11.54)	13.6	15.87	0.6
		(±8.29)	(±14.29)	
Average BSA:	24%	22.90%	24.90%	0.789
Min and Max:	6 – 76%	6 – 74%	6 – 76%	
Average PASI:	17.08	15.88	18.28	0.387
Min and Max:	5.4 – 38.8	7.4 - 23	5.4 – 38.8	
DLQI (n=4):*	16	18	16	
	18	24	20	
	20			
	24			
Pso:				
I. Scalp	30	15 (100%)	15 (100%)	>0.05
II. Nail	13	6/15 (40%)	7/15 (46.7%)	
III. Inverted (flexure)	19	11/15 (73.3%)	8/15 (53.3%)	
Comorbidities:				
Yes (absolute and percentage frequency):	24 (80%)	12/15 (80%)	12/15 (80%)	1
Average BMI (kg/m2)	29.93 (±5.65)	32.85 (±4.76)	27.02 (±5.04)	0.003
+ Standard deviation:				
PsA (absolute and percentage frequency): ∞			15 (50%)	
I. Peripheral			7 (46.66%)	
II. Entesis/Dactylitis			12 (80%)	
III. Axial			5 (33.33%)	
Average DAPSA (n=15):			23.11	
I. Remission:			1/15	
II. Low activity:			3/15	
III. Moderate activity:			6/15	
IV. High activity			5/15	
Average BASDAI (n=5)			4.98	
Obesity	15 (50%)	11/15 (73.3%)	4/15 (26.7%)	<0.001
I. Class I	11 (73.33%)			
II. Class II	2 (13.33%)			
III. Class III	2 (13.33%)			
Metabolic syndrome	14 (46.66%)	7/15 (46.7%)	7/15 (46.7%)	1
High Blood Pressure	12 (40%)	6/15 (40%)	6/15 (40%)	1
Diabetes	4 (13.33%)	2/15 (13.3%)	2/15 (13.3%)	1
Dyslipidemia	13 (43.44%)	5/15 (33.3%)	8/15 (53.3%)	<0.001
Hepatic steatosis	15 (50%)	7/15 (46.7%)	8/15 (53.3%)	0.876
I. Mild	7 (46.66%)			
II. Moderate	8 (53.33%)			
III. Severe	0			
Tabagism:	9 (30%)	3/15 (20%)	6/15 (40%)	<0.001
Sedentarism	20 (66.66%)	11/15 (73.3%)	9/15 (60%)	0.466
PESTπ (positive screening for PsA):	14 (46.66%)	3/15 (20%)	11/15γ(73.3%)	<0.001
Average VHS (mm 1H):	21.4	20.7	21.87	0.875
Average PCR (mg/dL):	3.72	2.77	4.67	0.476

*Those with BSA and PASI < 10 had DLQI > 10

∞ As for arthritis, clinical patterns overlap, with the same patient being able to present a peripheral pattern, in addition to axial involvement, for example.

π Psoriasis Epidemiology Screening Tool (PEST)

γ All 4 patients with negative arthritis and PEST had positive ultrasound

Source: Elaborated by the authors, 2022.

Table 2 Patients with psoriatic arthritis

Age:	Gen.:	Age Diag.:	Time Evol.:	PASI / BSA:	DAPSA:	BASDAI:	LEI:	SPARCC:	MASES:	USG:
54	Fem.	30	36	11.6 8%	29.4		1	1	1	Enthesitis of Aquileus
54	Masc.	53	1	22.4 20%	2.65		1	1	1	Enthesitis of Aquileus
58	Masc.	34	24	7.0* 5.60%	34.3		0	0	0	Enthesitis and Synovitis
46	Masc.	22	24	23 25%	4.6	5.2 [∞]	0	0	0	Psoriatic nail dystrophy, mild enthesitis and mild synovitis
45	Masc.	40	5	20.4 40%	5.13	2.2 [∞]	0	0	0	Discrete Aquileus and Plantar enthesitis
39	Fem.	1	38	22.6 50%	48.5		2	0	0	Synovitis and Enthesitis
40	Masc.	20	28	17.2 24%	40.6		16	6	13	Dactylitis and Enthesitis
61	Masc.	59	4	13.1 12%	41	5.7 [∞]	9	4	3	Plantar enthesitis
48	Fem.	28	20	16.1 12%	18.45	8.2 [∞]	0	3	0	Patellar and Plantar Enthesitis
46	Fem.	44	5	5.4* 6%	24.9		0	0	0	Synovitis, Tenosynovitis and Enthesitis
58	Masc.	33	25	38.8 76%	16.8		0	0	0	Synovitis, Tenosynovitis in the left wrist, Dactylitis in the toes
64	Masc.	14	50	18.5 20%	18.77	3.6 [∞]	0	0	0	Synovitis and Dactylitis
28	Masc.	28	3	13.1 16%	8.6		0	0	0	Synovitis
55	Fem.	47	8	32.4 40%	23.35		4	4	13	Synovitis and Enthesitis
34	Fem.	24	10	14 13%	21.7		1	4	1	Enthesitis

*Those with BSA and PASI < 10 had DLQI > 10

[∞] Magnetic resonance imaging confirming sacroiliitis.

Source: Elaborated by the authors, 2022.s

Discussion

Some aspects deserve to be highlighted. The case group presented equivalence between genders, mean age of 48 years and mean time of disease evolution of more than 10 years (14.7 years, SD ±11.54). This means that the population studied has a well-established disease. When comparing cases and controls, there was no statistically significant difference in terms of mean age and mean time of disease progression. Evolving to clinical characteristics, there was no difference in terms of average PASI and BSA, in addition to no difference between the presence of comorbidities. This homogeneity ensures comparability between groups.

However, for the same purpose, there was a significant predominance of women in the group without arthritis (60% vs. 40%). Another anomalous finding was the identification of a higher average BMI among patients without joint disease (p = 0.003) and, consequently, a greater number of obese patients also among patients without joint disease (p < 0.001).

The following are risk factors classically related to joint disease in patients with psoriasis vulgaris: onset of the disease in childhood/adolescence; severe/extensive skin disease, involvement of nails

and scalp, in addition to intergluteal cleft; family history of psoriatic arthritis in a first-degree relative; HLA-B27 positivity; obesity; uveitis; biomechanical stress and trauma.^{14,15} In the present sample, smoking and the presence of dyslipidemia were risk factors (both with p < 0.001). There was no difference in the presence or absence of nail psoriasis, involvement of the scalp or intergluteal groove (p > 0.05). As mentioned previously, unexpectedly, obesity was a protective factor (p < 0.001). Perhaps it represents a selection bias, where there was a significantly higher prevalence of obese people among those without arthritis.

It is worth highlighting that, from a screening point of view, the PEST tool was effective in differentiating patients with joint disease (20% The present study therefore found a sensitivity of 78.5% and specificity of 75%, in addition to a positive predictive value of 73.3% and a negative predictive value of 80%. Studies that validated the tool demonstrated high sensitivity (97%), with reasonable specificity (79%), which is strictly what is expected from a screening tool.¹⁶ In addition a negative predictive value of 99%, which is information very useful in practice: in the case of a negative PEST, you are reasonably certain that you are not dealing with a patient with psoriatic arthritis. At least, from the point of view of peripheral involvement, enthesitis

and dactylitis. The major exception to the applicability of PEST in clinical practice is the failure to consider the involvement of the axial skeleton. Therefore, it is recommended to add questions to the PEST regarding the presence of low back or hip pain, whether this pain is worse in the morning or whether it has woken the patient up during the night, and whether it is accompanied by a certain stiffness and is relieved with mobilization and stretching.

In the present study, acute phase inflammatory tests were not able to differentiate between patients with and without joint disease. There was a tendency towards a higher mean of ultrasensitive quantitative C-reactive protein (CRP) (4.67 x 2.77), however, like the 1-hour erythrocyte sedimentation rate (ESR), the difference did not reach statistical significance ($p = 0.476$). In fact, the literature shows that increased CRP can help in the interpretation of a patient with plaque psoriasis and arthralgia/arthritis, however, when negative, it should not rule out the diagnosis or even be indicative of controlled joint disease or in remission.¹⁷

Even so, the clinical evaluation correlated with the ultrasound findings allowed the diagnosis of joint involvement. This highlights the importance of ultrasound as a tool for early diagnosis. Ultrasound is a quick, affordable and non-invasive exam, and does not involve radiation or the use of contrast. On the other hand, it is operator dependent, requiring rigorous training in order to increase its accuracy. Another relevant aspect to be highlighted was the evolution of devices, with greater frequency, allowing the skin and nail system to be studied, complementing the evaluation of patients with psoriatic disease.^{18,19} The *European League Against Rheumatism* (EULAR) recommends that ultrasound should be included in the evaluation of all patients with chronic arthritis in order to increase diagnostic accuracy.^{20,21}

A recent study by Chen et al.,²² evaluated 490 patients with moderately severe plaque psoriasis. Among them, 384 were asymptomatic from a joint point of view and 106 with arthralgia and fatigue, included in what is understood as the prodromal phase of psoriatic arthritis. They also included 80 height controls without psoriasis. When compared to controls, patients with psoriasis without joint complaints, there was an important difference in the presence of synovium-enthesitis (1.3% x 16.1%, $p < 0.001$), the most common location being the knees. The results motivated researchers to recommend ultrasound screening in all patients with psoriasis, regardless of the presence of symptoms, especially in the lower limbs.

Finally, ultrasound allows not only the identification of established structural damage, but also minimal changes in blood flow in superficial, soft tissues, using the doppler tool. These flow changes correlate with recent, active inflammation. Thus, in addition to early diagnosis, it allows monitoring of disease activity.²³

Returning to our findings with the study of the intestinal microbiome in patients with and without arthritis, we demonstrated a greater expression of the Bacteroidaceae family, the Bacteroides genus and the Bacteroides uniformis species among patients with joint disease when compared to those with plaque psoriasis without joint involvement. This finding corroborated the study by Scher et al, from 2015, where it was postulated that increased expression of the Bacteroides genus is a hallmark of established joint disease. In fact, in the model of progression of psoriatic disease towards the transition to psoriatic arthritis, proposed by Scher and Merola in 2019, in addition to the previously mentioned risk factors, the authors speculated that microbiome changes could play a role in the transition from the prodromal phase of psoriatic arthritis to established joint disease.

Conclusion

In conclusion, the dermatologist must be the sentinel in early identification of patients at increased risk of psoriatic arthritis. Active questioning about joint pain, swelling, stiffness and limitation of movement, in addition to inspection and palpation of joints and entheses, should be part of the assessment consultation for patients with psoriasis. As demonstrated in the literature, PEST as a screening method tool can and should be implemented, being very practical and accessible, with the exception of not considering issues related to possible involvement of the axial skeleton. In parallel, multidisciplinary clinics with access to ultrasound certainly increase diagnosis in subclinical and prodromal phases of joint disease, possibly contributing to better outcomes. These findings need to be confirmed in prospective studies with long follow-up periods.

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Conflicts of interest

The authors declare no conflict of interest.

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