

disease incidence in a general population: findings from the Yamagata study. *J Epidemiol.* 2019. <http://dx.doi.org/10.2188/jea.JE20180249>.

4. De Francisco S, Torres C, de Andrés S, Millet A, Ricart MT, Hernández-Martínez-Esparza E, et al. Effectiveness of integrative laughter therapy to reduce anxiety improve self-esteem and increase happiness: a naturalistic study at a day hospital for addictive disorders. *Int J Environ Res Public Health.* 2019;16. <http://dx.doi.org/10.3390/ijerph16214194>, pii: E4194.
5. Sorgun MH, Kural MA, Yücesan C. Clinical characteristics and prognosis of neuro-Behçet's disease. *Eur J Rheumatol.* 2018;5:235–9.
6. Al-Araji A, Kidd DP. Neuro-Behçet's disease: epidemiology, clinical characteristics, and management. *Lancet Neurol.* 2009;8:192–204.
7. Casanova Peño IC, de las Heras Revilla V, Parejo Carbonella B, di Capua Sacotoa D, Fuentes Ferrer ME, García-Cobos R, et al. Neurobehçet disease: clinical and demographic characteristics. *Eur J Neurol.* 2012. <http://dx.doi.org/10.1111/j.1468-1331.2012.03706.x>.
8. Jenette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis Rheum.* 2013;65:1–11.

Gerardo Toantiu Jaimes-Piñon,^a Ildefonso Rodríguez-Leyva,^{b,c} Carlos Abud Mendoza^{b,c,*}

^a Hospital General número 50, Instituto Mexicano del Seguro Social (IMSS), San Luis Potosí, Mexico

^b Facultad de Medicina, Universidad Autónoma San Luis Potosí (UASLP), San Luis Potosí, Mexico

^c Hospital Central «Dr. Ignacio Morones Prieto», San Luis Potosí, Mexico

* Corresponding author.

E-mail address: cabudm@hotmail.com (C. Abud Mendoza).

<https://doi.org/10.1016/j.reumae.2020.01.001>

2173-5743/ © 2021 Elsevier España, S.L.U. and Sociedad Española de Reumatología y Colegio Mexicano de Reumatología. All rights reserved.

Growth factors: Do they play a role in enthesal involvement in psoriatic arthritis and undifferentiated spondyloarthritis patients?



Factores de crecimiento: ¿desempeñan un papel en el compromiso enteseal en pacientes de artritis psoriásica y espondiloartritis indiferenciada?

Dear Editor:

The role of growth factors (GFs) in arthritis is rarely investigated, reporting controversial results.^{1–4}

To the best of our knowledge, the serum levels of IGF-1, FGF-1, TGFβ in patients (pts) with undifferentiated spondyloarthritis (SpA) or psoriatic arthritis (PsA) have never been described in literature. Partsch et al. described a higher titer of GH in the sera of PsA pts compared to psoriatic pts.¹

We describe a study designed to evaluate the serum levels of GFs, IGF-1, FGF-1, GH and TGFβ, in PsA pts and SpA pts, with particular focus on the enthesal involvement. Our goal was to assess any differences in the concentration of these GFs between pts with different clinical and instrumental features.

Preliminary data were obtained on 15 pts (all female): 6 with a new diagnosis of PsA,⁵ 9 with a new diagnosis of SpA.⁶ The con-

trol group was formed by 5 age-matched healthy females (HC). The exclusion criteria were intestinal bowel disease, diabetes mellitus, body mass index >30, systemic hypertension, dyslipidemia, alteration of thyroid function.

Serum levels of IGF-1, FGF-1, GH and TGFβ were measured using enzyme-linked immunosorbent assay (ELISA). Moreover, an imaging evaluation was conducted on all pts: the presence of calcific enthesopathy (CE) was assessed using standard radiology; the ultrasound evaluation was conducted according to the Madrid Sonographic Enthesis Index (MASEI) score.⁷ Disease activity was assessed by means of Disease Activity Score (DAS28), Disease Activity in Psoriatic Arthritis (DAPSA) and Leeds Enthesitis Index (LEI). Comparisons between groups were made with one-way analysis of variance (ANOVA) (Table 1).

We found that serum levels of IGF-1 and TGFβ were remarkably but not significantly higher in SpA pts compared to PsA pts and HC. In particular, there was a tendency toward higher serum concentrations of TGFβ in pts with CE compared to those pts without and HC (1003.5 ± 208.5 vs. 999.5 ± 156.9 vs. 975.9 ± 61.7; *P* = .965). Furthermore, a statistically significant negative correlation between TGFβ levels and symptoms duration both in SpA and PsA pts was observed (*r*² = 0.582; *P* = .029). In addition, subjects with moderate (MA) or high disease activity (HA) according to DAPSA score showed a tendency toward higher GH (low activity

Table 1
Comparison of demographic, clinical characteristics and serum levels of growth factors between groups in study.

Variables	PsA	SpA	HC	<i>P</i>
Age	49.1 ± 15.7	43.8 ± 12.3	43.2 ± 13.1	.691
BMI	24.1 ± 3.2	24.2 ± 1.54	22.5 ± 3.6	.233
Symptoms duration	4.6 ± 3.2	4.00 ± 2.0		.424
ESR	16 ± 17.7	19.4 ± 14.6		.688
CRP	0.1 ± 0.2	0.2 ± 0.2		.813
LEI	3.5 ± 1.2	2.3 ± 1.3		.109
DAS28	3.2 ± 0.5	2.6 ± 1.1		.287
DAPSA	24.1 ± 5.7	20.7 ± 6.1		.305
MASEI	6.5 ± 5.6	5.3 ± 4.5		.665
SHARP score	33.3 ± 39.7	50.7 ± 33.9		.474
PARS	4.6 ± 1.1	6.5 ± 8.2		.708
IGF-1	378.3 ± 330.8	859.4 ± 923.4	366.5 ± 280.6	.638
FGF-1	9.6 ± 23.5	13.3 ± 22.5	3.5 ± 7.1	.242
GH	336.1 ± 694.0	991.2 ± 1082.6	593.1 ± 601.6	.679
TGFβ	968.8 ± 189	1024.3 ± 193.3	927.2 ± 121.1	.464

Data are expressed as mean ± standard deviation; significant *P* value was set to ≤ .05.

BMI: BODY MASS INDEX; CRP: C Reactive Protein; DAPSA: Disease Activity in Psoriatic Arthritis; DAS28: Disease Activity Score; ESR: Erythrocytes Sedimentation Rate; HC: Healthy Controls; LEI: Leeds Enthesitis Index; MASEI: MADRID Sonographic Enthesitis Index; PARS: Psoriatic Arthritis Ratingen Score; PsA: Psoriatic Arthritis; SpA: undifferentiated Spondyloarthritis.

(LA): 310.8 ± 449.4 , MA: 533.8 ± 967.4 , HA: 630 ± 1074.4 ; $P = .903$) and IGF-1 (LA: 389.4 ± 532.8 , MA: 467.7 ± 825.2 , HA: 491.7 ± 585.6 ; $P = .908$) levels, while TGF β levels were higher only in DAPSA HA (LA: 954.6 ± 257.3 , MA: 910.1 ± 170.5 , HA: 1049.5 ± 44.1 ; $P = .653$). Interestingly, this tendency was not observed when assessing the disease activity using the DAS28 score, except for the HA group (LA: 954.6 ± 257.3 , MA: 903.8 ± 207.7 , HA: 974.5 ± 124.2 ; $P = .91$).

The differences we found were not statistically significant most presumably given the small sample size. Since no statistically significant differences in age and BMI were observed between the groups, a difference in the GFs concentration due to physiological hormonal variations can be excluded.^{8,9}

The evidences about DAS28 may be owed to the focus of this score on joint involvement, while enthesitis is not evaluated, as in DAPSA.

The most remarkable result is the significant higher TGF β serum levels in pts with shorter symptoms duration, suggestive for a potential role of TGF β as an early biomarker of disease.

This preliminary study, although lacking statistically significant results, support the hypothesis of an important role played by GFs IGF-1, GH and TGF β rather in the pathogenesis of enthesitis than of joint inflammation. In particular, TGF β should have a key role in earlier phases of SpA and PsA. Further studies, with a larger sample size, are necessary to clarify the role of GFs in the pathogenesis of enthesopathy, and more broadly of spondylarthritis.

Funding

No funding was received for this study.

Conflict of interest

None.

Acknowledgements

We would like to thank Prof. Addolorata Corrado and Dr. Giovanni Bellantuono for their contribution in this study.

References

1. Partsch G, Schwarzer C, Dunky A, Mayer F, Gschnait F, Neumüller J, et al. Determination of growth hormone in plasma of psoriatic arthritis, psoriasis vulgaris and seronegative spondylarthritis. *Z Rheumatol.* 1985;44:267–9.
2. Denko CW, Boja B, Moskowitz RW. Growth factors, insulin-like growth factor-1 and growth hormone, in synovial fluid and serum of patients with rheumatic disorders. *Osteoarthritis Cartilage.* 1996;4:245–9.
3. van Tok MN, Yeremenko NG, Teitsma CA, Kream BE, Knaup VL, Lories RJ, et al. Insulin-like growth factor I does not drive new bone formation in experimental arthritis. *PLoS ONE.* 2016;11:e0163632, <http://dx.doi.org/10.1371/journal.pone.0163632>.
4. François RJ, Neure L, Sieper J, Braun J. Immunohistological examination of open sacroiliac biopsies of patients with ankylosing spondylitis: detection of tumour necrosis factor alpha in two patients with early disease and transforming growth factor beta in three more advanced cases. *Ann Rheum Dis.* 2006;65:713–20, <http://dx.doi.org/10.1136/ard.2005.037465>.
5. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. *Arthritis Rheumatol.* 2006;54:2665–73.
6. Amor B, Dougados M, Mijiyawa M. Criteria of the classification of spondylarthropathies. *Rev Rhum Mal Osteoartic.* 1990;57:85–9.
7. de Miguel E, Cobo T, Muñoz-Fernández S, Naredo E, Usón J, Acebes JC, et al. Validity of enthesitis ultrasound assessment in spondyloarthropathy. *Ann Rheum Dis.* 2009;68:169–74, <http://dx.doi.org/10.1136/ard.2007.084251>.
8. Nimura A, Katsumata N, Tanaka T. Serum levels of free insulin-like growth factor (IGF)-I in normal children. *Clin Pediatr Endocrinol.* 2004;13:71–8, <http://dx.doi.org/10.1297/cpe.13.71>.
9. Blizzard RM, Martha PM, Kerrigan JR, Mauras N, Rogol AD. Changes in growth hormone (GH) secretion and in growth during puberty. *J Endocrinol Invest.* 1989;12:65–8.

Cinzia Rotondo Daniela Cici* Francesco Paolo Cantatore

Rheumatology Clinic, Department of Medical and Surgical Sciences, University of Foggia, Ospedali Riuniti Foggia, Viale Pinto 1, 71121 Foggia, Italy

* Corresponding author.

E-mail address: daniela.cici@gmail.com (D. Cici).

<https://doi.org/10.1016/j.reuma.2020.01.002>

1699-258X/ © 2020 Elsevier España, S.L.U. and Sociedad Española de Reumatología y Colegio Mexicano de Reumatología. All rights reserved.