Letters to the Editors

An adult-onset Still's disease during infection with *Chlamydia* trachomatis

Sirs,

Adult-onset Still's disease (AOSD) is a rare and sporadic systemic autoinflammatory disease. It mainly occurs in young adults between 18 and 45 years old, with a similar prevalence between sex (1). The main signs are high fever (>39°C), transient maculopapular rash, arthralgia or arthritis, odynophagia, elevated white blood cell count with $\ge 80\%$ polymorphonuclear cells, and elevated ferritin with low glycosylated ferritin (≤20%) (2-4). AOSD is a serious condition with potentially life-threatening complications (5). Various conditions, especially infectious diseases may trigger it. Similar to the phenomenon encountered in other autoinflammatory diseases, microbial pathogen-associated molecular patterns would activate macrophages, responsible for the over-activation of innate immune responses.

Genital infections have been suggested as potential triggers of AOSD (2). *Chlamydia trachomatis* is an obligate intracellular, Gram-negative bacterium, which may induce genital symptoms, eye inflammation, and more rarely reactive arthritis (7). Genital symptoms, especially in women, may be completely silent.

We report the case of a young postpartum woman who developed AOSD concomitant with documented *Chlamydia trachomatis* infection, suggesting a causal relationship between these two diseases.

An 18-year-old woman was admitted in our Rheumatology department for a 3-week polyarthritis, transient maculopapular rash concomitant to fever peaks up to 39°C (Fig. 1), severe pharyngitis, and right mucopurulent conjunctivitis, that occurred four months after childbirth. Cervical and a right preauricular lymphadenopathies were present. Initial blood tests showed elevated polymorphonuclear cells (12,000/mm³) and C-reactive protein level (150 mg/L). Classical viral serologies were all negative as the autoimmune tests. The ferritin level was elevated (2300 mg/L), whereas the glycosylated ferritin was deeply decreased (10%). Thus, the diagnosis of AOSD was retained. Given the association between arthritis and conjunctivitis, we performed a urinary polymerase chain reaction (PCR) for Chlamydia trachomatis, which was positive. The Chlamydia trachomatis infection appeared to be recent, since there was no sign of any genital infection on an endocervical swab performed during her pregnancy. We treated the infection resulting in a rapid improvement of conjunctivitis. Corticoids were initiated with an insufficient



 $Fig. \ 1. \ {\rm Transient\ maculopapular\ rash,\ concomitant\ with\ the\ fever\ peaks.}$

clinical improvement. Thus, a complementary treatment with anakinra allowed a rapid and durable regression of the clinical and biological manifestations.

The aetiology of AOSD and its underlying pathogenetic mechanisms are still unknown. Several infections have been found to be associated with the onset of this disease as viral ones but occasionally, it can be triggered by bacterial infections (2). To our knowledge, this is the first reported case of AOSD during a bacteriologically confirmed *Chlamydia trachomatis* infection. A case of AOSD following a likely *Chlamydia trachomatis* infection has previously been described, but there was no direct evidence of current infection (only an elevated antibody titer) (8).

The characteristics of the conjunctivitis (non-itchy, mucopurulent, with a preauricular lymphadenopathy) lead us to suspect Chlamydia trachomatis infection (9). Although a coincidental association cannot be ruled out, the absence of other causes associated with AOSD onset, and the symptomatic expression of concomitant Chlamydia trachomatis infection argue for a potential causal relationship between these two conditions. In addition, there may be an overlap between the diagnoses of AOSD and reactive arthritis caused by Chlamydia trachomatis. Several cases of association of autoinflammatory syndrome and spondyloarthritis have recently been reported and raised the question of shared pathogenic pathways. Indeed, HLAB27 has been shown to activate innate immunity, and durable elevation of IL-1 β and IL-18 levels in patients with persistent autoinflammatory states may affect T-cell differentiation, promoting occurrence of spondyloarthritis (10).

This case suggests that, in addition to the classically recommended serologies for AOSD, *Chlamydia trachomatis* should be sought in presence of suggestive symptoms. Because the health consequences for women who are infected may be substantial, treatment of this infection is crucial.

I. KOUKI¹, MD I. SACCO¹, MD F. EYMARD¹, MD, PhD B. FAUTREL², MD, PhD X. CHEVALIER¹, MD, PhD L. PINA VEGAS¹, MD, MPH ¹Department of Rheumatology, AP-HP, Henri Mondor Hospital, Créteil; ²Department of Rheumatology, AP-HP, Pitié Salpétrière Hospital, Paris, France. Please address correspondence to: Laura Pina Vegas Service de Rhumatologie, Hôpital Henri Mondor, 51 Avenue du Maréchal de Lattre de Tassigny, 94010 Créteil Cedex, France. E-mail: laura.pinavegas@aphp.fr

Competing interests: X. Chevalier has received consultancies and/or honoraria from Ibsa and Nordic Pharma. The other authors have declared no competing interests.

© Copyright CLINICAL AND

EXPERIMENTAL RHEUMATOLOGY 2022.

References

- MAGADUR-JOLY G, BILLAUD E, BARRIER JH et al.: Epidemiology of adult Still's disease: estimate of the incidence by a retrospective study in west France. Ann Rheum Dis 1995; 54: 587-90.
- FEIST E, MITROVIC S, FAUTREL B: Mechanisms, biomarkers and targets for adult-onset Still's disease. *Nat Rev Rheumatol* 2018; 14: 603-18.
- FAUTREL B: Adult-onset Still disease. Best Pract Res Clin Rheumatol 2008; 22: 773-92.
- DROUOT MH, HACHULLA E, HOUVENAGEL E et al.: Cardiac complications in adult onset Still disease: from pericarditis to tamponade as manifestations. *Rev Med Interne* 1994; 15: 740-3.
- BAE C-B, JUNG J-Y, KIM H-A, SUH C-H: Reactive hemophagocytic syndrome in adult-onset Still disease: clinical features, predictive factors, and prognosis in 21 patients. *Medicine* (Baltimore) 2015; 94: e451.
- KELLEY N, JELTEMA D, DUAN Y, HE Y: The NLRP3 Inflammasome: an overview of mechanisms of activation and regulation. *Int J Mol Sci* 2019; 20: 3328.
- MISHORI R, MCCLASKEY EL, WINKLERPRINS VJ: Chlamydia trachomatis infections: screening, diagnosis, and management. *Am Fam Physician* 2012; 86: 1127-32.
- ANDRÈS E, IMLER M: A patient with adult Still's disease and high Chlamydia trachomatis titers. *J Infect Chemother* 2003; 9: 194.
- AZARI AA, BARNEY NP: Conjunctivitis: a systematic review of diagnosis and treatment. JAMA 2013; 310: 1721-9.
- MITROVIC S, HASSOLD N, KAMISSOKO A et al.: Erratum to: Adult-onset Still's disease or systemiconset juvenile idiopathic arthritis and spondyloarthritis: overlapping syndrome or phenotype shift? *Rheumatology* (Oxford) 2022; 61: 882.