reparative process. An MRI study of bone ankylosis in the hands of a cohort of consecutive RA patients could help understand the true frequency and significance of this finding.

**Rheumatology key message**

- Bone ankylosis of the wrist joints in RA may be a reparative process.

**Disclosure statement**: The authors have declared no conflicts of interest.

**Francesca Barbieri**, **Massimiliano Parodi**, **Giuseppe Zampogna**, **Francesco Paparo** and **Marco A. Cimmino**

1 Dipartimento di Medicina Interna, Clinica Reumatologica and 2 Dipartimento di Medicina Interna, Sezione di Diagnostica per Immagini, Università di Genova, Genova, Italy

Accepted 12 February 2010

Correspondence to: Marco A. Cimmino, Dipartimento di Medicina Interna, Clinica Reumatologica, Università di Genova, Viale Benedetto XV, 6, 16132 Genova, Italy. E-mail: cimmino@unige.it

**References**


Rheumatology 2010;49:1416–1418
doi:10.1093/rheumatology/keq074
Advance Access publication 18 March 2010

**Dysregulation of P2X7 receptor-inflammasome axis in SAPHO syndrome: successful treatment with anakinra**

Sir, The syndrome of Synovitis Acne Pustulosis Hyperostosis Osteitis (SAPHO) is a rare condition characterized by a variable combination of osteoarticular and cutaneous manifestations [1]. Although often related to the SpAs, emerging evidence suggests that SAPHO might be a primitive inflammatory osteitis, probably related to polygenic auto-inflammatory disorders [2]. In this report, we describe a dysregulation of extracellular ATP-dependent P2X7-IL1β axis in a case of SAPHO syndrome effectively treated with the IL-1 receptor antagonist (IL-1Ra) anakinra.

A 47-year-old female, was admitted to our unit in July 2007 with a 3-year history of remitting pain and swelling of anterior chest wall (ACW) structures, and a 10-year history of severe palmoplantar pustulosis (PPP). During adolescence she suffered from acne conglobata. Total white blood cell (WBC) count was 14.5 × 10^9/l; ESR was 35 mm/h (normal range <20) and CRP was 1.8 mg/dl (normal range <0.6). HLA-B27 antigen was negative. A CT scan of ACW revealed massive osteitis with periostitic erosive aspects. A diagnosis of SAPHO syndrome was made, and therapy with SSZ (3 g/day) was set up for 6 months without any significant improvement. The patient was further evaluated in February 2008, after appearance of intermittent right knee arthritis. A slight leucocytosis and elevated acute-phase markers were still present (ESR and CRP were 28 mm/h and 1.1 mg/dl, respectively). At that time, the patient also referred low-grade fever and asthenia. Joint SF showed 7800 cells (65% of monocytes). SF cultures for Propionibacterium acnes resulted negative and so did the PCR for 16S ribosomal RNA and lipase genes. Technetium 99m (⁹⁹mTc) bone scan revealed hypercapta-

![ATP-dependent P2X7-IL1β axis](https://example.com/atp-dependent_p2x7-il1beta-axis.png)

The authors have declared no conflicts of interest.

1416
To understand the molecular basis of the higher P2X7-stimulated IL-1β release in SAPHO PBMCs, we measured the level of expression of the inflammasome constituents NLRP3 and ASC. While NLRP3 expression did not differ, ASC was expressed at higher level in SAPHO than in healthy controls (net intensity ratio: 3.4 (0.12) and 4.54 (0.35) for the expression of ASC in healthy and SAPHO subjects, respectively; Fig. 1D). Finally, measurement by firefly luciferin-luciferase assay showed that plasma ATP level in SAPHO patient was much higher than that in 13 healthy controls [1689 (11.54) and 1016 (160) nM, respectively, average (S.D.) of three determinations from SAPHO patient and healthy controls].

These findings suggested a possible dysregulation of the IL-1β processing machinery, which prompted us to start off label treatment with anakinra 100 mg/day, in late March 2008 after local ethics committee approval from The Ethical Committee of Azienda Ospedaliero – Universitaria Sant’Anna, Ferrara, and patient’s written informed consent was obtained. By June 2008, the painful osteoarticular symptomatology, the cutaneous lesions and the systemic symptoms had disappeared. Peripheral synovitis at the right knee remitted, and laboratory parameters were within the normal range. A 99mTc bone scintigraphy showed complete resolution of previous uptake abnormality at the manubrium sterni and a considerable reduction of tracer uptake in the right sternoclavicular joint. The dosage of anakinra was then gradually reduced to 100 mg every 2 days and the patient is still symptom free.

In conclusion, we wish to suggest that these findings and response to anakinra should be taken as the criteria to include SAPHO syndrome in the growing family of auto-inflammatory disorders. However, since a positive

Fig. 1 (A) Measurement by ELISA of IL-1β release in the supernatant of SAPHO (closed bars) and healthy control (open bars) PBMCs. Cells were left untreated (control) or primed for 2 h in the presence of 1 μg/ml LPS. Treated PBMCs were also incubated for 30 min with increasing concentrations of BzATP. To block P2X7, PBMCs were incubated for 2 h in the presence of 600 μM oxidized ATP (oATP) and then washed before addition of stimulators. Data from the SAPHO patients are averages (s.e.) of the same experiment, performed in triplicate. Control data are averages (s.e.) of three experiments performed with PBMCs from three different controls. (B–D) Expression of inflammasome components in healthy controls (H) and SAPHO (S) PBMCs. Quantitation of P2X7 transcript was performed by real-time PCR (B). Primers and probes were selected from Applied Biosystems Taqman™ Gene Expression Custom Assay (Foster City, CA, USA). Data are averages (s.e.) of expression of P2X7 evaluated in two different controls and in the SAPHO PBMCs. Amplifications were performed in triplicate for each sample. P2X7, NLRP3 and ASC protein expression levels were measured by western blot. For statistical analysis: *P < 0.05, **P < 0.005, ***P < 0.001, vs healthy subjects.
response to anti-TNF-α agents has also been observed [7, 8] the precise pathogenetic role of IL-1β and TNF-α is a matter for further investigations.

Rheumatology key message

- IL-1 is involved in the pathogenesis of SAPHO syndrome.

Acknowledgements

Funding: This research was supported by grants from the Italian Association for Cancer Research, Telethon of Italy (no. GGP06070), the Italian Space Agency (ASI-OSMA), the Italian Ministry of University and Scientific Research (PRIN), the Commission of European Communities (Seventh Framework Program HEALTH-F2-2007-202231), the Emilia-Romagna Region, the Fondazione Cassa Di Risparmio di Ferrara and institutional funds from the University of Ferrara.

Disclosure statement: F.D.V. acts as a consultant for Cordex Pharma Inc. and Afectis Pharma AG, Biotech Companies involved in the development of ATP-based drugs.

Matteo Colina1, Cinzia Pizzirani2,3, Micheline Khodeir4, Simonetta Falzoni2,3, Marco Bruschi1, Francesco Trotta1 and Francesco Di Virgilio2,3

1Department of Clinical and Experimental Medicine, Rheumatology Section, 2Interdisciplinary Center for the Study of Inflammation (ICSI), 3Department of Experimental and Diagnostic Medicine, Section of General Pathology, University of Ferrara and 4Department of Radiology and Clinical Pathology, Microbiology Section, Azienda Ospedaliero-Universitaria di Ferrara Arcispedale Sant’Anna, Ferrara, Italy

Accepted 16 February 2010
Correspondence to: Matteo Colina, Department of Clinical and Experimental Medicine, Rheumatology Section, University of Ferrara, Corso della Giovecca 203, Ferrara 44100, Italy. E-mail: teocolina@libero.it

References


Comment on: Monitoring Achilles enthesitis in ankylosing spondylitis during TNF-α antagonist therapy: an ultrasound study

Sir, I read with great interest the recent report by Aydin et al. [1] highlighting the potential role of ultrasound including grey scale and power-Doppler imaging. I would appreciate commenting on some issues raised by the authors.

At baseline, both grey scale and power-Doppler ultrasound features were recorded, which were re-evaluated after 2 months of TNF-α antagonist therapy. In addition to the outcome measures used by the authors, one should consider the validated Victorian Institute of Sports Assessment-Achilles (VISA-A) questionnaire, which quantifies the pain and activity level with scores ranging from 0 (worse) to 100 (perfect) [2]. It has been applied in a number of publications dealing with Achilles tendinopathy and, thus, might be applicable for patients suffering from AS.

As far as gender is concerned, the authors found that men had higher baseline ultrasound abnormality values than females, albeit similar Bath Ankylosing Spondilitis Disease Activity Index (BASDAI), ESR and CRP levels.

Treatment response, however, was similar, but not displayed by the authors. From a microcirculatory perspective, tendon microcirculatory changes between symptomatic females and males suffering from Achilles tendinopathy have been described previously [3]. Although there were similar pain levels on a visual analogue scale [VAS 0–10, < 5.3 (2.2) vs > 5.4 (2); P = 0.864], females had a superior tendon oxygenation and reduced post-capillary venous filling pressures than symptomatic males. Notably, treatment response is not necessarily the same for both genders, at least in Achilles tendinopathy, which might be different to AS. As far as painful eccentric training is concerned in Achilles tendinopathy, symptomatic females do not benefit as much as symptomatic males from eccentric training alone over 12 weeks of treatment [4].

Rheumatology 2010;49:1418–1419
doi:10.1093/rheumatology/keq069
Advance Access publication 31 March 2010

www.rheumatology.oxfordjournals.org