

COMPLICATIONS OF ADULT-ONSET STILL'S DISEASE: DATA ANALYSIS OF THE SPANISH STILL'S REGISTRY

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BACKGROUND

Adult-onset Still’s disease (AOSD) is a rare systemic disorder typically characterized by fever, arthritis, skin rash, leukocytosis, and hyperferritinemia, which are the hallmarks of the disease. Other frequent manifestations include odynophagia, myalgias, hepatic involvement, lymphadenopathy and splenomegaly. However, its clinical picture may be burdened by the occurrence of atypical or non-classical complications, which can be severe and potentially life-threatening

OBJECTIVE

To investigate the prevalence and clinical spectrum of complications in AOSD beyond macrophage activation syndrome (MAS), and to identify factors linked to their occurrence.

METHODS

Hospital-based registry with national coverage of patients with a diagnosis or suspected diagnosis of sJIA or AOSD according to the responsible physician and at least one year of follow-up. Descriptive variables (classification criteria, clinical manifestations, complications, family and personal history) were collected at the onset of the disease and during follow-up.

RESULTS

The cohort included 107 patients (67% women) from 14 centers in various autonomous communities in Spain. Table 1 summarizes their general characteristics and main clinical and laboratory data. Among them, 64 (59.8%) patients had one or more of the following complications, retrospectively recorded in the electronic Data Collection Form:

- MAS in 10 out of 105 patients (Prevalence: 9.5%, 95% CI 14.2 to 34.3).
- Atypical skin manifestations in 38 out of 98 patients (38.8%, 95% CI 27.4 to 53.2) The most common lessions were persistent pruritic papules and plaques with a linear configuration resembling flagellate erythema, and urticaria-like eruptions.
- Cardiac involvement in 22 out of 97 patients (22.7%, 95% CI 14.2 to 34.3), comprising 18 cases of pericardial disease, 4 cases of myocarditis, 6 cases of suspected pulmonary arterial hypertension (PAH) by imaging, and 1 case of inflammatory valvular involvement
- Pleural disease in 28 out of 97 and transient pulmonary infiltrates in 4 out of 100 patients, with prevalences of 28.9% (19.2 to 41.7) and 4% (1.1 to 10.2), respectively.
- Secondary amyloidosis in 1 out of 104 patients (0.96%, 95% CI 0.2 to 5.3).
- Significant headache as a presenting symptom in 13 out of 92 patients (14.1%, 95% CI 7.5 to 24.2), with some cases objectively confirmed as aseptic meningitis.
- Peritonitis confirmed by peritoneal effusion on imaging in 9 out of 107 patients (8.4%, 95% CI 3.8 to 16).

In the comparative study (Table 2), patients with complications exhibited a higher incidence of lymphadenopathy (52.4% vs. 27.8%; p=0.018) and, as expected due to its composition, higher values in the Systemic Score System index (6.6 vs 5.3; p=0.0002)

They also more frequently exhibited a chronic clinical course, higher ferritin levels, alterations in liver function tests, a higher frequency of hepatomegaly, and a greater need for high-dose steroids and biological therapy, although these differences did not reach statistical significance

Table 1. Main characteristics of the 107 patients with AOSD

Number of patients*	N=107
Demographic characteristics	
Women/Men	71 (67%) / 36 (33%)
Age of onset, P ₅₀ (P ₂₅ -P ₇₅)	40.7 (28.4 - 56.3)
Age at diagnosis, P ₅₀ (P ₂₅ -P ₇₅)	40.6 (30.2 - 53.8)
Start-diagnosis years, P ₅₀ (P ₂₅ -P ₇₅)	0.13 (0.06 - 0.44)
Family history	16 (30.2%)
Fullfiment of Criteria Diagnosis	
Yamaguchi	91 (85%)
Fautrel	58 (54.2%)
Cush	63 (58.9%)
Baseline characteristics	
Fever	98 (100%)
Typical exanthema	81 (82.6%)
Constitutional syndrome	44 (44.4%)
Arthralgia	101 (99%)
Arthritis	71 (68.9%)
Persistent arthritis	34 (43%)
Odynophagia	80 (78.4%)
Splenomegaly	27 (28.4%)
Hepatic involvement	28 (29.5%)
Lymphadenopathy	43 (43.4%)
Serositis	30 (32.3%)
Laboratory data	
ESR ≥ 30 mm/h (n=302)	90 (92.8%)
Ferritin ≥ 1,500 (ng/dl)	52 (56.5%)
Ferritin values (mean ± SD), ng/dl	6053 ± 9779
Haemoglobin <12 g/dl	39 (37.1%)
Leukocytes ≥15,000 /mm ³	45 (43.7%)
Platelets ≥400,000/mm ³	26 (29.5%)
ALT ≥40 U/L	52 (57.8%)
AST ≥40 U/L	52 (57.8%)
GGT ≥40 U/L	61 (73.5%)
Treatments	
Need of glucocorticoids	63 (63.6%)
Need of biologics	57 (58.8%)
Type of evolution	
Mono-episodic	29 (27.4%)
Poly-episodic	29 (27.4%)
Persistent	48 (45.3%)

Data represent n (%), except where other statistics are specified.

*The results (percentages) in each variable were calculated considering only the number of patients in which the data have been documented.

Table 2.- Results of the comparative study

	Without complications (N=43)	With complications (N=64)	P value
Fever	34 (100%)	64 (100%)	-
Typical exanthema	22 (64.7%)	32 (50.0%)	0.164
Splenomegaly	8 (25.8%)	19 (29.7%)	0.694
Hepatomegaly	7 (22.6%)	21 (32.8%)	0.305
Odynophagia	27 (71.0%)	53 (82.8%)	0.163
Lymphadenopathy	10 (27.8%)	33 (52.4%)	0.018
Arthritis	27 (69.2%)	44 (68.7%)	0.959
Shoulder involvement	-	2 (22.2%)	1.000
Type of evolution			0.112
Mono-episodic	11 (26.2%)	18 (28.1%)	
Poly-episodic	16 (38.1%)	13 (20.3%)	
Persistent	15 (35.7%)	33 (51.6%)	
Need for high doses of GC	30 (55.6%)	43 (68.2%)	0.206
Need of biologics	30 (55.6%)	37 (60.7%)	0.622
Age at onset	39.4 ± 16.6	44.2 ± 17.8	0.256
ESR (mm/h)	80.4 ± 26.4	73.9 ± 30.8	0.281
CRP (mg/dl)	25.4 ± 36.9	34.1 ± 61.3	0.776
Ferritin values (ng/dl)	4879 ± 6797	6741 ± 11164	0.955
Hemoglobin(g/dl)	11.1 ± 1.6	11.5 ± 1.7	0.212
Leucocytes /mm ³	14118 ± 6177	14286 ± 5905	0.836
ALT	69.1 ± 89.6	84.9 ± 122.7	0.942
AST	77 ± 65.7	83.3 ± 121.9	0.440
GGT	103.7 ± 87.2	163 ± 195.7	0.428
SSC index	5.3 ± 1.5	6.6 ±1.7	0.0002

Results are presented as mean ± standard deviation (SD) or number of cases with frequencies

*The percentages in each variable were calculated considering only the number of patients in which the data have been documented.

CONCLUSION

In addition to typical clinical manifestations and MAS, a significant proportion of patients with AOSD develop uncommon or exceptional complications. These should be considered in the evaluation and follow-up of patients, particularly those with chronic or persistent disease progression. Early recognition and prompt management are crucial to significantly reduce morbidity and mortality.

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