

## Original Article

# Clinical features and prognosis of adult-onset Still's disease: 75 cases from China

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**Abstract:** This study evaluated the clinical characteristics, treatment outcomes, and complications of patients with adult onset Still's disease (AOSD) in our local Chinese population. Patients with AOSD attending our hospital from 2008 to 2011 were identified and followed up. Their clinical and laboratory features at presentation, as well as their disease progression, treatments, and outcomes were recorded and compared with other reported series. A total of 75 patients with AOSD were identified. Forty-four were female. Thirty-nine had disease onset between 16 and 35 years of age. The most common presenting features were fever (96%), arthritis (57.33%), rash (78.67%), and sore throat (49.3%). The acute phase response was marked in most patients, with elevated erythrocyte sedimentation rates (77.05%) and C-reactive protein levels (84.06%). Hyperferritinemia was present in 74.14% of cases, and serum ferritin (SF) levels declined after treatment in most cases. Liver abnormalities were usually transient, but were more severe in 5 patients. Most patients (92%) required corticosteroid therapy; of these, 33.3% also received disease-modifying antirheumatic drugs or immunosuppressive drugs. Sixty-four and 45.33% patients with AOSD achieved partial and complete remission, respectively, after 2 weeks of treatment, and 92% and 74.67%, respectively, after 1 month. The cumulative relapse rate was 45.3%. Patients with AOSD had complex symptoms with no specific laboratory findings. Reduced SF levels after treatment and liver abnormalities may be used to follow treatment outcome.

**Keywords:** Adult onset Still's disease, serum ferritin, liver dysfunction, clinic feature

## Introduction

AOSD is a rare rheumatic inflammatory disorder of unknown etiology first described by Eric Bywaters in 1971 [1]. Its etiopathogenesis remains unknown and there is evidence supporting both genetic and environmental factors. The disease affects young people, with a bimodal age distribution at 15-25 and 36-46 years of age; however, there are several reports of new cases of AOSD in older individuals [2, 3]. The disease is slightly more prevalent in women [4, 5].

The clinical presentation of AOSD is nonspecific and heterogeneous. Symptoms commonly include high spiking fever, arthralgia or arthritis, transient maculopapular rash, and sore throat. Blood tests usually reveal leukocytosis with neutrophilia, liver function abnormalities, increased C-reactive protein levels, and negative findings for rheumatoid factors and antinuclear antibody tests [4, 6-14]. High ferritin levels are common in this disease [4, 15, 16], but

are generally a nonspecific finding because high levels are also common in various conditions such as infections and hematologic disorders. The most commonly used classification criteria proposed by Yamaguchi et al [17] have been shown to be the most sensitive (93.5%) [18] and are based on the exclusion of other diseases such as chronic infection, tumors, and other autoimmune disorders.

Aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended for initial AOSD treatment, but the response rate is reportedly as low as 20% to 25% [19]. Since response to NSAID monotherapy is not generally sufficient, most patients also receive corticosteroids during the course of their disease, with an efficacy of up to 95%.

## Materials and methods

We retrospectively reviewed the medical records of 75 adult patients at the Department of Infectious Diseases, West China Hospital

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**Table 1.** Clinical features of patients with AOSD

	Patients (n=75) (%)	Zeng et al [6] (n=61) (%)	Cagatay et al [4] (n=84) (%)	Franchini et al [7] (n=66) (%)	Fautrel et al [8] (n=72) (%)	Riera et al [9] (n=41) (%)
	China	Turkey	Italy	French	Spain	
Female	44 (58.67)	45 (73.8)	59 (70.24)	38 (58)	NA	25 (61)
Onset between 16~35 years	39 (52)	29 (47.5)	45 (54)	30 (45)	NA	NA
Fever ( $\geq 39^{\circ}\text{C}$ )	72 (96)	61 (100)	81 (95.2)	63 (95)	61 (84.7)	41 (100)
Evanescent rash	59 (78.67)	54 (88.5)	50 (59.5)	52 (79)	51 (70.8)	38 (92.6)
Arthralgia/arthritis	43 (57.33)	50 (82.0)	81 (96.4)	52 (79)	64 (88.8)	40 (97.5)
Sore throat	39 (49.3)	44 (72.1)	55 (65.5)	38 (58)	38 (52.7)	37 (90.2)
Lymphadenopathy	18 (24)	32 (52.5)	28 (33.3)	36 (54)	32 (44.4)	17 (41.5)
Splenomegaly	14 (18.67)	23 (37.7)	24 (28.6)	25 (38)	32 (44.4)	7 (17)
Pleuritis	11 (14.67)	11 (18)	8 (9.52)	12 (18)	NA	6 (14.6)
Pericarditis	6 (8)	15 (24.6)	10 (11.9)	9 (14)	15 (20.8)	5 (12)

of Sichuan University, from January 2008 to January 2011 who were diagnosed with AOSD. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Sichuan University. Written informed consent was obtained from all participants. The diagnosis was based on criteria from Yamaguchi et al [17]. Briefly, 5 or more criteria were required for diagnosis, including 2 or more of the following major criteria: fever ( $> 39^{\circ}\text{C}$ ), arthralgia or arthritis, evanescent rash, and leukocytosis with granulocytosis. Minor criteria included sore throat, liver dysfunction, lymphadenopathy or splenomegaly, and negative antinuclear antibodies (ANA) and rheumatoid factor (RF) test results. Infections, malignancies, and other autoimmune disorders were excluded for all patients. We retrospectively reviewed medical records, laboratory data, and telephone follow-ups concerning patient symptoms for 1 year.

### Clinical manifestations

Clinical information was recorded, including patient age, gender, and clinical symptoms. Constitutional symptoms included high-spiking fevers, characteristic rash, arthritis/arthralgias, myalgia, sore throat, pleuritis, peritonitis, and pericarditis.

### Laboratory data

Laboratory tests results included hemogram, liver function tests, and erythrocyte sedimentation rate (ESR), as well as C-reactive protein (CRP), antinuclear antibody (ANA), and serum ferritin (SF) levels. Microbiological investigations, imaging studies, and bone marrow and

lymph node biopsies (with lymph node enlargement) were performed.

### Treatment and prognosis

Medicines used in the course of the disease were recorded. Relapse and remission rates were also analyzed. Complete remission was defined according to Fautrel et al [20] as complete disappearance of clinical symptoms such as fever, evanescent rash, polyarthralgia, lymphadenopathy, and hepatosplenomegaly and normalization of laboratory test results such as white blood cell counts (WBC), liver enzyme levels, ESR, and SF levels. Partial remission was defined as partial improvement of clinical symptoms, and more than 50% decrease in laboratory findings such as leukocytosis, elevated liver enzyme levels, ESR, and SF levels. Relapse was defined as AOSD patients who had achieved complete remission who re-developed clinical symptoms and laboratory findings.

### Statistical analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 19.0. All results were expressed as mean values  $\pm$  standard deviation (SD). Data were compared using Chi-square tests. The significance level was set at  $P < 0.05$ .

## Results

### Clinical manifestations of patients with AOSD

The demographic features, clinical manifestations, and laboratory findings of the 75 patients in this study and in the literature are shown in **Table 1**. In the present study, 31 patients were

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**Table 2.** Laboratory features of patients with AOSD

	Patients (n=75) (%)	Zeng et al [6] (n=61) (%)	Cagatay et al [4] (n=84) (%)	Franchini et al [7] (n=66) (%)	Fautrelb et al [8] (n=72) (%)	Riera et al [9] (n=41) (%)
	China	Turkey	Italy	French	Spain	
Positive ANA	4 (5.33)	7 (11.67)	NS	6(9)	6 (8.3)	0
Elevated of ESR	47/61 (77.05)	61 (100)	79 (94)	66 (100)	NA	41 (100)
Elevated of CRP	58/69 (84.06)	47/59 (79.7)	NA	NA	NA	41 (100)
SF > 5 N (*> 1000 ng/ml)	43/58 (74.14)	43/54 (79.6) <sup>#</sup>	32 (38.10) <sup>#</sup>	43 (70) <sup>#</sup>	28 (38.9)	19/37 (51)
Elevated of WBC	56 (74.67)	51 (83.6)	69 (82.1)	52 (79)	64 (88.8)	38 (93)
20×10 <sup>9</sup> /L (*> 15×10 <sup>9</sup> /L)	25 (33.33)	31 (50.8)	48 (57.14) <sup>*</sup>	41 (62) <sup>*</sup>	NA	9 (22)
30×10 <sup>9</sup> /L	2 (2.67)	NA	NA	NA	NA	4 (10)
Neutrophilia	68 (90.67)	NA	35/63 (55.56)	54 (88)	NA	NA
HGB < 10 g/L	23 (30.67)	9 (14.8)	30 (35.7)	25 (38)	NA	10 (24)
Abnormal transaminase	27 (36)	14 (23)	30 (35.71)	52 (79)	53 (73.6)	21 (51)
Albumin level < 35 g/L	51 (68)	NA	35 (41.67)	43 (65)	NA	NA

<sup>#</sup>SF > 1000 ng/ml; <sup>\*</sup>WBC > 15×10<sup>9</sup>/L.

men and 44 were women. They were all ethnic Chinese. The median age at disease onset was 35.75±13.25 years (range 16-82 years). Most of the patients (52%) were between 16 and 35 years of age at onset. However, 6 patients had disease onset after the age of 60. Seventy-two patients had fevers with a maximum body temperature ≥ 39°C for more than 2 weeks; the fever was remitting or irregular in most patients. A typical salmon-pink macular or maculopapular rash, evanescent and concurrent with fever, was observed in 59 (78.67%) patients. The rash was most frequently observed on the proximal limbs and trunk, which could be mildly pruritic and associated with a burning sensation. Arthritis was noted in 43 (57.33%) patients. The most commonly affected joints were the knees, wrists, ankles, and the proximal interphalangeal joints of both hands. A total of 49.3% patients complained of sore throat that usually coincided with fever spikes and subsided when the body temperature returned to normal. Lymphadenopathy was observed in 18 patients (24%), with the cervical lymph nodes most frequently involved. Lymph node biopsy was performed in 14 patients, which revealed reactive hyperplasia in all patients. Bone marrow biopsy studies were not revealing in 66 patients. Slight to moderate splenic enlargement was observed in 14 patients (18.67%). There were 11 (14.67%), 2 (2.67%), and 6 (8%) cases of pleuritis, peritonitis, and pericarditis, respectively.

### Laboratory findings

Features correlated with laboratory findings are shown in **Table 2**. Fifty-six patients (74.67%)

had leukocytosis, 68 (90.67%) revealed neutrophilia, and 1 patient presented with leukopenia. The mean WBC was 15.72±7.19×10<sup>9</sup>/L (range 3.01-36.43×10<sup>9</sup>/L). Normochromic normocytic anemia (hemoglobin < 10 g/dL) was found in 23 cases (30.67%). Thrombocytosis was present in 28 patients (37.33%). ESR and CRP were 38.59±17.42 mm/h (range 13-87) and 89.79±53.4 mg/L (range 5.64-250), respectively. Elevated SF levels were observed in 91.38% of patients in this study (range 24-336 ng/mL) and 74.14% showed hyperferritinemia of more than 5 times the upper limit of the normal range. ANA (1:100) were detected in 4 patients (5.33%). Abnormal transaminases were observed in 27 patients. The mean serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), and albumin (Alb) levels of the 75 patients were 65.5±119.39 IU/L (range 6-732), 63.11±104.26 IU/L (range 8-713), 379.76±210.22 IU/L (range 123-1490), and 32.59±5.71 g/L (range: 21.1-42.9), respectively. Two patients (2.67%) had total serum bilirubin level above normal (range: 5.0-28.0). Albumin levels were decreased (< 35 g/L) in 51 patients (68%). None of the patients had manifestations of chronic liver disease, such as palm erythema, spider telangiectasia, and varicose veins.

### Treatment and prognosis

Sixty-nine patients (92%) received corticosteroids, including prednisone, prednisolone, methylprednisolone, and hydrocortisone. Among these patients, the steroid dosage was more than 40 mg/d (prednisone-equivalent). Disease-modifying anti-rheumatic drugs (DMARDs) or

immunosuppressive drugs were administered to 23 patients, including 18 who received methotrexate, 3 who received cyclophosphamide, 5 who received leflunomide, 4 who received hydroxychloroquine, 1 who received azathioprine, and 1 patient who received tripterygium wilfordii. Seven patients received 2 or more DMARDs.

Sixty-four percent and 45.33% of patients with AOSD achieved partial and complete remission, respectively, after 2 weeks of treatment. After 1 month of treatment, partial and complete remission rates were as high as 92% and 74.67%, respectively. In our series, all patients were followed up for 1 year. The cumulative relapse rate was 45.3% (34 patients); most of the relapses happened when tapering corticosteroids, regardless of DMARDs administration. Among relapsed patients, 27 relapsed once and 7 relapsed at least twice.

Elevated serum transaminase levels were transient and returned to normal after corticosteroid or NSAIDs treatment in most patients. However, serum transaminase levels were higher during treatment in 5 patients, and became high in 2 patients whose serum transaminase levels were initially normal. None of the patients from our study group developed acute liver failure. Among patients with abnormal liver function tests, 1 was taking NSAIDs and 3 were taking methotrexate (MTX). The percentages of patients with aggravation of abnormal liver function were compared between those who were taking NSAIDs and those who were not, and also between those patients who were taking MTX and those who were not. No significant differences were found. Eighteen patients with moderate to severe liver dysfunction, including 7 patients whose liver function worsened during treatment, were administered 1 or 2 hepatoprotective drugs such as glutathione, diammonium glycyrrhizinate, bifendate, inosine, ademetonine, ursodeoxycholic acid, and vitamin C. All patients attained complete recovery of liver abnormalities without stopping or adjusting NSAIDs, MTX, or corticosteroid dosages. Partial and complete remission rates were 51.85% (14/27) and 25.93% (7/27) after 2 weeks of treatment in patients with elevated serum transaminase levels, and 92.59% (25/27) and 66.66% (18/27) at the end of 1 month of treatment. The percentages of partial and complete remission were compared between patients with liver abnormalities and

those with normal liver function. Chi-square tests revealed significant differences in the group with partial remission after 1 month and complete remission after 2 weeks ( $P < 0.05$ ).

We monitored dynamic SF changes in 55 patients with elevated levels. SF levels declined to 50% their original values in 36 patients after 1 month of treatment, and fell to within normal range in 6 patients. In 43 patients with hyperferritinemia of more than 5 times the upper limit of the normal range, we observed a 5-fold decline in 26 patients and a return to normal ferritin levels in 5 patients. Partial and complete remission rates were 95.23% (40/42) and 85.71% (36/42) in patients whose SF levels had declined. Seventeen patients relapsed once in the follow-up period, and 4 patients relapsed twice or more. The percentages of partial and complete remission and cumulative relapse were compared between patients whose SF levels declined and those whose SF levels remained high. Significant differences were found in partial remission after 1 month based on Chi-square tests ( $P > 0.05$ ).

### Discussion

We described a series of 75 patients with AOSD who were diagnosed and treated at a Chinese tertiary teaching hospital. Persistent fever, evanescent rash, arthritis, and sore throat were the most prevalent and nonspecific symptoms in our series. Except for the incidence of arthralgia/arthritis and lymphadenopathy, which were lower compared to other studies presented in **Table 1**, the incidences of the remaining symptoms were similar. Elevated ESR and leukocytosis of more than  $10 \times 10^9/L$  or neutrophilia were present in almost all patients with AOSD. We found significant differences in laboratory findings of different studies shown in **Table 2**, including elevated ESR and leukocytosis, SF levels more than 5 times normal, and abnormal transaminase levels.

Mild, transient elevations in liver enzyme levels accompanying only the active phase of the disease were seen in three-quarter of cases [10, 21]. Progression to severe liver failure has been also reported [10, 22, 23]. Our data confirm that liver involvement in patients with AOSD may be mild to severe, and liver dysfunction was present in up to one-third of patients, a lower prevalence than other studies. Pathologic examination of liver biopsy samples was unne-

essary because pathologic changes cannot identify the specific cause of liver damage in AOSD [21, 22]. Sustained macrophage activation and cytokine production may play a role in the pathogenesis of these liver abnormalities [21, 24]. The abnormalities could be related to medications, particularly some NSAIDs, immunosuppressive drugs, and antibiotics. However, pathologic examination of fine-needle liver biopsy samples has not revealed drug-induced hepatitis among AOSD-associated liver abnormalities [21]. Our data showed transient elevation of liver enzyme levels, exacerbation of liver damage during the course of treatment, and complete recovery of liver abnormalities in all patients who received hepatoprotective drug treatment, without discontinuing or adjusting the dosage of NSAIDs, MTX, and corticosteroids. Thus, the liver damage was more likely related to macrophage activation and cytokine production, rather than use of these drugs.

High ferritin levels are also seen in other diseases such as liver disease, infections, malignancies, and hemophagocytic syndrome. Moreover, ferritin levels in AOSD are usually higher than those found in other autoimmune or inflammatory diseases [15, 16]. Hyperferritinemia in AOSD is not related to iron metabolism and is likely to be a consequence of cytokine secretion induced by the reticuloendothelial system [4, 15, 25]. The validity of the diagnostic test for AOSD has been evaluated in a retrospective study, where a 5-fold increase in SF levels has 41% specificity and 80% sensitivity [26]. Furthermore, SF levels correlate with disease activity and normalize after remission. Our data showed that ferritin levels in most patients increased to more than 5 times the upper limit of the normal range and quickly declined in nearly 80% of patients after corticosteroid therapy. A drop in glycosylated ferritin levels may be a more specific diagnostic marker. In AOSD, decreased levels of glycosylated ferritin, an isoform of ferritin, were noted in comparison with other inflammatory diseases. However, glycosylated ferritin cannot be used to monitor disease activity or response to treatment, because its level remains low for many months after disease remission [27, 28]. Because this test was not available in our hospital, we were unable to analyze this factor.

Management of patients with AOSD is based on use of NSAIDs, corticosteroids, and DMARDs. NSAIDs are recommended as the ini-

tial treatment in AOSD, but the response rate is reportedly low [19]. In our study, only 6 patients received NSAID monotherapy at the beginning of treatment. Three patients achieved partial remission; the remaining patients switched to a steroid combination therapy due to lack of response. MTX was widely used in this study. The prognosis of AOSD is typically good, but the relapse rate is high. Appenzeller [12] reported that about 75% of patients relapsed in 6.9 years of follow-up. Peripheral blood leukocyte counts of more than  $30 \times 10^9/L$ , ESR levels greater than 100 mm/h, SF levels of more than 1,500 ng/mL, and insufficient steroid starting dose (less than 40 mg/d prednisone) are factors correlated with relapse. We did not observe a correlation between relapse and these factors in our series, however. Most of the relapses happened when tapering corticosteroids, likely related to the speed of tapering and maintenance dose. Significant differences were found in partial remission after 1 month and complete remission after 2 weeks between patients with liver abnormalities and with normal liver function, and in partial remission after 1 month between patients with reduced SF levels after treatment and those whose SF levels remained high. These observations suggest that these 2 factors may be correlated with treatment outcome. However, additional studies with larger sample sizes will be necessary in future studies.

### Disclosure of conflict of interest

None.

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### References

- [1] Bywaters EG. Still's disease in the adult. *Ann Rheum Dis* 1971; 30: 121-133.
- [2] Kurasawa M, Kotani K, Kurasawa G, Shida K, Yamada S and Tago T. Adult-onset Still's disease in a patient over 80 years old successfully treated with low-dose methotrexate therapy. *Age Ageing* 2007; 36: 104-106.
- [3] Ichiki H, Shishido M and Nishiyama S. [Two cases of adult onset of Still's disease in the elderly]. *Nihon Ronen Igakkai Zasshi* 1992; 29: 960-964.

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- [4] Cagatay Y, Gul A, Cagatay A, Kamali S, Karadeniz A, Inanc M, Ocal L, Aral O and Konice M. Adult-onset Still's disease. *Int J Clin Pract* 2009; 63: 1050-1055.
- [5] Mehrpoor G, Owlia MB, Soleimani H and Ayatollahi J. Adult-onset Still's disease: a report of 28 cases and review of the literature. *Mod Rheumatol* 2008; 18: 480-485.
- [6] Zeng T, Zou YQ, Wu MF and Yang CD. Clinical features and prognosis of adult-onset Still's disease: 61 cases from China. *J Rheumatol* 2009; 36: 1026-1031.
- [7] Franchini S, Dagna L, Salvo F, Aiello P, Baldissera E and Sabbadini MG. Adult onset Still's disease: clinical presentation in a large cohort of Italian patients. *Clin Exp Rheumatol* 2010; 28: 41-48.
- [8] Fautrel B, Zing E, Golmard JL, Le Moel G, Bissery A, Rioux C, Rozenberg S, Piette JC and Bourgeois P. Proposal for a new set of classification criteria for adult-onset still disease. *Medicine (Baltimore)* 2002; 81: 194-200.
- [9] Riera E, Olive A, Narvaez J, Holgado S, Santo P, Mateo L, Bianchi MM and Nolla JM. Adult onset Still's disease: review of 41 cases. *Clin Exp Rheumatol* 2011; 29: 331-336.
- [10] Pouchot J, Sampalis JS, Beaudet F, Carette S, Decary F, Salusinsky-Sternbach M, Hill RO, Gutkowski A, Harth M, Myhal D, et al. Adult Still's disease: manifestations, disease course, and outcome in 62 patients. *Medicine (Baltimore)* 1991; 70: 118-136.
- [11] Mok CC, Lau CS and Wong RW. Clinical characteristics, treatment, and outcome of adult onset Still's disease in southern Chinese. *J Rheumatol* 1998; 25: 2345-2351.
- [12] Appenzeller S, Castro GR, Costallat LT, Samara AM and Bertolo MB. Adult-onset Still disease in southeast Brazil. *J Clin Rheumatol* 2005; 11: 76-80.
- [13] Pujol R, Valverde J, Pastor F and Garrigosa R. [Still's disease in the adult]. *Med Clin (Barc)* 1983; 80: 112-114.
- [14] Efthimiou P, Paik PK and Bielory L. Diagnosis and management of adult onset Still's disease. *Ann Rheum Dis* 2006; 65: 564-572.
- [15] Meijvis SC, Endeman H, Geers AB and ter Borg EJ. Extremely high serum ferritin levels as diagnostic tool in adult-onset Still's disease. *Neth J Med* 2007; 65: 212-214.
- [16] Kelly J, Chowieńczyk P and Gibson T. Sore throat and hyperferritinaemia. *J R Soc Med* 2001; 94: 400-401.
- [17] Yamaguchi M, Ohta A, Tsunematsu T, Kasukawa R, Mizushima Y, Kashiwagi H, Kashiwazaki S, Tanimoto K, Matsumoto Y, Ota T, et al. Preliminary criteria for classification of adult Still's disease. *J Rheumatol* 1992; 19: 424-430.
- [18] Masson C, Le Loet X, Liote F, Dubost JJ, Boissier MC, Perroux-Goumy L, Bregeon C and Audran M. Comparative study of 6 types of criteria in adult Still's disease. *J Rheumatol* 1996; 23: 495-497.
- [19] Kadar J and Petrovicz E. Adult-onset Still's disease. *Best Pract Res Clin Rheumatol* 2004; 18: 663-676.
- [20] Fautrel B, Sibilia J, Mariette X and Combe B. Tumour necrosis factor alpha blocking agents in refractory adult Still's disease: an observational study of 20 cases. *Ann Rheum Dis* 2005; 64: 262-266.
- [21] Andres E, Kurtz JE, Perrin AE, Pflumio F, Ruellan A, Goichot B, Dufour P, Blickle JF, Brogard JM and Schlienger JL. Retrospective monocentric study of 17 patients with adult Still's disease, with special focus on liver abnormalities. *Hepatology* 2003; 50: 192-195.
- [22] Chen DY, Lan JL, Hsieh TY and Chen YH. Clinical manifestations, disease course, and complications of adult-onset Still's disease in Taiwan. *J Formos Med Assoc* 2004; 103: 844-852.
- [23] Zhu G, Liu G, Liu Y, Xie Q and Shi G. Liver abnormalities in adult onset Still's disease: a retrospective study of 77 Chinese patients. *J Clin Rheumatol* 2009; 15: 284-288.
- [24] Arlet JB, Le TH, Marinho A, Amoura Z, Wechsler B, Papo T and Piette JC. Reactive haemophagocytic syndrome in adult-onset Still's disease: a report of six patients and a review of the literature. *Ann Rheum Dis* 2006; 65: 1596-1601.
- [25] ten Kate J, Drenth JP, Kahn MF and van Deursen C. Iron saturation of serum ferritin in patients with adult onset Still's disease. *J Rheumatol* 2001; 28: 2213-2215.
- [26] Fautrel B, Le Moel G, Saint-Marcoux B, Taupin P, Vignes S, Rozenberg S, Koeger AC, Meyer O, Guillevin L, Piette JC and Bourgeois P. Diagnostic value of ferritin and glycosylated ferritin in adult onset Still's disease. *J Rheumatol* 2001; 28: 322-329.
- [27] Vignes S, Le Moel G, Fautrel B, Wechsler B, Godeau P and Piette JC. Percentage of glycosylated serum ferritin remains low throughout the course of adult onset Still's disease. *Ann Rheum Dis* 2000; 59: 347-350.
- [28] Hamidou MA, Denis M, Barbarot S, Boutoille D, Belizna C and Le Moel G. Usefulness of glycosylated ferritin in atypical presentations of adult onset Still's disease. *Ann Rheum Dis* 2004; 63: 605.