Reumatol Clin. 22 (2026) 502126

Sociedad Española de Reumatología - Colegio Mexicano de Reumatología

Reumatología Clínica

www.reumatologiaclinica.org

Case Report

Autoinflammatory syndromes in adults: report of 8 cases

Nuria Garvín Grande,[a,*] Paloma Turiel Hernández,[a] Manuel Beladiez Giner,[a] Giancarlo Ernesto Candela Ganoza,[b] Nicolás Silvestre Torner,[c] Paz Collado Ramos[a]

[a] *Departamento de Reumatología, Hospital Universitario Severo Ochoa, Leganés, Madrid, Spain*
[b] *Departamento de Medicina Interna, Hospital Universitario Severo Ochoa, Leganés, Madrid, Spain*
[c] *Departamento de Dermatología, Hospital Universitario Severo Ochoa, Leganés, Madrid, Spain*

ARTICLE INFO

Article history:
Received 17 September 2025
Accepted 19 February 2026
Available online 10 April 2026

Keywords:
Autoinflammatory syndromes
Adult patients
Anakinra
Canakinumab
Genetic mutations
Case report

ABSTRACT

Introduction: Retrospective study documenting the clinical features, demographic and analytical parameters and therapeutic management in a cohort of adult patients with AIS.
Clinical description: Eight patients (50% male) were included, the majority of whom were Caucasian. The most frequent AIS was AOSD (37,5%). The mean age at symptom onset was 40 ± 23,1 years. The mean diagnostic delay was 5,7 ± 5 years. Fever, skin rash and myalgias were the most prevalent symptoms. The mean CRP value was 187,1 ± 110 mg/L and ESR rate of 95,2 ± 38 mm/h. 100% were treated with systemic corticosteroids, 50% with int i-IL-1. 3 patients required a switch from anakinra to canakinumab due to intolerance or lack of efficacy.
Conclusions: Given its increasing prevalence, this study emphasizes the importance of not underestimating the existence of AIS in adults, regardless of the level of health care. Early diagnosis and treatment with i-IL-1 are essential to control disease activity and prevent serious complications.

© 2026 Sociedad Española de Reumatología (SER), Colegio Mexicano de Reumatología (CMR) and Elsevier España, S.L.U. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

Síndromes autoinflamatorios en edad adulta: reporte de 8 casos

Palabras clave:
Síndromes autoinflamatorios
Adultos
Anakinra
Canakinumab
Mutaciones genéticas
Serie de casos

RESUMEN

Introducción: Estudio retrospectivo donde se describen las características clínicas, demográficas, analíticas y terapéuticas de una serie de pacientes adultos con SAI.
Descripción clínica: Se incluyeron 8 pacientes (50% hombres) en su mayoría caucásicos. El SAI más frecuente fue la AOSD (37,5%). La media de edad al debut fue de 40 ± 23,1 años. El retraso diagnóstico medio fue de 5,7 ± 5 años. La fiebre, el rash cutáneo y las mialgias fueron los síntomas más prevalentes. El valor medio de PCR de 187,1 ± 110 mg/L y de VSG de 95,2 ± 38 mm/h. El 100% recibió tratamiento con corticoesteroides sistémicos, el 50% con i-IL-1. En 3 pacientes fue necesario cambiar anakinra por canakinumab debido a intolerancia o ineficacia.
Conclusión: Dada su creciente prevalencia, este estudio enfatiza la importancia de no subestimar la existencia de los SAI en adultos, independientemente del nivel asistencial sanitario. El diagnóstico precoz y el tratamiento con i-IL-1 son fundamentales para controlar la actividad de la enfermedad y prevenir complicaciones graves.

© 2026 Sociedad Española de Reumatología (SER), Colegio Mexicano de Reumatología (CMR) y Elsevier España, S.L.U. Se reservan todos los derechos, incluidos los de minería de texto y datos, entrenamiento de IA y tecnologías similares.

* Corresponding author.
E-mail address: nuria.garvin@gmail.com (N. Garvín Grande).

2173-5743/© 2026 Sociedad Española de Reumatología (SER), Colegio Mexicano de Reumatología (CMR) and Elsevier España, S.L.U. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

Introduction

Autoinflammatory syndromes (AIS) are a heterogeneous group of inherited disorders characterised by aberrant activation of the innate immune system, with recurrent or persistent systemic inflammation. They include monogenic and polygenic forms, associated with mutations in genes that regulate inflammatory pathways. Although AIS usually present in childhood, cases have been reported in adults. Clinical non-specificity and phenotypic variability contribute to delayed diagnosis; therefore, a high clinical index of suspicion and genetic testing are key to their identification.[1,2]

Clinical description

A retrospective case series study was conducted involving adult patients (aged 16 years and over) with high suspicion for AIS, who attended the rheumatology clinic of a medium-sized hospital between 2005 and 2023. Demographic, clinical, laboratory and genetic data were collected.

When genetic testing was not possible, clinical criteria were used for diagnosis, employing the Yamaguchi et al.[3] criteria for adult-onset Still's disease (AOSD) and the Eurofever criteria[4] for tumour necrosis factor receptor-associated periodic syndrome (TRAPS). Other infectious, neoplastic or autoimmune causes were excluded. A descriptive analysis was performed considering the distribution of the variables.

Eight patients were included in the study; most were Caucasian and there was no predominance in terms of sex. AOSD was the most common AIS (37.5%, three patients). The mean age at onset was reported as 40 ± 23.1 years and the mean age at diagnosis as 45.6 ± 20.7 years. Genetic testing was required to confirm the diagnosis in 3 patients, while clinical diagnostic classification criteria were applied to the remainder. A mean diagnostic delay of 5.7 ± 5 years was observed, most strikingly in the case of familial cold autoinflammatory syndrome (FCAS), with symptom onset occurring at the age of 4. Symptoms began in adulthood in 87.5% (n = 7) of cases.

Clinically, fever, skin rash, and myalgia were the predominant symptoms (Table 1). All patients presented with elevated acute-phase reactants (APRs), with a mean value of 187.1 ± 110 mg/l for CRP and 95.2 ± 38 mm/h for ESR. Ferritin showed a median of 923.5 ng/mL [329–15,410].

All patients received corticosteroids. Four patients received interleukin-1 inhibitors (i-IL-1), starting with anakinra; 3 of them required a switch to canakinumab due to intolerance or lack of response.

At the most recent cohort follow-up (2025), 75% (n = 6) of patients were in a state of clinical stability. Twenty-five percent (n = 2) discontinued canakinumab: one due to clinical remission (with subsequent relapse) and the other due to lack of response.

Discussion

Traditionally, AIS have been considered rare diseases presenting in the paediatric population. However, their identification in adults is becoming increasingly common, as this study demonstrates. In line with other recent series,[2,5] AOSD and TRAPS are the most common AIS.

Table 1
Baseline characteristics of the cohort of patients with autoinflammatory syndromes (AIS).

Characteristics, n (%)	AOSD (n = 3)	FCAS2 (n = 1)	FCAS (n = 1)	TRAPS (n = 1)	FMF (n = 1)	SCHNITZLER (n = 1)	Total (n = 8)
Age at onset of symptoms[a]	57.7 (± 8.6)[a]	53	4	20	16	54	40 (± 23.1)[a]
Age at diagnosis[a]	59 (± 7)[a]	58	19	27	18	66	45.6 (± 20.8)[a]
Sex, n (%)							
Female	2 (66.7%)	1 (100)	0 (0)	0 (0)	0 (0)	1 (100)	4 (50)
Male	1 (33.3%)	0 (0)	1 (100)	1 (100)	1 (100)	0 (0)	4 (50)
Genetic mutation	NA	NLRP12 c.753C > G p. Asn251Lys	NLRC4 c > g; p. (Asp1009Gly)	NA	MEFV c.2177 T > C p. (Val726Ala)	NA	
Clinical characteristics							
Fever	3 (100)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)	8 (100)
Abdominal pain	1 (33.3)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	2 (25)
Genital involvement	1 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (12.5)
Pericarditis/Chest pain	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	1 (12.5)
Joint pain	2 (66.6)	1 (100)	1 (100)	0 (0)	0 (0)	1 (100)	5 (62.5)
Arthritis	1 (33.3)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	2 (25)
Myalgia	3 (100)	1 (100)	1 (100)	0 (0)	0 (0)	0 (0)	5 (62.5)
Skin rash	3 (100)	1 (100)	1 (100)	1 (100)	0 (0)	1 (100)	7 (87.5)
Facial oedema	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	1 (100)	2 (25)
Leukocytoclastic vasculitis	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	1 (12.5)
Oral ulcers	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	1 (12.5)
Ocular manifestations	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	1 (12.5)
Odynophagia	3 (100)	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)	5 (62.5)
Lymphadenopathy	2 (66.6)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	3 (37.5)
Splenomegaly	1 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (12.5)
Hepatosplenomegaly	1 (33.3)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	2 (25)
Drugs							
Colchicine	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	1 (100)	2 (25)
Prednisone	3 (100)	1 (100)	1 (100)	1 (100)	0 (0)	1 (100)	7 (87.5)
Methotrexate	2 (66.6)	0 (0)	1 (100)	0 (0)	0 (0)	1 (100)	4 (50)
Anakinra	1 (33.3)	1 (100)	1 (100)	0 (0)	0 (0)	1 (100)	4 (50)
Canakinumab	0 (0)	1 (100)	1 (100)	0 (0)	0 (0)	1 (100)	3 (75)

AOSD: adult-onset Still's disease; FCAS: familial cold autoinflammatory syndrome; FCAS2: type 2 familial cold autoinflammatory syndrome; FMF: familial Mediterranean fever; NA: not applicable; Schnitzler: Schnitzler's syndrome; TRAPS: tumour necrosis factor receptor-associated periodic syndrome.

[a] Values expressed as the mean (± standard deviation).

The diagnostic delay observed is consistent with the existing literature, due to clinical non-specificity and the lack of specific biomarkers.[6] Elevated APR, particularly ferritin, were a common and expected finding, underscoring their usefulness as an indirect biomarker of severe systemic inflammation.[5,7]

IIL-1 inhibitors have been shown to be an effective therapy for controlling disease activity, particularly in patients with AOSD refractory to conventional treatments[8] or with serious complications such as MAS, reported in up to 15% of patients.[7]

Despite its limitations (retrospective design and small sample size), this study highlights the need to recognise and manage AIS in adults, including in medium-complexity hospitals, emphasising the importance of considering AIS in the differential diagnosis of febrile syndromes of unknown origin.[9]

Conclusion

Given its increasing prevalence, the study emphasises the importance of maintaining a high clinical index of suspicion when diagnosing AIS in adults. Early diagnosis and IL-1 inhibitors are essential for appropriate management of the condition. Further longitudinal studies involving larger populations are needed to improve our understanding of AIS in adults.

Funding

This research study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

The authors have no conflict of interests to declare.

References

1. Hernández-Rodríguez J. Introducción y fisiopatología de las enfermedades autoinflamatorias. In: En Manual de Enfermedades Autoinflamatorias, J. Yagües Ribes. Madrid: Panamericana; 2022. p. 3–15.
2. González García A, Patier de la Peña JL, Ortego Centeno N. Enfermedades autoinflamatorias en el adulto. Características clínicas e implicaciones pronósticas. Rev Clín Esp. 2017;217(2):108–16, http://dx.doi.org/10.1016/j.rce.2016.08.004.
3. Yamaguchi M, Ohta A, Tsunematsu T, Kasukawa R, Mizushima Y, Kashiwagi H, et al. Preliminary criteria for classification of adult Still's disease. J Rheumatol. 1992;19(3):424–30. PMID: 1578458.
4. Federici S, Sormani MP, Ozen S, Lachmann HJ, Amaryan G, Woo P, et al., Paediatric Rheumatology International Trials Organisation (PRINTO) and Eurofever Project. Evidence-based provisional clinical classification criteria for autoinflammatory periodic fevers. Ann Rheum Dis. 2015;74(5):799–805, http://dx.doi.org/10.1136/annrheumdis-2014-206580. Epub 2015 Jan 30. PMID: 25637003.
5. Riera Alonso E, Olivé Marqués A, Sallés Lizarzaburu M, Holgado Pérez S, García Casares E, Tena Marsà X. Enfermedad de Still del adulto: revisión de 26 casos. Med Clin (Barc). 2007;129(7):258–61.
6. Caterson H, Papadopoulou C, Peet C, Lachmann HJ. Systemic autoinflammatory disease diagnoses in a single year from a UK national referral centre. Rheumatology. 2025, keaf165.
7. Giacomelli R, Ruscitti P, Shoenfeld Y. A comprehensive review on adult onset Still's disease. J Autoimmun. 2018;93:24–36, http://dx.doi.org/10.1016/j.jaut.2018.07.018. Epub 2018 Aug 1. PMID: 30077425.
8. Siddiqui M, Putman MS, Dua AB. Adult-onset Still's disease: current challenges and future prospects. Open Access Rheumatol. 2016;8:17–22, http://dx.doi.org/10.2147/OARRR.S83948. PMID: 27843366; PMCID: PMC5098765.
9. Hernández-Rodríguez J, Ruíz-Ortiz E, Tomé A, Espinosa G, González-Roca E, et al. Clinical and genetic characterization of the autoinflammatory diseases diagnosed in an adult reference center. Autoinmmun Rev. 2016;15(1):9–15, http://dx.doi.org/10.1016/j.autrev.2015.08.008. Epub 2015 Aug 21. PMID:26299986.