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Clinical Characteristics of Japanese Patients with Elderly-Onset Adult-Onset Still's Disease

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The aim of this study was to compare the characteristics of Japanese patients with elderly-onset Adult-onset Still's disease (AOSD) and those with younger-onset AOSD. Patients were classified into elderly-onset (≥ 65 years, n = 20) and younger-onset (< 65 years, n = 62) groups according to age at AOSD diagnosis. Analyses included the comparison of clinical features, treatments, and Pouchot and modified Pouchot (mPouchot) scores between the two groups. The frequencies of sore throat, lymphadenopathy, and splenomegaly were significantly lower in the elderly-onset group than in the younger-onset group (30.5% vs. 80.6%, p = 0.0004; 15.0% vs. 54.8%, p = 0.0019; 30.0% vs. 61.3%, p = 0.0203; respectively). There were no significant differences in the frequencies of complications, such as macrophage activation syndrome and disseminated intravenous coagulation, between the patients with elderly-onset or younger-onset AOSD. Serum ferritin levels were higher in the elderly-onset group than in the younger-onset group, albeit without statistical significance (median, 9,423 vs. 4,164 ng/mL, p = 0.1727). Pouchot score was lower in the elderly-onset group than in the younger-onset group (median score, 5.5 vs. 4.0, p = 0.0008); however, there was no significant difference in the mPouchot score between the two groups. Our analyses revealed that elderly-onset AOSD was associated with certain characteristics that were distinct from those of younger-onset AOSD and that the disease severity in patients with elderly-onset AOSD, determined by Pouchot score at the time of AOSD diagnosis, was similar to or less than that in patients with younger-onset AOSD.

Keywords: adult-onset Still's disease; elderly; ferritin; prednisolone; systemic score
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Introduction

Adult-onset Still's disease (AOSD) is a systemic auto-inflammatory disease with innate immune activation driven by a combination of genetic and environmental factors (Giacomelli et al. 2018). The etiology and pathogenesis of AOSD remain unclear; however, the excessive production of proinflammatory cytokines, such as interleukin (IL)-1β, IL-6, IL-18, and interferon-γ, produced by activated macrophages are considered to play an important role in AOSD (Sfriso et al. 2018). AOSD is characterized by spiking fever, skin rash, arthritis, and multisystem involvement. Other clinical features including sore throat, elevated liver enzymes, lymphadenopathy, hepatosplenomegaly, and liver involvement are heterogeneous with various clinical manifestations (Kalyoncu et al. 2016). Laboratory tests show a strong inflammatory response associated with leukocytosis, anemia, increased serum levels of acute-phase reactants, hyperferritinemia, and elevated hepatic enzymes. Usually, the disease follows monocyclic, polyphasic, and chronic patterns in 30%, 30%, and 40% of patients with AOSD, respectively (Gerfaud-Valentin et al. 2014a). The combination of heterogeneous symptoms, complex laboratory results, and a polymorphic phenotype hinder the prediction of prognosis in patients with AOSD (Guilpain and Le Quellec 2017). AOSD is primarily diagnosed in young adults, with median age at diagnosis of approximately 36 years (Gerfaud-Valentin et al. 2014a, b). However, patients with elderly-onset AOSD have also been reported (Kurasawa et al. 2007; Ertugrul et al. 2012; Sakata et al. 2016; Suda et al. 2020). In fact, a 1994 Japanese nationwide epidemiological survey on AOSD revealed that the

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mean age at diagnosis was 38.1 years (Wakai et al. 1997). However, a 2010-2011 nationwide survey of AOSD in Japan revealed that the mean age at onset was 46 years (Asanuma et al. 2015). It is therefore thought that the age of onset of AOSD has recently increased. Several heterogeneous clinical features appear to be associated with elderly-onset AOSD (Maruyama et al. 2021; Mollaeian et al. 2021). The accumulation and characterization of patients with elderly-onset AOSD is an important aspect of AOSD treatment.

In the present retrospective study, we aimed to compare the clinical features between elderly-onset and younger-onset AOSD.

Materials and Methods

Patients

This retrospective study included 82 patients with AOSD who were diagnosed and treated in the Department of Rheumatology at Fukushima Medical University Hospital between December 1, 2013 and September 30, 2020. All patients were diagnosed with AOSD according to the Yamaguchi criteria (Yamaguchi et al. 1992), after the exclusion of infectious, hematologic, and autoimmune diseases. The study considered all three clinical AOSD courses: (1) monocyclic course defined as a single episode that subsequently resolved and was followed by persistent good health for one year or more of follow-up; (2) polycyclic course defined as complete remission followed by one or more exacerbations; and (3) chronic course defined as persistently active disease, usually associated with polyarthritis (Gerfaud-Valentin et al. 2014a). The study was approved by the Ethics Committee of Fukushima Medical University (approval no. 2020-110). The requirement for informed consent was waived because of the retrospective study design.

Data collection

Demographic characteristics, comorbidities, clinical features, laboratory values, and treatment strategies were collected. The following clinical features were recorded: fever, skin rash, arthritis, leukocytosis, sore throat, lymphadenopathy, splenomegaly, and liver dysfunction. The presence of splenomegaly and lymphadenopathy was determined by ultrasonography or computed tomography. Data on the levels of rheumatoid factor, anti-nuclear antibody, C-reactive protein, and ferritin were collected. The collected data also included information on complications such as pleuritis, disseminated intravascular coagulation (DIC), and macrophage activation syndrome (MAS), and treatments. The systemic score for AOSD proposed by Pouchot et al. (1991) was calculated to evaluate disease activity and severity. The Pouchot systemic scoring system assigns one point for the presence of each of the following 12 manifestations: fever, skin rash, pleuritis, pneumonia, pericarditis, hepatomegaly or abnormal liver function tests, splenomegaly, lymphadenopathy, leukocyte count > 15,000/mm^3, sore throat, myalgia, and abdominal pain. Rau et al. (2010) proposed the modified Pouchot (mPouchot) score, which includes arthritis and serum ferritin > 3,000 μg/L as new factors and excludes abdominal pain and splenomegaly (Mueller and Sheriff 2010). The mPouchot score was also calculated.

Statistical analysis

Variables were presented as frequencies (%) for categorical variables and as medians [interquartile range (IQR)] for continuous data. Continuous data between the elderly-onset and younger-onset groups were compared using the Mann–Whitney *U* test, and proportions were analyzed using Fisher's exact or the chi-square test, as appropriate. All *p* values were two-sided, and a *p* value of < 0.05 was considered to indicate statistical significance. All statistical analyses were performed using IBM SPSS Statistics for Mac, version 26.0 (IBM, Armonk, NY, USA).

Results

Demographic data of patients with AOSD

The characteristics of 82 patients with AOSD included in the present study are summarized in Table 1. The median age at AOSD diagnosis was 52 (IQR 33.3-64.3) years, and female sex was predominant (88.3%). The most common clinical features at presentation were fever (98.8%), skin rash (96.3%), arthralgia (86.6%), leukocytosis (68.3%), and sore throat (69.5%).

Clinical findings of patients with elderly-onset AOSD

In the present study, patients with elderly-onset and younger-onset AOSD were defined as those diagnosed with AOSD at ≥ 65 years (n = 20) and < 65 years (n = 62) of age, respectively. The clinical features of patients with elderly-onset and younger-onset AOSD are summarized in Table 2. Briefly, there were 16 female and 4 male patients

Table 1. Baseline characteristics of patients.

Characteristics	Overall (number = 82)
Female, number (%)	55 (83.3)
Age at onset (year), median (IQR)	52.0 (33.3-64.3)
Disease duration (year), median (IQR)	2.0 (1.0-5.0)
Fever, number (%)	81 (98.8)
Skin rash, number (%)	79 (96.3)
Arthralgia, number (%)	71 (86.6)
Leukocytosis, number (%)	56 (68.3)
Sore throat, number (%)	57 (69.5)
Lymphadenopathy, number (%)	37 (45.1)
Splenomegaly, number (%)	44 (53.7)
Liver dysfunction, number (%)	69 (84.1)
Negative of rheumatoid factor, number (%)	76 (92.7)
Negative of antinuclear antibodies, number (%)	68 (82.9)

IQR, interquartile range.

Table 2. Comparison of the clinical features, course and diagnosis of adult-onset Still's disease patients with younger- and elderly-onset.

	Younger-onset	Elderly-onset	*p* value
Number	62	20	
Age at onset (years), median (IQR)	43.0 (30.0-57.3)	72.5 (68.5-75.8)	< 0.0001
Female, number (%)	50 (80.6)	16 (80.0)	1.0000
Clinical course			
Monocyclic, number (%)	15 (24.2)	6 (30.0)	
Polycyclic, number (%)	39 (62.9)	13 (65.0)	0.6663
Chronic, number (%)	7 (11.3)	1 (5.0)	
Clinical Features			
Fever, number (%)	62 (100)	19 (95.0)	0.2439
Skin rash, number (%)	60 (96.8)	19 (95.0)	1.0000
Arthralgia, number (%)	53 (85.5)	18 (90.0)	1.0000
Leukocytosis, number (%)	39 (62.9)	17 (85.0)	0.0966
Sore throat, number (%)	50 (80.6)	7 (35.0)	0.0004
Lymphadenopathy, number (%)	34 (54.8)	3 (15.0)	0.0019
Splenomegaly, number (%)	38 (61.3)	6 (30.0)	0.0203
Liver abnormalities, number (%)	52 (83.9)	17 (85.0)	1.0000

IQR, interquartile range.

Table 3. Comparison of the laboratory findings, complications and treatments of adult-onset Still's disease patients with younger- and elderly-onset.

	Younger-onset	Elderly-onset	*p* value
Number	62	20	
Laboratory findings			
Ferritin (ng/ml), median (IQR)	4,164 (1,903-15,563)	9,423 (3,539-17,730)	0.1727
CRP (mg/dl), median (IQR)	10.20 (5.74-17.29)	12.17 (7.38-27.59)	0.1925
Positivity of ANA, number (%)	12 (19.4)	2 (10.0)	0.4995
Positivity of RF, number (%)	3 (4.8)	3 (15.0)	0.1521
Complications			
MAS	15 (24.2)	4 (20.0)	1.0000
DIC	8 (12.9)	3 (15.0)	1.0000
Pleurisy	1 (1.6)	1 (5.0)	0.4306
Treatments			
PSL (mg/day), median (IQR)	40 (30-60)	40 (40-55)	0.6184
mPSL pulse therapy, number (%)	44 (71.0)	11 (55.0)	0.2733
Tocilizumab, number (%)	21 (33.9)	5 (25.0)	0.5831

ANA, antinuclear antibody; CRP, C-reactive protein; DIC, disseminated intravascular coagulation; IQR, interquartile range; MAS, macrophage activation syndrome; mPSL, methyl-prednisolone; PSL, prednisolone; RF, rheumatoid factor.

in the elderly-onset AOSD group and 50 female and 22 male patients in the younger-onset AOSD group. There was no significant difference in the sex distribution between the two groups: female ratio of elderly-onset AOSD was 80.0% and that of younger-onset AOSD was 80.6% (p = 1.0000). The median age at AOSD diagnosis was 72.5 (68.5-75.8) years in the elderly-onset group and 43.0 (30.0-57.3) years in the younger-onset group. The monophasic, polyphasic, and chronic articular disease courses were present in 6, 13, and 1 patient with elderly-onset AOSD, respectively, and in 15, 39, and 7 patients with younger-onset AOSD, respectively. The frequencies of sore throat, lymphadenopathy and splenomegaly were lower in patients with elderly-onset AOSD than in those with younger-onset

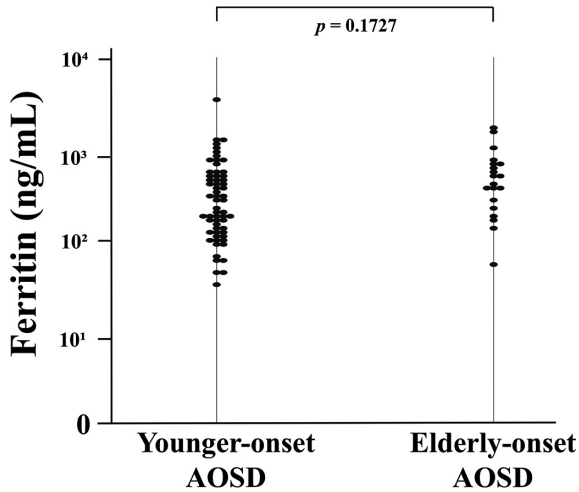

Fig. 1. Comparison of serum levels of ferritin between patients with elderly-onset and younger-onset adult-onset Still's disease.
Albeit not statistically significant, serum levels of ferritin are higher in patients with elderly-onset adult-onset Still's disease (AOSD) than in those with younger-onset AOSD [9,423 (3,539-17,730) vs. 4,146 (1,903-15,563) ng/mL, $p = 0.1727$].

AOSD (30.5% vs. 80.6%, $p = 0.0004$; 15.0% vs. 54.8%, $p = 0.0019$; 30.0% vs. 61.3%, $p = 0.0203$; respectively). In contrast, there were no significant differences in the frequencies of other clinical features between the two groups. In addition, there were no significant differences in the frequencies of complications such as MAS and DIC between the patients with elderly-onset and those with younger-onset AOSD.

Comparison of laboratory data between the elderly-onset and younger-onset AOSD groups

As shown in Table 3, the comparison of laboratory data between the elderly-onset and younger-onset AOSD groups revealed that, albeit not statistically significant, serum ferritin levels were higher in the elderly-onset group than in the younger-onset group [9,423 (3,539-17,730) vs. 4,146 (1,903-15,563) ng/mL, $p = 0.1727$] (Fig. 1). There were no significant differences in C-reactive protein levels and positivity for anti-nuclear antibody or rheumatoid factor between the two groups.

Comparison of treatment approaches between the elderly-onset and younger-onset AOSD groups

The comparison of treatments used for first induction between the elderly-onset and younger-onset AOSD groups (Table 3) revealed that all patients received steroids at different dosages and that median prednisolone dosage was comparable between the two groups [40 (30-60) vs. 40 (40-55) mg/mL, $p = 0.6184$]. Additionally, there was no significant difference in the use of methylprednisolone pulse therapy or tocilizumab between the two groups (55.0% vs. 71.0%, $p = 0.2733$; 25.0% vs. 33.9%, $p = 0.5831$; respectively).

Table 4. Comparison of Pouchot's and modified Pouchot's score of adult-onset Still's disease patients with younger- and elderly-onset.

	Younger-onset	Elderly-onset	*p* value
Number	62	20	
Factors of Pouchot's and mPouchot's score			
Fever, number (%)	62 (100)	19 (95.0)	0.2439
Skin rash, number (%)	60 (96.8)	19 (95.0)	1.0000
Sore throat, number (%)	50 (80.6)	7 (35.0)	0.0004
Myalgia, number (%)	0 (0)	0 (0)	NA
Pleuritis, number (%)	1 (1.6)	1 (5.0)	0.4306
Pericarditis, number (%)	1 (1.6)	0 (0)	1.0000
Pneumonia, number (%)	0 (0)	0 (0)	NA
Lymphadenopathy, number (%)	34 (54.8)	3 (15.0)	0.0019
Hepatomegaly or elevated live enzymes, number (%)	52 (83.9)	17 (85.0)	1.0000
Leukocyte count > 15,000/μl, number (%)	30 (48.4)	13 (65.0)	0.2118
Splenomegaly, number (%)†	38 (61.3)	6 (30.0)	0.0203
Abdominal pain, number (%)†	0 (0)	0 (0)	NA
Arthritis, number (%)‡	53 (85.5)	18 (90.0)	1.0000
Ferritin > 3,000 ng/ml, number (%)‡	36 (58.1)	16 (80.0)	0.1095
Pouchot's score, median (IQR)	5.5 (5.0-6.0)	4.0 (4.0-5.0)	0.0008
mPouchot's score, median (IQR)	6.0 (5.0-6.8)	6.0 (5.0-7.0)	0.1659

†Factors including only in Pouchot's score, ‡Factors including only in mPouchot's score.
IQR, interquartile range; mPouchot's, modified Pouchot's; NA, not applicable.

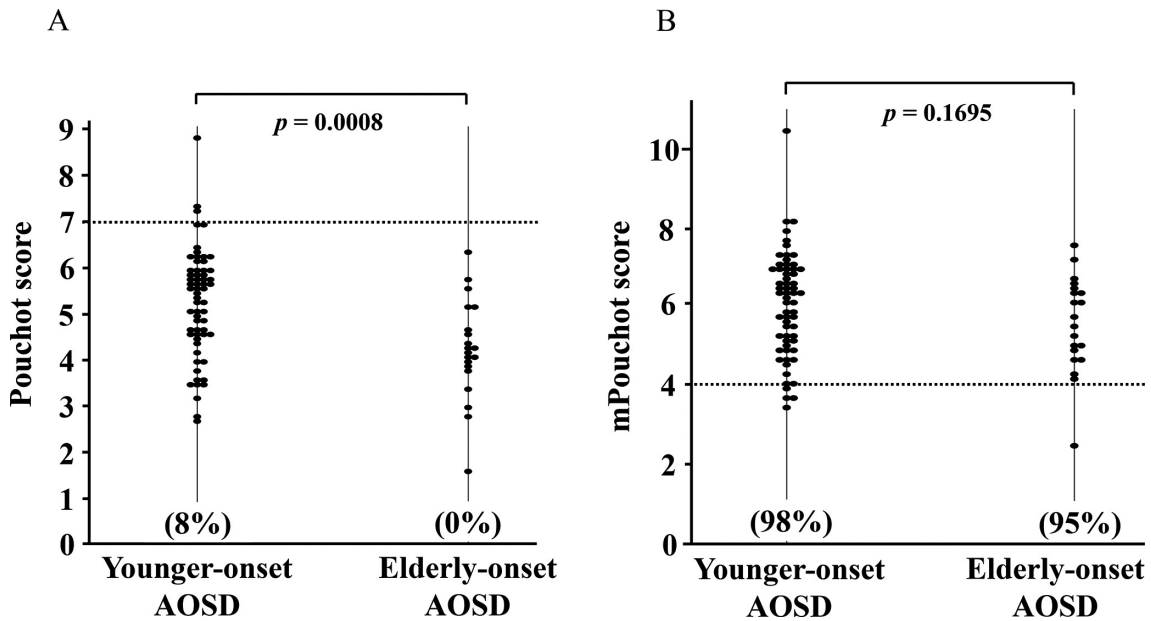

Fig. 2. Comparison between patients with elderly-onset and younger-onset adult-onset Still's disease.
(A) Pouchot scores are significantly lower in patients with elderly-onset adult-onset Still's disease (AOSD) than in those with younger-onset AOSD [5.5 (5.0-6.0) vs. 4.0 (4.0-5.0), $p = 0.0008$]. There is no significant difference in the proportion of patients with a Pouchot score of ≥ 7.0 between the two groups (0% vs. 8%, $p = 0.3277$). (B) The modified Pouchot (mPouchot) scores are not significantly different between patients with elderly-onset adult-onset Still's disease (AOSD) and those with younger-onset AOSD [6.0 (5.0-6.8) vs. 6.0 (5.0-7.0), $p = 0.1659$]. There is no significant difference in the proportion of patients with an mPouchot score of ≥ 4.0 between the two groups (98% vs. 95%, $p = 0.4306$).

Comparison of the Pouchot score between the elderly-onset and younger-onset AOSD groups

The systemic score for disease activity, which was developed by Pouchot et al. (1991), has a sensitivity of 92% and a specificity of 93% for discriminating active and non-active AOSD. We compared the Pouchot score between the patients with elderly-onset and younger-onset AOSD (Table 4) and found that the Pouchot scores were significantly lower in patients with elderly-onset AOSD than in those with younger-onset AOSD [5.5 (5.0-6.0) vs. 4.0 (4.0-5.0), $p = 0.0008$]. In contrast, there was no significant difference in the proportion of patients with a Pouchot score ≥ 7.0 between the two groups (0% vs. 8%, $p = 0.3277$) (Fig. 2A). Furthermore, there was no significant difference in the mPouchot score (Rau et al. 2010) between the elderly-onset and younger-onset AOSD groups [6.0 (5.0-6.8) vs. 6.0 (5.0-7.0), $p = 0.1659$]. Finally, there was no significant difference in the proportion of patients with the mPouchot score ≥ 4.0 between the elderly-onset and younger-onset AOSD groups (98% vs. 95%, $p = 0.4306$) (Fig. 2B).

Discussion

The typical clinical presentation of AOSD comprises systemic manifestations including spiking fever, evanescent rash, and lymphadenopathy with arthritis or arthralgia (Kalyoncu et al. 2016). Not all symptoms may be present at disease onset, and atypical presentations may occur; therefore, the pleiotropic presentation of AOSD is a source of diagnostic dilemma (Hu et al. 2012; Mehta et al. 2016). Disease complexity arising from the pathophysiological processes underlying AOSD and heterogeneous clinical AOSD phenotypes hinder the ability to predict patient outcomes (Guilpain and Le Quellec 2017). The diagnosis of AOSD is challenging and depends on clinical findings because there are no single diagnostic tests or characteristic autoantibodies or histopathological findings (Mimura et al. 2018). AOSD is considered to develop primarily in young adults (Gerfaud-Valentin et al. 2014a). However, recent studies demonstrate that disease onset has shifted toward older ages (Asanuma et al. 2015; Sakata et al. 2016). Furthermore, elderly-onset AOSD has been suggested to be associated with specific clinical features, such as higher incidence of MAS or DIC, and poor prognosis (Maruyama et al. 2021; Mollaeian et al. 2021).

In the present study, we found that age at disease diagnosis impacted the clinical manifestations. Our data indicated that elderly-onset AOSD was characterized by lower frequencies of sore throat, lymphadenopathy, and splenomegaly. In a recent study, Maruyama et al. (2021) reported that patients with elderly-onset AOSD exhibited several distinct clinical features, including less typical skin lesions, sore throat, splenomegaly, high serum ferritin levels, and a high frequency of DIC, compared to patients with younger-onset AOSD. The clinical manifestations observed in the present study are consistent with the findings of Maruyama et al. (2021). This report shows the differences in frequency of sore throat and splenomegaly between patients with elderly-onset and younger-onset AOSD. Tomaras et al.

(2021) reported that frequency of sore throat was approximately 50%-60%. A report by Maruyama et al. (2021) also showed that patients with elderly-onset AOSD had less complicated sore throat compared to those with younger-onset AOSD. Nguyen and Weisman (1997) reported that there were no specific topical pharyngeal findings in patients with AOSD, and that sore throat was a frequent early symptom of AOSD. However, Maruyama et al. (2021) could not identify the difference in time to diagnosis between elderly-onset and younger-onset. We also showed that the frequency of splenomegaly was significantly lower in patients with elderly-onset AOSD than in those with younger-onset AOSD. Berardicurti et al. (2021) reported that patients with AOSD had different genetic backgrounds and pathogenetic mechanisms according to phenotypic subgroups. Hence, the age is also a factor that may affect the heterogeneity of AOSD. Furthermore, although the etiology of AOSD remains unknown, malignancy and infection are considered trigger candidates for the development of AOSD (Gerfaud-Valentin et al. 2014a). Malignant and analogous diseases are more common in the elderly. It is possible that differences in the triggers of development of AOSD may reflect differences in clinical symptoms. Further, increased serum ferritin levels are shown to be associated with increased disease activity and chronic or recurrent forms of AOSD (Giacomelli et al. 2018). In the present study, serum ferritin levels were higher in the elderly-onset group than in the younger-onset group, although the difference was not statistically significant. The presence of serious organ involvement, including MAS, kidney failure, and myocarditis, may be associated with increased mortality in AOSD (Mitrovic and Fautrel 2018). MAS and DIC are important, life-threatening complications of AOSD. MAS has been reported in up to 15% of patients with AOSD (Giacomelli et al. 2018), whereas DIC has occurred in 1%-5% of patients with AOSD (Tomaras et al. 2021). Age-based prevalence of MAS or DIC was reported in several reports, but with varied results. Sakata et al. (2016) reported that severe complications, including MAS and DIC, among age groups were also not significant, but mortality increased with age. Maruyama et al. (2021) reported that patients with elderly-onset AOSD developed DIC more often compared with those with younger-onset AOSD; however, the frequency of MAS was not statistically different in the two groups. Suda et al. (2020) stated that the presence of MAS and DIC was more frequent in their literature review. However, there were no significant differences in the rates of MAS and DIC between the elderly-onset and younger-onset groups in the present study. Table 5 summarizes comparisons of former reports, including clinical features and complications. AOSD is a rare disease, and the number of patients with MAS and DIC is even lower; therefore, the accumulation of cases tends to be low. As such, there are few reports on the difference in the

Table 5. Comparison of clinical characteristics of patients of elderly-onset adult-onset Still's disease between previous reports.

Author name (publication year)	Maruyama et al. (2021)	Mollaeian et al. (2021)	Suda et al. (2020)	Our cases
Number	47	42	25	20
Definition of elderly-onset	≧ 60	≧ 70	≧ 70	≧ 65
Age at onset (years), median or average	71.2	75	76.6	72.5
Female, number (%)	39 (83.0)	34 (81.0)	18 (72.0)	16 (80.0)
Clinical Features and laboratory findings				
Fever, number (%)	37 (78.7)	42 (100)	25 (100)	19 (95.0)
Skin rash, number (%)	37 (78.7)	34 (81.0)	17 (68.0)	19 (95.0)
Arthralgia, number (%)	35 (74.5)	38 (90.5)	19 (76.0)	18 (90.0)
Sore throat, number (%)	26 (55.3)†	22 (52.4)	16 (64.0)	7 (35.0)†
Lymphadenopathy, number (%)	24 (51.1)	NA	9 (36.0)	3 (15.0)†
Splenomegaly, number (%)	12 (25.5)†	14 (33.3)	7 (28.0)	6 (30.0)†
Liver abnormalities, number (%)	NA	NA	21 (84.0)	17 (85.0)
Leukocytosis (/μl), median	14,400	13,700	NA	NA
Ferritin (ng/ml), median	12,700‡	5,336	NA	9,423
Complications				
Pleuritis	13 (27.7)‡	7 (16.7)	NA	1 (5.0)
MAS (%)	8 (17.0)	NA	5 (20.0)	4 (20.0)
DIS (%)	9 (19.1)‡	NA	5 (20.0)	3 (15.0)

†Significantly lower in elderly-onset adult-onset Still's disease patients, ‡Significantly higher in elderly-onset adult-onset Still's disease patients.
DIC, disseminated intravascular coagulation; MAS, macrophage activation syndrome; NA, not applicable.

frequency of MAS and DIC between the elderly and young. Furthermore, it has been reported that the patient population of AOSD is heterogeneous (Berardicurti et al. 2021), and the triggers involved in the pathogenesis of AOSD may be more diverse in the elderly compared with the young. (Gerfaud-Valentin et al. 2014a). Therefore, the results may vary across each report. Due to the cross-sectional study design, we were not able to analyze the clinical outcomes of patients with elderly-onset AOSD, and future cohort studies are warranted to determine whether elderly-onset AOSD is associated with worse prognosis due to organ involvement.

The Pouchot score has been shown to successfully predict poor outcomes in patients with AOSD. Of note, a Pouchot score above the cutoff of 7.0 was shown to exhibit a strong prognostic impact in identifying patients at risk of AOSD-related death (Pouchot et al. 1991). Ruscitti et al. (2016) also demonstrated that a higher Pouchot score and the presence of AOSD-related complications, including MAS, were significantly associated with poor outcomes in patients with AOSD. In the present study, the Pouchot score was significantly lower in patients presenting with elderly-onset AOSD than in those presenting with younger-onset AOSD. However, there was no significant difference in the proportion of patients with a Pouchot score of ≥ 7.0 between the two groups. Although we did not perform prospective analyses for clinical outcomes due to the study design, our results suggest that elderly-onset AOSD might have some distinct clinical features; however, there was no difference in the severity of AOSD between the patients with elderly-onset and younger-onset AOSD at the time of diagnosis. Nonetheless, survival in patients with elderly-onset AOSD might be modulated by various complications including infections as a consequence of aging. Therefore, more attention is warranted for the clinical management of patients with elderly-onset AOSD to improve prognosis.

The mPouchot score proposed by Rau et al. (2010) includes arthritis and serum ferritin > 3,000 ng/mL, which replace abdominal pain and splenomegaly included in the Pouchot score. The mPouchot score, which comprises typical clinical signs and laboratory findings, can differentiate between patients with AOSD and those with bacterial sepsis. Furthermore, the mPouchot score cutoff of ≥ 4 exhibits a sensitivity of 92% and a specificity of 93% for the diagnosis of AOSD (Rau et al. 2010). In the present study, there was no significant difference in the mPouchot score between the patients with elderly-onset AOSD and those with younger-onset AOSD and most of the patients with elderly-onset AOSD exceeded this cutoff value. Taken together, these findings suggest that the patients with elderly-onset AOSD were consistent with the typical AOSD phenotype and presented with expected or less severe disease based on the Pouchot score determined at the time of disease onset.

The present study has several limitations which should be acknowledged. First, due to the retrospective study design, it was not possible to completely exclude the effects of confounding factors such as treatments. Second, the clinical course and patient outcomes were not surveyed in the present cross-sectional study. Furthermore, the study included hospitalized patients in a tertiary hospital, which might have led to selection bias. As a result, multi-center prospective studies are warranted to verify the results of the current study. Given the cross-sectional analysis utilized in the present study, not all clinical manifestations that occurred during the disease course could be determined. Finally, the study included only Japanese patients with AOSD and future studies including non-Japanese patients with AOSD are warranted to compare elderly-onset and younger-onset AOSD.

In conclusion, AOSD can develop even in elderly individuals and patients with elderly-onset AOSD present with the classical clinical manifestations in addition to several distinct features compared to patients with younger-onset AOSD. The frequencies of severe complications, such as MAS, were comparable between the patients with elderly-onset and younger-onset AOSD, and elderly-onset AOSD was not associated with higher disease severity, which would indicate worse prognosis, at the time of AOSD diagnosis.

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Conflict of Interest

The authors declare no conflict of interest.

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