

# Adult-onset Still's disease: clinical, serological and therapeutic considerations

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## Abstract

### Objectives

*This paper aims to describe the clinical manifestations, laboratory abnormalities and treatment of adult-onset Still's disease (AOSD) in Greek patients.*

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### Methods

*This is a retrospective observational study. Forty-four patients, diagnosed with AOSD, followed since 1985 up to June 2011, were included. The disease course and treatment were recorded and compared to previously published studies.*

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### Results

*Twenty-one males and 23 females were identified. Mean age at diagnosis was 38.3 years. The most common clinical manifestations were fever (100%), arthralgias (97.7%), arthritis (93.2%), salmon-coloured rash (84%), myalgias (50%) and sore throat (38.6%). Characteristic laboratory abnormalities were leucocytosis with neutrophilia (81.8%), elevated C-reactive protein (100%) and erythrocyte sedimentation rate (100%). Elevated liver enzymes and hyperferritinaemia were found in 50% and in 59% of the patients respectively. Very high ferritin serum levels ( $>5000 \mu\text{g/l}$ ) were found in 22.7%. Rheumatoid factor and antinuclear antibodies were negative in all patients. Thirty patients (68.2%) received non-steroidal anti-inflammatory drugs or aspirin with or without corticosteroids. Response to corticosteroids was common (58.9%). When this treatment was ineffective, a disease-modifying anti-rheumatic drug (DMARD), usually methotrexate, was added with a response rate of 63.6%. Anakinra was used in cases resistant to conventional immunosuppressive treatment. Ten out of 44 patients (22.7%) were treated with anakinra and response was achieved in all of them.*

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### Conclusion

*Our results regarding clinical manifestations and laboratory abnormalities were similar to those of previous reports. High ferritin serum levels were reported in all studies of AOSD and are considered as diagnostically valuable. When treatment with corticosteroids and DMARDS had failed, biologic agents such as anakinra were successfully applied.*

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### Key words

adult-onset Still's disease, corticosteroids, methotrexate, C-reactive protein, anakinra

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## Introduction

Adult-onset Still's disease (AOSD) is a multisystem inflammatory disease of unknown etiology (1-3). Although some factors, such as genetic predisposition, infectious agents, immune-complexes and stress have been implicated, the exact pathophysiological mechanism has not been fully elucidated (2). It is a rare disease with an annual incidence of 0.16 cases per 100,000 people (4). In most studies both genders are affected equally (2, 4). There is a bimodal age distribution, with one peak between the ages of 15 and 25, and the other between the ages of 36 and 46 (2, 4). However, it may affect older people as well (2).

AOSD typically begins with spiking fever that often exceeds 39°C, a characteristic but evanescent rash, arthralgias or true arthritis, myalgias and sore throat (1-3). A common mode of onset is fever of unknown origin (2). Other frequent clinical manifestations are lymphadenopathy, hepatomegaly or splenomegaly and serositis (pleurisy, pericarditis) (1-3). The most common laboratory abnormalities of AOSD are leucocytosis with neutrophilia, elevated acute phase reactants, such as C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR), elevated liver enzymes and serum ferritin levels (1-3). Antinuclear antibodies (ANA) and rheumatoid factor (RF) are negative in most cases (1-3). The course of AOSD can be monophasic, recurrent or chronic (1, 3).

Regarding treatment, non-steroidal anti-inflammatory drugs (NSAIDs), aspirin and corticosteroids are used as first line agents. When corticosteroids are ineffective, disease-modifying anti-rheumatic drugs (DMARDs) such as methotrexate (MTX) are added (1-3). Biologic agents such as tumour necrosis factor (TNF- $\alpha$ ) blockers, rituximab, anakinra and tocilizumab, although not formally approved for AOSD, have been reported to be effective in cases resistant to conventional immunosuppressive treatment (5-17). Anakinra, a recombinant human interleukin (IL) 1 receptor antagonist, and tocilizumab, a humanised monoclonal antibody against IL-6 receptor, seem to be most promising in cases of refractory AOSD (2, 3).

This is a retrospective study of clinical and laboratory manifestations, treatment modalities applied and outcome in Greek patients with AOSD. The findings are compared to those of other populations (18-24).

## Methods

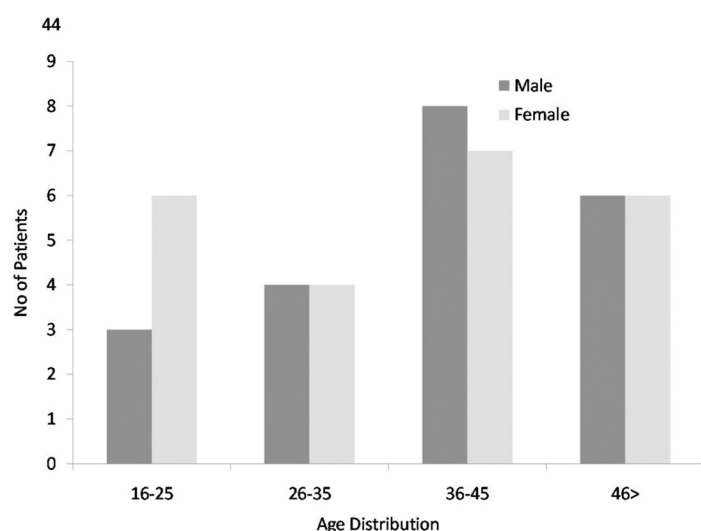
We retrospectively reviewed the medical files of all patients diagnosed with AOSD and followed by the Rheumatology Clinic of the University Hospital of Ioannina between 1985 and June 2011. Forty-four patients who satisfied Yamaguchi (25), Fautrel (26) or Cush (27) criteria for AOSD were identified. Clinical symptoms and signs as well as laboratory abnormalities were recorded. Disease activity was estimated according to modified Pouchot score (28), at disease onset, and one year later, so correlations between disease activity and its progression or treatment's efficacy could be made. Modified Pouchot score includes twelve characteristics of the disease clinical and laboratory parameters. These are: fever, evanescent rash, sore throat, arthritis, myalgias, pleuritis, pericarditis, pneumonitis, lymphadenopathy, hepatomegaly or abnormal liver function tests, leucocytosis  $>15,000/\mu\text{l}$  and serum ferritin  $>3,000 \mu\text{g/l}$ . Medications used response to treatment and long-term outcomes were also recorded and compared to those of previous studies (18-24).

## Results

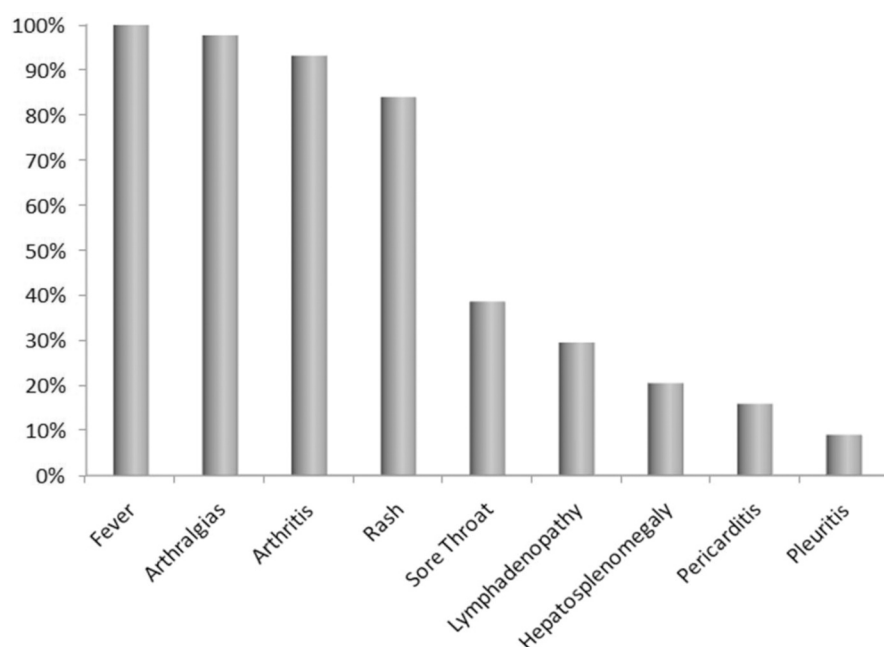
### Epidemiology

The 44 patients were 21 males and 23 females. All patients were Caucasian. Mean age at diagnosis was 38.3 years old (median 37, range 16–78 years). Age distribution at disease onset was as follows: 9 patients between 16 and 25 years old, 8 patients 26–35 years old, 15 patients 36–45 years old and 12 patients 46 years old or older. Of the last group, the oldest patient was 54 years old except one, who was 78 years old at the time of onset (Fig. 1). The mean time between symptom onset and diagnosis was 3.5 months (median 2, range 0.5–6 months). Half of the cases were initially described as fever of unknown origin.

Competing interests: none declared.



**Fig. 1.** Age distribution of adult-onset Still's disease.



**Fig. 2.** Main clinical manifestations of adult-onset Still's disease at onset.

### Clinical manifestations

The main clinical features are illustrated in Figure 2 and Table I. Fever  $>39^{\circ}\text{C}$  occurred at the onset of the disease in all patients. In most cases, it was characterised by spikes and accompanied by shaking chills and sweating. Typical salmon-coloured macular or maculopapular rash was present in 37 patients (84%). It usually affected the trunk and extremities and was short-lived, coinciding with the febrile spikes. In two patients, brisk dermographism was noted and one patient had subcutaneous nodules. Sore throat was an onset symptom in 17 patients (38.6%).

Arthralgias was a universal symptom and affected 43 patients (97.7%). Arthritis was present in 41 patients (93.2%). In 33 cases (75%) arthritis was symmetric or migratory and mainly involved the large joints, most often wrists, knees and ankles. Shoulder involvement was present in 7 patients (15.9%), while hip involvement was reported in 5 patients (11.4%). Involvement of shoulders and hips was associated with more severe course of the disease. Arthritis of temporomandibular joint developed in one patient. Small joints of hands and feet were involved in 20 cases (45.5%). Radiological findings were joint space

narrowing of the intercarpal and the carpometacarpal joints. True erosive disease was not observed. The erosive disease was estimated using x-rays to all patients. Myalgias were reported by 22 patients (50%). Lymphadenopathy occurred in 13 patients (29.5%). A lymph node biopsy was performed in 5 patients that showed non-specific reactive lymphadenopathy without evidence of malignancy. A bone marrow biopsy was performed in 6 patients. In three of them it showed no pathological changes, while in the rest a reactive bone marrow was noted. Hepatosplenomegaly was present in 9 patients (20.5%) using ultrasound evaluation and computed tomography. Abdominal ultrasound revealed homogeneous liver parenchyma or fatty infiltration. Pericarditis occurred in 7 patients (15.9%), and pleural effusion in 4 (9%). Other less common symptoms present at the disease onset were: headache in three patients, Raynaud's phenomenon in two patients, cough in another two patients, vomiting, diarrhea and abdominal pain in one patient and dysphagia, mouth ulcers and conjunctivitis in one patient each. None of our patients developed macrophage activation syndrome, a rare but life-threatening complication of AOSD.

### Laboratory findings

One of the most common laboratory abnormalities in AOSD is leucocytosis with predominance of neutrophils. Leucocytosis was present in 36 patients (81.8%). Leucocytes were more than  $15,000/\text{mm}^3$  in 16 patients (36.4%) and more than  $10,000/\text{mm}^3$ , but less than  $15,000/\text{mm}^3$  in 20 patients (45.5%). Anaemia and thrombocytosis were found in equal proportion – in 8 patients (18.2%) each. Elevated liver enzymes were found in 22 patients (50%). CRP and ESR were increased in all patients (100%).

Elevated ferritin levels were found in 26 patients (59.1%). The highest value recorded was  $20,323 \mu\text{g/l}$ . Ferritin levels up to 2 times normal were found in 7.7%, from 2 to 5 times over normal in 42.3%, from 5 to 10 times over normal in 27%, and 10 times and more over normal in 23% of the patients. The mean

**Table I.** Clinical manifestations at the onset of adult-onset Still's disease and comparison with published literature.

Clinical manifestations (%)	Present study (n=44)	Jiang (18) (n=70)	Riera (19) (n=41)	Colina (20) (n=76)	Kong (21) (n=104)	Cagatay (22) (n=84)	Mehrpoor (23) (n=28)	Appenzeller (24) (n=16)
Fever	100	94.3	100	100	100	95.2	100	100
Rash	84	75.7	92.6	58	95	59.5	85	100
Arthralgias	97.7	80	97.5	72	–	96.4	92	100
Arthritis	93.2	–	88	72	90	69	60	100
Myalgias	50	41.4	–	13	–	–	–	50
Sore throat	38.6	72.8	90.2	37	–	65.5	83	56
Lymphadenopathy	29.5	–	41.4	–	66	33.3	57	50
Hepatomegaly	20.5	–	22	–	44	–	–	81
Splenomegaly	20.5	–	17	–	44	28.6	32	31.2
Pericarditis	15.9	–	12	–	–	11.9	21	12.6
Pleurisy	9	–	14.6	–	–	–	–	6.3

ferritin level was 4,483 µg/l, while the median value was 1,382µg/l. ANA and RF were negative in all patients. Main laboratory findings from our and other series are shown on Table II.

#### Disease activity score

According to modified Pouchot score (28) at disease onset, our patients are distributed as follows: score 3 was found in 2 patients (4.5%), score 4 in 8 patients (18.2%), score 5 in 17 patients (38.6%), score 6 in 8 patients (18.2%), score 7 in 6 patients (13.6%), and finally 3 patients (6.8%) had disease score activity 8 at onset. Mean modified Pouchot score at disease onset among our patients, was estimated 5.44. One year later, the modified Pouchot score is distributed as follows: 0 in 43.5% of the patients, 1 in 43.5%, and 2 in 13% of them, with mean disease activity score of 0.57.

#### Treatment and outcome

Thirty patients (68.2%) were treated with NSAIDs including aspirin, and 39 patients (88.6%) were treated with corticosteroids with or without concomitant NSAIDs. DMARDs were added to corticosteroids in resistant cases. Eleven patients (25%) received MTX, while cyclosporine A (CsA) was prescribed to 8 patients (18.2%) who were not suitable for or intolerant to MTX. Response, which was defined as remission of systemic manifestations (fever, rash, raised inflammatory markers) and arthritis, was attained by 58.9% of patients treated with corticosteroids. MTX produced a response in 63.6% and CsA in 50% of treated patients. NSAID monotherapy

**Table II.** Laboratory findings in adult-onset Still's disease in the present and previous studies.

Parameter*	Present study (n=44)	Riera (19) (n=41)	Kong (21) (n=104)
Leucocytosis			
White blood cell >10,000/mm <sup>3</sup>	36 (81.8)	38 (92.7)	103 (99.0)
White blood cell >15,000/mm <sup>3</sup>	16 (36.4)	16 (39.0)	
Anaemia	8 (18.2)	27 (65.9)	72 (69.2)
Thrombocytosis	8 (18.2)		27 (26.0)
Elevated liver enzymes	22 (50.0)	21 (51.2)	67 (64.4)
Elevated C-reactive protein	44 (100)	41 (100)	86 (82.7)
Elevated erythrocyte sedimentation rate (>40 mm/h)	44 (100)	41 (100)	91 (87.5)
Hyperferritinaemia	26 (59.1)	19 (46.3)	

\*Values are number of patients (%).

**Table III.** The adult-onset Still's disease treatment and response in our series.

Treatment	Patients n (%)	Response n (%)
Non-steroidal anti-inflammatory drugs / Aspirin	30 (68.2)	9 (30.0)
Corticosteroids	39 (88.6)	23 (58.9)
Methotrexate	11 (25.0)	7 (63.6)
Cyclosporine A	8 (18.2)	4 (50.0)
Anakinra	10 (22.7)	10 (100)

was efficacious in a minority of patients (13.6%). Anakinra, an IL-1 blocking agent, was introduced at a dose of 100 mg per day in 10 patients (22.7%) who were resistant to treatment with corticosteroids and DMARDs. Clinical remission and corticosteroid tapering were achieved in all of them. Excluding treatment failure/active disease, no major adverse events (requiring hospitalisation, life-threatening or fatal) related to treatment were recorded during follow-up. The treatment applied to our patients and the response rates are shown in Table III.

In association with the modified Pouchot score (28), the treatment provided to our patients could be distributed as

follows: all patients with score 3 or 4 at disease onset received only corticosteroids and NSAIDs as a treatment, and they experienced a fairly good response. In the group of modified Pouchot score 5 or 6, the mentioned treatment with corticosteroids and NSAIDs was proved to be sufficient to half of patients. In the other half, it was necessary to add a conventional DMARD (MTX or CsA), and only two of them (one from each score group 5, 6) needed a biologic agent (anakinra). Finally, all patients with high score (7 or 8), had to be treated with combination of corticosteroids, NSAIDs, conventional DMARDs and/or anakinra.

In our study, the course of the disease

was monophasic in 18 patients (40.9%), who went into complete remission within the first two years of the disease onset. In the rest of the patients the disease ran a polyphasic or chronic course and the patients were maintained on long-term treatment to control the disease. However, after a median follow-up of 7 (range 2–19) years, most of them (85.3%) had a good functional status, absent systemic features and none or mild articular symptoms.

## Discussion

Adult-onset Still's disease is a rare systemic inflammatory disease of unknown cause and a worldwide distribution (2). We present a series of 44 patients with AOSD diagnosed and treated in our clinic. In this study, male and female genders were equally affected and the disease onset occurred both in young and middle-aged patients. These results are similar to the already reported ones (18–24).

Feverish polyarthritis with evanescent rash was the most common clinical presentation. Other features such as sore throat, arthritis, arthralgias, myalgias, lymphadenopathy and hepatosplenomegaly were also quite common. AOSD should be suspected in patients with fever of unknown origin and myoskeletal complaints or arthritis (2). However, as AOSD is a diagnosis of exclusion, infections and malignancies should also be excluded, due to similar clinical presentations in some cases (1, 2, 18–21, 23). Regarding the clinical features of AOSD, our results are similar to those previously reported. The most common clinical features such as fever, arthritis, arthralgias, myalgias and the typical rash appeared in similar rates. We found a lower rate of sore throat (38.6%) than in other series, but similar to that reported in an Italian study (20). This might be due to a common genetic background and/or environmental factors. Conversely, Spanish patients developed sore throat in higher rates (19) than Greeks and Italians. Lymphadenopathy was reported in similar rates in the Spanish (19) and Turkish (22) studies, but it was found twice as frequent in Chinese (21) and Iranian (23) studies. Hepatosplenomegaly was also reported

twice as frequently in Chinese (21) and Brazilian (24) patients. Genetic diversity, environmental factors or even random variation might again account for the observed differences in the clinical presentation. Regarding laboratory findings, leucocytosis with neutrophilia was noted in a high proportion in several studies, including our own. Elevated acute phase reactants (CRP and ESR) are common features of AOSD. High CRP and ESR were reported in 100% of our patients. Anaemia was reported in 18.2% of our patients, much less frequently than in the Spanish (66%) and Chinese (69%) series (19, 21). Liver enzyme abnormalities were reported in similar rates in our and previous studies. Hyperferritinaemia (up to 5 times above normal) is a common feature at the disease onset and it may be normalised with treatment or in periods of remission (18–24). Serum ferritin levels were significantly higher in patients with AOSD than in patients with different disease entities including infectious, malignant, haematologic or other autoimmune diseases (29). In our study, the mean serum ferritin level was 4,483 µg/l. In several studies, very high levels of serum ferritin (>5,000 µg/l) have been suggested as a significant diagnostic and prognostic marker for AOSD and have been proposed to be used as criteria of AOSD (30, 31). RF and ANA, which are negative in AOSD almost by definition (1–3, 25–27), were also negative in the whole of our patients.

Regarding the disease activity score (28), most patients were presented with quite high score (mean score: 5.44 at onset, but one year later a significant reduction was noticed [mean score: 0.57]). This could be explained by early diagnosis and early and appropriate therapeutic intervention. It should be noted that a more aggressive treatment such as conventional DMARDs and biologic agents is related to greater reduction, up to zero, of disease activity score.

Concerning treatment of AOSD, NSAIDs, aspirin and corticosteroids were used as first-line therapy in our study as well as in previous studies (1–3, 19–24). Although in our series, the response rate to NSAIDs was higher than in other reports (2) it should be

noted that in most cases NSAIDs were combined with corticosteroids. When treatment with corticosteroids had failed, DMARDs were used. There was a 63.6% response rate to treatment with MTX. In line with previous reports (1–3, 19–24, 32) MTX was effective in controlling AOSD symptoms and allowing corticosteroid tapering. CsA was effective in 50% of our patients who were treated with this agent. Its effectiveness varies in different studies (1–3, 19–24, 33, 34).

Several reports have been published supporting the use of biologic agents for attainment of clinical remission, normalisation of laboratory markers such as CRP, ESR, leucocyte counts and serum ferritin levels, and for corticosteroid tapering (1–3, 5–17, 19–24, 34). In our series, anakinra was the only biologic agent prescribed in case of corticosteroid and DMARD failure and was proven effective in all cases. Anakinra has been reported to be efficacious in several studies as well (1–3, 5–8, 19–24). Other biological agents such as TNF-blockers (14–16), tocilizumab (9–13) and rituximab (17) have also been successfully used in previous studies. However, most consistently anakinra and tocilizumab appeared to be the most effective and most promising biologic agents so far for the treatment of refractory AOSD (5–13).

AOSD is a multisystem inflammatory disease of unknown cause. High fever, rash, arthralgia/arthritis, myalgias and sore throat are the most frequent clinical manifestations. Fever of unknown origin is a common presentation of AOSD. Leucocytosis with neutrophilia and elevated acute phase reactants are usual laboratory abnormalities. Differential diagnosis from infections and malignancies should be made and high serum ferritin levels may be a useful tool for differentiation. When treatment with NSAIDs and/or corticosteroids fails, conventional DMARDs and ultimately biologic agents may be helpful in treating these patients. However, prospective studies are needed to identify baseline predictive factors of persistent disease and to evaluate effectiveness, safety and appropriate place of the various therapeutic modalities available so far.



## References

- BAGNARI V, COLINA M, CIANCIO G, GOVONI M, TROTTA F: Adult-onset Still's disease. *Rheumatol Int* 2010; 30: 855-62.
- OWLIA MB, MEHRPOOR G: Adult-onset Still's disease: a review. *Indian J Med Sci* 2009; 63: 207-21.
- FAUTREL B: Adult-onset Still disease. *Best Pract Res Clin Rheumatol* 2008; 22: 773-92.
- MAGADUR-JOLY G, BILLAUD E, BARRIER JH: Epidemiology of adult Still's disease: Estimate of the incidence by a retrospective study in west France. *Ann Rheum Dis* 1995; 54: 587-90.
- LAHIRI M, TENG GG: A case of refractory adult-onset Still's disease treated with anakinra. *Int J Rheum Dis* 2010; 13: e36-41.
- NAUMANN L, FEIST E, NATUSCH A: IL-1-receptor antagonist anakinra provides long-lasting efficacy in the treatment of refractory adult-onset Still's disease. *Ann Rheum Dis* 2010; 69: 466-7.
- MOULIS G, SAILLER L, ASTUDILLO L, PUGNET G, ARLET P: May anakinra be used earlier in adult onset Still disease? *Clin Rheumatol* 2010; 29: 1199-200.
- LEQUERRE T, QUARTIER P, ROSELLINI D et al.: Societe Francophone pour la Rhumatologie et les Maladies Inflammatoires en Pediatrie (SOFREMIP); Club Rhumatismes et Inflammation (CRI) Interleukin - 1 receptor antagonist (anakinra) treatment in patients with systemic-onset juvenile idiopathic arthritis or adult onset Still disease: preliminary experience in France. *Ann Rheum Dis* 2008; 67: 302-8.
- THONHOFFER R, HILLER M, JUST H: Treatment of refractory adult-onset still's disease with tocilizumab: report of two cases and review of the literature. *Rheumatol Int* 2011; 31: 1653-8.
- NANIWA T, ITO R, WATANABE M et al.: Case report: successful use of short-term add-on tocilizumab for multirefractory systemic flare of adult-onset Still's disease. *Clin Rheumatol* 2010 Sep 15.
- PUECHAL X, DEBANDT M, BERTHELOT JM et al.: Club Rhumatismes et Inflammation. Tocilizumab in refractory adult Still's disease. *Arthritis Care Res (Hoboken)* 2011; 63: 155-9.
- PERDAN-PIRKMAJER K, PRAPROTNIK S, TOMŠIĆ M: A case of refractory adult-onset Still's disease successfully controlled with tocilizumab and a review of the literature. *Clin Rheumatol* 2010; 29: 1465-7.
- RECH J, RONNEBERGER M, ENGLBRECHT M et al.: Successful treatment of adult-onset Still's disease refractory to TNF and IL-1 blockade by IL-6 receptor blockade. *Ann Rheum Dis* 2011; 70: 390-2.
- KRAETSCH HG, ANTONI C, KALDEN JR, MANGER B: Successful treatment of a small cohort of patients with adult onset of Still's disease with infliximab: first experiences. *Ann Rheum Dis* 2001; 60 (Suppl. 3): iii55-7.
- DECHANT C, SCHAUENBERG P, ANTONI CE, KRAETSCH HG, KALDEN JR, MANGER B: Longterm outcome of TNF blockade in adult-onset Still's disease. *Dtsch Med Wochenschr* 2004; 129: 1308-12.
- FAUTREL B, SIBILIA J, MARIETTE X, COMBE B; CLUB RHUMATISMES et al.: Inflammation Tumour necrosis factor alpha blocking agents in refractory adult Still's disease: an observational study of 20 cases. *Ann Rheum Dis* 2005; 64: 262-6.
- BARTOLONI E, ALUNNO A, LUCCIOLI F, SANTOBONI G, GERLI R: Successful treatment of refractory adult-onset Still's disease with anti-CD20 monoclonal antibody. *Clin Exp Rheumatol* 2009; 27: 888-9.
- JIANG L, WANG Z, DAI X, JIN X: Evaluation of clinical measures and different criteria for diagnosis of adult-onset Still's disease in a Chinese population. *J Rheumatol* 2011; 38: 741-6.
- RIERA E, OLIVÉ A, NARVÁEZ J et al.: Adult onset Still's disease: review of 41 cases. *Clin Exp Rheumatol* 2011; 29: 331-6.
- COLINA M, ZUCCHINI W, CIANCIO G, ORZINCOLO C, TROTTA F, GOVONI M: The Evolution of Adult-Onset Still Disease: An Observational and Comparative Study in a Cohort of 76 Italian Patients. *Semin Arthritis Rheum* 2011; 41: 279-85.
- KONG XD, XU D, ZHANG W, ZHAO Y, ZENG X, ZHANG F: Clinical features and prognosis in adult-onset Still's disease: a study of 104 cases. *Clin Rheumatol* 2010; 29: 1015-9.
- CAGATAY Y, GULA, CAGATAY A et al.: Adult-onset Still's disease. *Int J Clin Pract* 2009; 63: 1050-5.
- MEHRPOOR G, OWLIA MB, SOLEIMANI H, AYATOLLAHI J: Adult-onset Still's disease: a report of 28 cases and review of the literature. *Mod Rheumatol* 2008; 18: 480-5.
- APPENZELLER S, CASTRO GR, COSTALLAT LT, SAMARA AM, BÉRTOLO MB: Adult-onset Still disease in southeast Brazil. *J Clin Rheumatol* 2005; 11: 76-80.
- YAMAGUSHI M, OHTA A, TSUNEMATSU T et al.: Preliminary criteria for classification of adult Still's disease. *J Rheumatol* 1992; 19: 424-30.
- FAUTREL B, ZING E, GOLMARD JL et al.: Proposal for a new set of classification criteria for adult-onset still disease. *Medicine (Baltimore)* 2002; 81: 194-200.
- CUSH JJ, MEDSGER TA JR, CHRISTY WC, HERBERT DC, COOPERSTEIN LA: Adult-onset Still's disease: Clinical course and outcome. *Arthritis Rheum* 1987; 30: 186-94.
- RAU M, SCHILLER M, KRIENKE S, HEYDER P, LORENZ H, BLANK N: Clinical manifestations but not cytokine profiles differentiate adult-onset Still's disease and sepsis. *J Rheumatol* 2010; 37: 2369-76.
- LIAN F, WANG Y, YANG X, XU H, LIANG L: Clinical features and hyperferritinemia diagnostic cutoff points for AOSD based on ROC curve: a Chinese experience. *Rheumatol Int* 2012; 32: 189-92.
- NOVAK S, ANIC F, LUKE-VRBANIĆ TS: Extremely high serum ferritin levels as a main diagnostic tool of adult-onset Still's disease. *Rheumatol Int* 2012; 32: 1091-4.
- FAUTREL B, LE MOEL G, SAINT-MARCOUX B et al.: Diagnostic value of ferritin and glycosylated ferritin in adult onset Still's disease. *J Rheumatol* 2001; 28: 322-9.
- MANGER B, RECH J, SCHETT G: Use of MTX in adult-onset Still's disease. *Clin Exp Rheumatol* 2010; 28 (Suppl. 61): S168-71.
- MITAMURA M, TADA Y, KOARADA S et al.: Cyclosporin A treatment for Japanese patients with severe adult-onset Still's disease. *Mod Rheumatol* 2009; 19: 57-63.
- FRANCHINI S, DAGNA L, SALVO F, AIELLO P, BALDISSERA E, SABBADINI MG: Efficacy of traditional and biologic agents in different clinical phenotypes of adult-onset Still's disease. *Arthritis Rheum* 2010; 62: 2530-5.