Review

Adult onset Still's disease: review of 41 cases

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ABSTRACT

Objective. *To describe the clinical, laboratory and radiological features, treatment and prognosis of patients with adult onset Still's disease (AOSD).*

Methods. *Specific clinical features were retrospectively recorded in 41 patients fulfilling the Yamaguchi criteria. Patients were reviewed in two academic hospitals with a referral area of 700,000–1,000,000 inhabitants. Laboratory tests including haemogram, ferritin, biochemistry and autoimmunity were reviewed. Radiological studies, treatment and ACR functional class were determined.*

Results. *Forty-one patients with AOSD were identified, 25 of whom were female. Mean age at diagnosis: 38.19 years (range 17–68). Feverish polyarthritis was the most common clinical presentation. Acute phase reactants were invariably high in all patients. Serum ferritin levels were elevated in 86% of patients. Anti-cyclic citrullinated peptide antibodies (anti-CCP antibodies) were negative in all patients except one. The course of the disease was monocyclic in 44% of the patients, polycyclic in 26%, and chronic articular in 30%. ACR class was as follows: 29 (72.5%) class I, 7 (17.5%) class II, 2 (5%) class III and 2 (5%) class IV. As for the treatment received, aspirin or NSAIDs controlled the disease in eight patients (19.5%) and high-dose corticosteroids (0.5–1 mg/kg/day) in 32 (78%). Almost half of the patients (49%) required an additional disease-modifying agent, usually methotrexate. Finally, in seven of them (17%) a biological treatment with TNF-α or specially anti-IL-1 had to be added to control the disease.*

Conclusions. *The clinical and laboratory findings were similar to previous studies. Anti-CCP antibodies were almost always negative. A monocyclic course was associated with a good prognosis. Most of the patients were in ACR functional class I and II. Biological agents were required in 7 patients (17%).*

Introduction

Adult onset Still's disease (AOSD) is a rheumatic inflammatory disease of unknown etiology first described by Eric Bywaters (1) in 1971. He reported 14 adult patients with arthritis and systemic features similar to those in systemic juvenile idiopathic arthritis (Still's disease). It was initially recognised as a distinct clinical disorder, but nowadays they are considered the same entity (2). Adult onset Still's disease is not frequent, with prevalence estimated to be lower than 1 case per 100,000 people (3, 4).

Patients typically present with high spiking fever, arthralgia or arthritis, transient maculopapular rash, sore throat, lymphadenopathy, hepatosplenomegaly and serositis. Blood tests usually reveal leukocytosis with neutrophilia, and the rheumatoid factor and antinuclear antibodies are negative (5-13). Diagnosis is difficult, often delayed and established on the basis of a classification criteria set due to the wide range of clinical manifestations and the absence of diagnostic tests. Exclusion of other entities such as sepsis, malignancy and other autoimmune diseases is mandatory (5, 7, 14-16).

In this paper we present a series of 41 patients with AOSD. Clinical, laboratory and radiological features, treatment received, evolution and prognosis in patients with AOSD from two Catalan university hospitals are described.

Patients and methods

Subjects were included if the diagnosis of AOSD occurred between 1984 and 2008. Diagnosis of AOSD was based

on the criteria set by Yamaguchi *et al*. (15), with special attention being given to the serum ferritin value (17). The recent criteria proposed by Fautrel *et al*. (16) were not used because most patients were diagnosed before these criteria were published, and because of a lack of data for glycosylated ferritin. All patients were diagnosed at the rheumatology unit of two university hospitals located in Catalonia, Spain: Hospital Universitari Germans Trias i Pujol de Badalona (Barcelona), with a referral area of 700,000 inhabitants, and Hospital Universitari Bellvitge de l'Hospitalet de Llobregat (Barcelona), with a referral area of 1,000,000 inhabitants. All the patients were followed by the clinical researchers. Two of them retrospectively reviewed the medical records using a standard data extraction form and standardised definitions.

An intermittent fever pattern was defined as a daily elevation of the body temperature above normal with a decrease in the temperature to normal each day. A remittent fever pattern referred to a temperature fall each day, but not to the normal values. Joint involvement was classified according to the number of affected joints within the first 6 months of disease course: oligoarticular if synovitis involved 4 or fewer joints and polyarticular if synovitis involved 5 or more joints. Hepatomegaly and splenomegaly were considered when an enlargement of liver or spleen was confirmed by ultrasound or computer tomography. Lymphadenopathy was defined as the enlargement of lymph nodes in at least 2 different sites. Diagnosis of pericarditis was considered when the patient presented with chest pain with a pericardial rub or an effusion documented by echocardiogram. Pleuritis was identified by the presence of pleuritic pain or pleural effusion.

The following laboratory parameters were analysed at diagnosis and on subsequent visits: complete blood count, erythrocyte sedimentation rate (ESR), ferritin levels, full liver and renal function tests, C-reactive protein (CRP) by nefelometry, rheumatoid factor (nefelometry), antinuclear antibodies (Hep2), C3, C4 (nefelometry). Other investigations to exclude infectious diseases such as cultures and serologies (parvovirus B19, Epstein-Barr virus, cytomegalovirus, salmonella, human immunodeficiency virus, hepatitis B and C virus) were performed. The joint radiographs carried out were reviewed to determine the presence of joint space narrowing, erosions or bony ankylosis. The number of disease relapses in our patients on follow-up was recorded. The clinical course patterns were classified according to those described by Cush *et al*. (5). A cyclical systemic pattern referred to patients in whom systemic disease activity dominated the course of the illness. This was subdivided into a monocyclic pattern, defined as an initial, single systemic flare disease followed by clinical and serological remission; and a polycyclic pattern, which was characterised by 2 or more episodes of systemic relapses with inter-episode clinical and serological remissions that lasted a minimum of 2 months. The chronic articular pattern identified patients in whom articular disease dominated the disease course.

The treatment received during the follow-up was recorded. The treatment regimen was as follows: all patients were initially treated with aspirin or NSAIDs. If articular or systemic symptoms persisted despite NSAIDs, corticosteroids at high doses (0.5–1 mg/kg/day) were added. An antirheumatic agent was added when the combination of NSAIDs and corticosteroids failed, or when a reduction in the requirement for steroids was desired. Finally, in those patients refractory to previous treatments, a biological agent (TNF-α blocker or anti-IL-1) was added.

Moreover, ACR functional class, which is a classification of global functional status in rheumatoid arthritis, was determined in all patients during the last recorded visit.

Results

Forty-one patients with AOSD were identified. All of them had an adult onset and did not have a similar disease in childhood. Twenty-five were female (61%); the female to male ratio was 1.6:1. Mean age at diagnosis was 38.19 years (range 17-68). All of them were Caucasian except for three Hispanic Americans. The clinical presentation was as follows: fevered polyarthritis in 30 (73%), fever and arthralgia in 3 (7.3%), fever and sore throat in 4 (9.7%), fever of unknown origin in 2 (4.8%), fever with rash in 1 (2.4%) and fever and pericarditis in one patient (2.4%).

The clinical features and laboratory results of our AOSD cases are summarised in Table 1. A high spiking fever (>39ºC) with 1 or 2 spikes daily was reported by all patients. Fever was intermittent in 32 patients (78%) and remittent in 9 (22%). The typical salmon-pink maculopapular exanthema was present in 38 patients (92.6%). In most patients it was evanescent, non-itchy and occurred during fever. The most common sites of involvement were the trunk and limbs, although in 4 cases (9.7%) the face was also involved. Symptoms were preceded by sore throat in 37 patients (90.2%). Almost all patients, 40 (97.5%), had polyarthralgia and 36 (88%) had arthritis, with a polyarticular involvement in 29 (80.5%) and oligoarticular in 7 (19.5%) cases. Joint involvement was especially common in wrists, knees and ankles. The frequency of the joints involved is shown in Table II. Arthrocentesis was performed in 6 patients (14.5%) and synovial fluid analysis revealed a cell count >5,000/mm^3 with predominance of neutrophils in all patients. A synovial biopsy was also performed in one patient, showing a chronic unspecific synovitis with focal synovial hyperplasia. Lymph node enlargement was detected in 17 patients (41.4%); the cervical region was the most common site of localisation followed by the axilar and inguinal region. A lymph node biopsy was performed in 6 patients and indicated reactive lymphadenitis with non-malignant cellular infiltrates. Hepatomegaly was found in 9 patients (22%) and splenomegaly in 7 (17%). In two patients suspected to have other diseases a liver biopsy was performed, showing minimal changes without granulomas. Abdominal pain was present in 4 patients (9%); all had elevated serum liver enzymes but just one had hepatosplenomegaly. A pleural effusion, usually small, occurred in six

Table I. Clinical manifestations of cases of AOSD in the current series and other reported series.

Clinical Manifestations	Cush *et al*.[5] (n=21) n. (%)	Wouters *et al*.[6] (n=45) n. (%)	Reginato *et al*.[7] (n=23) n. (%)	Ohta *et al*.[8] (n=90) n. (%)	Pouchot *et al*.[9] (n=62) n. (%)	Mok *et al*.[10] (n=16) n. (%)	Appenzeller *et al*.[11] (n=16) n. (%)	Our series (n=41) n. (%)
Fever	21 (100)	38 (84)	23 (100)	90 (100)	62 (100)	15 (94)	16 (100)	41 (100)
Arthralgia	–	–	–	86 (96)	–	16 (100)	16 (100)	40 (97.5)
Arthritis	21 (100)	44 (98)	23 (100)	90 (100)	44 (98)	15 (94)	16 (100)	36 (88)
Myalgia	16 (76)	–	8 (25)	50 (56)	52 (84)	7 (44)	8 (50)	–
Constitutional syndrome	14 (67)	38 (84)	–	40 (56)	41 (76)	11 (69)	6 (37'5)	–
Rash	16 (86)	37 (82)	22 (96)	72 (87)	54 (87)	14 (88)	16 (100)	38 (92.6)
Sore throat	19 (90)	19/28 (68)	21 (91)	53 (70)	57 (92)	10 (63)	9 (56)	37 (90.2)
Lymphadenopathy	19 (90)	32 (71)	12 (52)	59 (69)	46 (74)	6 (38)	8 (50)	17 (41.4)
Hepatomegaly	8 (38)	–	6 (23)	42 (48)	27 (44)	7 (44)	13 (81)	9 (22)
Splenomegaly	11 (52)	16 (36)	5 (22)	56 (65)	34 (55)	6 (38)	5 (31.2)	7 (17)
Abdominal pain	10 (48)	–	2 (9)	–	30 (48)	–	7 (43.8)	4 (9.7)
Pleuritis	11 (53)	14 (31)	7 (30)	11 (89)	33 (53)	3 (19)	1 (6.3)	6 (14.6)
Pericarditis	7 (33)	10 (22)	3 (23)	9 (10)	23 (37)	3 (19)	2 (12.6)	5 (12)

Table II. Distribution of arthritis in our 41 patients with AOSD.

Joint	n. (%)
Wrist	26 (63)
Knee	25 (61)
Ankle	13 (32)
Shoulder	11 (27)
MCP	11 (27)
Elbow	9 (22)
Hip	8 (20)
PIP	8 (20)
MTP	2 (5)
DIP	1 (2)
Tarsus	1 (2)
Cervical	1 (2)
Temporomandibular	1 (2)

MCP: metacarpophalangeal joint; PIP: proximal interphalangeal joint; MTP: metatarsophalangeal joint; DIP: distal interphalangeal joint.

Table III. Laboratory results of cases of AOSD in the current and previous series.

Laboratory features	Wouters *et al*.[6] n=45 n. (%)	Ohta *et al*.[8] n=90 n. (%)	Pouchot *et al*.[9] n=62 n. (%)	Mok *et al*.[10] n=16 n. (%)	Our series n=41 n. (%)
WBC (x 10^9 / L)					
>10	44 (98)	80 (85)	58 (94)	16 (100)	38 (93)
>15	24 (35)	–	50 (81)	12 (75)	16 (39)
>20	–	–	–	10 (63)	9 (22)
>30	–	–	–	–	4 (10)
Elevated ESR (>40 mm/h)	45 (100)	85/89 (96)	62 (100)	16 (100)	41 (100)
Hb <12 (g/dl)	–	–	–	–	27 (65)
Hb <10 (g/dl)	–	53 (59)	–	11 (69)	10 (24)
Hyperferritinemia					
>5 x normal	–	22/32 (69)	–	9/10 (90)	19/37 (51)
>60 x normal	–	–	–	4/10 (40)	11/37 (30)
CRP (normal <1 mg/dl)	–	–	–	11 (69)	41 (100)
Elevated hepatic enzymes	38 (64)	74/87 (85)	47 (78)	15 (94)	21 (51)
Negative RF	43 (96)	84/89 (94)	58 (94)	16 (100)	41 (100)
Negative ANA	43 (96)	88/88 (94)	55 (89)	14 (88)	41 (100)

patients (14.5%); all of them had pleuritic chest pain. A thoracocentesis was performed in two patients and revealed a sterile exudate in both. Finally, pulmonary infiltrates were reported in 2 patients (5%), both with alveolitis and focal areas of interstitial fibrosis. Pericarditis was documented in 5 patients (12%); all of them had concomitant pleural effusion and none developed pericardial tamponade. None of our patients developed a macrophagic activation syndrome.

The results of selected laboratory tests are summarised in Table III. Thirty-eight patients (92%) presented leukocytosis (range 5.8-36.2x10^9/L). Sixteen patients (39%) had a leukocyte count above 15x10^9/L, 9 patients (22%) were above 20x10^9/L and 4 patients (10%) above 30x10^9/L. Thirty-six patients (88%) had neutrophilia. A bone marrow aspirate was performed in three patients. It was normal in the first two and revealed a reactive bone marrow in the third, in which the bone marrow biopsy found a mild granulocytic and eosinophylic hyperplasia; hemophagocytosis was not reported in any patient. A normochromic normocyte anemia (Hb<12 g/dl) was found in 27 patients (65%); and 10 of them (24%) had a hemoglobin count below 10 g/dl. Serum ferritin levels were present in 37 patients and were high in 32 of them (86%). The mean ferritin level was 6783. ng/ml (range 68-85,000). All patients had an elevation of ESR and CRP. The mean ESR was 89 mm/1h (range 29-140) and the mean CRP was 130 mg/L (range 5-408). Liver function abnormalities were detected in 21 patients (51%); five patients had elevated liver parenchymal enzymes (AST or ALT), four patients had elevated ductal enzymes (alkaline phosphatase or GGT) and 12 patients had both. The rheumatoid factor and ANA were negative in all patients. Anti-cyclic citrullinated peptide antibody counts were performed in 23 patients (56%) and were negative in all except for one patient (4.3%) who had coxitis at the moment of the revision. This patient has a chronic articular pattern with polycyclic systemic flares, and does not fulfill rheumatoid arthritis criteria.

Joint radiographs performed at initial evaluation were normal in most cases, except for some cases where swelling

of soft tissue was observed. At the moment of the review bone erosions were observed in 4 patients (10%), especially in wrist and hip; carpal ankylosis was observed in 4 patients (10%) and hip ankylosis in 4 patients (10%).

As to the treatment received (Table IV), all patients were initially treated with aspirin (AAS) or NSAIDs (mostly indomethacin). This regimen of therapy controlled the disease in 8 patients, which means a response rate of 19.5%. Corticosteroids at high doses (0.5-1mg/kg/day) were added to NSAIDs at some point during the course of the disease in 32 patients (78%) and helped to control the systemic and joint disease in 12 patients (37.5%). A disease-modifying antirheumatic drug had to be added in 20 patients (49%) either due to inefficiency of corticosteroids (especially in chronic articular disease) or in order to reduce their dose. In 15 patients (36.5%) the first DMARD used was methotrexate with a response rate of 66.6% (10/15 patients). In 5 patients several DMARDs in succession were used: gold salts (2 patients), salazopyrin (1 patient), cyclosporine A (1 patient), azathioprine (1 patient), hydroxychloroquine (1 patient), leflunomide (1 patient). None of these DMARDs were effective and methotrexate was needed. Finally, in seven patients (17%) refractory to previous drug treatment, a biological treatment was added (TNF-α blocker or anakinra); five of them had only been treated with methotrexate and two had been treated with several DMARDs including methotrexate. Five patients received a TNF-α blocker that was effective in 2 patients (1 adalimumab and 1 etanercept) and had to be changed to anakinra in 3 patients (3 infliximab). Anakinra was used in 5 patients; as a first biological treatment in two and after a TNF-α blocker failure in three, and induced remission in all of them (5/5, 100%). None of our patients was treated with intravenous immunoglobulin or tocilizumab.

The course of the disease was monocyclic in 18 patients (44%), polycyclic in 11 patients (26%), and chronic articular in 12 patients (30%). Even though there are differences in the duration of follow-up between the subjects of the three groups, all patients were followed up for at least 12 months. Only one patient with a self-limited disease was lost after 14 months' follow-up in remission and without treatment.

Table IV. Treatment received and response rates in AOSD.

Treatment	Patients n. (%)	Response n. (%)
NSAID	41 (100)	8 (19.5)
Prednisone	32 (78)	12 (37.5)
Methotrexate	20 (49)	13 (65)
Leflunomide	1 (2.4)	0 (0)
Azathioprine	1 (2.4)	0 (0)
Hydroxychloroquine	1 (2.4)	0 (0)
Salazopyrin	1 (2.4)	0 (0)
Cyclosporine A	1 (2.4)	0 (0)
Infliximab	3 (7.3)	0 (0)
Etanercept	2 (4.8)	1 (50)
Adalimumab	1 (2.4)	1 (100)
Anakinra	5 (12)	5 (100)

The mean follow-up time of our patients was 112.85 months (standard deviation 60 months). Currently 17 patients (42.5%) are free of disease without treatment. The mean duration of disease of this group of patients is 114.74 months with standard deviation (SD) of 105.65 months, and they have been totally asymptomatic for a mean of 72.55 months (SD 30.75). Of these, fifteen patients had a monocyclic pattern and two a polycyclic one.

Twenty-three patients (57.5%) still need treatments to control the disease. The mean duration of disease of these patients is 110.96 months (SD 70.22). Three patients are being treated with AAS, 8 with NSAIDs, prednisone and methotrexate, 4 with methotrexate alone and 7 with NSAIDs, prednisone, methotrexate and biological treatment. Of these, two patients have presented a monocyclic course, 9 a polycyclic course, and 12 a chronic articular course.

During the follow-up different comorbid conditions were recorded: 29 drug-related events (mainly linked to corticosteroids) and 8 infectious events. Some of them were mild and related to corticosteroids, such as corticoid acne (1 patient), dyslipidemia (2 patients), hyperglycemias (4 patients), and Cushing syndrome (14 patients); in all cases, the symptoms resolved when corticosteroids were withdrawn. Five patients had fragility fractures. 4 of them were women in postmenopausal age and had at least one vertebral fracture. One woman had two femoral fractures (at the age of 67 and 69) and another had a Colles fracture and ischiatic branch fracture (at the age of 58 and 59 respectively). The only man with a fracture was 30 years old and had an acetabular fracture in relation to a very erosive hip arthritis with a normal bone densitometry. Finally, in relation to corticosteroids, 4 women were diagnosed as having proximal myopathy with a compatible electromyography. Besides drug-related adverse effects, infections were also present. Two patients were diagnosed with ocular herpes that resolved with topic treatment. Three severe systemic infections were reported: one disseminated herpes zoster that required intravenous antiviral treatment and two Legionella infections; one was a nosocomial pneumonia and the other was a community-acquired pneumonia. Both of them resolved with appropriate antibiotics. In all cases, patients were on treatment with an immunosuppressive drug that was temporarily withdrawn. Three out of 41 patients were of Hispanic-American origin, and all of them had a *Salmonella enteritidis* bacteraemia while on immunosuppressive treatment; two of them had a symptomatic severe gastroenteritis that coursed with hypovolemic shock and required admission to the intensive care unit.

Finally, two other co-morbid conditions related to the disease itself were recorded: one patient had an asymptomatic AA amyloidosis, and one patient needed a total hip arthroplasty in both hips due to severe ankylosis.

Disability in our patients was determined primarily by the course of the arthritis, using the ACR functional class. At the last evaluation the ACR class was as follows: 29 patients (72.5%) in class I, 7 (17.5%) in class II, 2 (5%) in class III and 2 (5%) in class IV.

Discussion

We present a series of 41 patients afflicted with adult onset Still's disease, diagnosed and treated in two Catalan hospitals. The most common clinical features were fever, arthritis and exanthema. The fever was present in every single patient, being the most characteristic and needed sign for diagnostic purposes. Fevered polyarthritis was the most common clinical presentation, and the joints most involved were wrists, knees and ankles. The joint radiographs revealed erosions and ankylosis in 4 patients each. Typical exanthema was present in 92% of the patients, being a major criterion needed for diagnosis. The prevalence of clinical manifestations in our series is similar to that observed by other authors. Most notably, there was a large prevalence of sore throat as in other series (5, 7, 9) and, as reported by the Chinese (10) and Brazilian (11) studies, a lower incidence of pleuritis and pericarditis compared to American (5) and European (9) studies. The joints affected are similar, as are the radiological findings, especially a carpal ankylosis which is a well-known articular sequel of AOSD with carpometacarpal and intercarpal fusion and a pericapitate involvement without associated radiocarpal alterations (18).

Regarding the laboratory tests, leukocytosis with neutrophilia, elevation of acute phase reactants (ESR, CRP and ferritin), anemia of chronic disease and abnormalities in liver function were usually present. No major discrepancies in the laboratory results were observed between our patients and other series. We want to emphasise the important role of the serum ferritin level, which seems to be critical in this disease, because it can be used not only as an indicator of disease activity but also as a diagnostic marker, as reported (19-21). The glycosylated ferritin, an isoform of serum ferritin, has also been proposed as an AOSD diagnostic marker (22). This glycosylated component may be potentially more useful in clinical practice since its level is relatively constant over time and appears to be independent of fluctuations in disease activity (22). A new set of classification criteria for AOSD have been proposed, including glycosylated ferritin as a major criterion that provides higher sensitivity and specificity without requiring exclusion criteria (23). Lastly, some of our patients (56%) were tested for anti-cyclic citrullinated peptide antibodies (ACCP). This is the first report of a series of patients with AOSD in which these antibodies have been determined. All were negative except in one patient who had a chronic articular pattern with a severe erosive arthritis. The precise role of ACCP in AOSD requires prospective studies and large cohorts; however our results suggest that they are usually negative.

The optimal treatment strategy of AOSD is difficult to determine because of the absence of large-scale prospective studies. Moreover, the response to treatment in different series is hard to compare because of heterogeneity of diagnostic criteria, lack of long-term controlled studies, the small number of patients involved and the remittent nature of the disease. The objective of the treatment is to induce remission of the systemic symptoms and avoid progression of the disease, especially chronic arthritis. We observed a response rate to NSAIDs of 20% which is quite more than previous studies, where the efficiency rate of NSAIDs was around 7–15% of cases (8, 9, 24) probably due to a greater percentage of patients with a monocyclic course. As in other series, around 80% of the patients required corticosteroids, but there was a positive response in 38% of them. There are only 2 studies where the response rate to corticosteroids is defined, ranging from 46 to 76% (6, 24). Methotrexate in a mean dose of 15 mg/week (range 7.5–20 mg/week) was effective in up to 65% of the patients, while other DMARDs used were all ineffective. The response rate to DMARDs is also variable in the existing literature from 44 to 88% (6, 25) but is higher when the DMARD is methotrexate (around 66–88% (24-26)). Finally, we observed an excellent response to anakinra (5/5) even in patients refractory to TNF-α blockers in concordance to the literature (27). The response to TNF-α blockers in our series was variable. Infliximab could not control the disease in any of the 3 patients, while the overall response rate published in eleven studies (44 patients) is up to 91% of the cases (28). Etanercept was effective in one patient (1/2, 50%) but the other one required anakinra. Again, the overall response rate of 25 patients from 5 studies is up to 72% (28). Lastly, there is a single case report referring to clinical improvement with adalimumab in disease refractory to methotrexate and corticosteroids (29), the same as our single case.

As described, those patients who respond frequently to NSAIDs or systemic corticosteroids had a good prognosis with monocyclic or polycyclic course (9). This is in agreement with our data, in which most of the patients who at the time of revision were free of treatment, had had a self-limiting course; while those patients that where still on treatment had had a polycyclic or chronic articular course.

In our series, the outcome of articular involvement measured by the ACR functional class is worse than a series by Pouchot *et al*. (9) where, despite the fact that 35% of the patients had a chronic disease course, at follow-up 90% of patients were in ACR class I, only 6.4% in class II and 3% in class III, and no patient was in ACR class IV. In contrast, when compared to a previous series by Wouters *et al*. (6), the outcome of articular involvement is better.

In summary, we describe the clinical presentation, treatment, comorbidity and outcome of a series of patients with AOSD in Catalonia (Spain). The clinical spectrum and laboratory tests were similar, with mild differences to other series. The differences may be attributed to methodological factors in addition to ethnic ones. Moreover, comparison with other published series is very difficult and misleading because of the various diagnostic criteria used. Anticyclic citrullinated peptide antibodies

are usually negative. Seven patients (17%) required a biological agent and the response to anakinra was excellent. Prognosis seems to be good, with just 2 patients in ACR class III (5%) and 2 patients in class IV (5%).

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