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1 **Musculoskeletal ultrasound findings in adult-onset Still's disease: A case series**

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17 **Highlights**

- 18 ● Arthritis is common in AOSD patients, but inflammatory changes remain unclear.
- 19 ● A wide variety of MSKUS findings are observed in patients with AOSD.
- 20 ● MSKUS findings in AOSD require differentiation from other rheumatic diseases.

21

22 **Abstract**

23 Adult-onset Still’s disease (AOSD) is a rare systemic inflammatory disorder of unknown
24 etiology characterized by high spiking fever, salmon-like skin rash, arthritis, and elevated serum
25 ferritin levels. Early detection of AOSD is remarkably difficult because of the lack of serologic
26 biomarkers, nonspecific presentation, and rarity of the disease. Although arthralgia and arthritis are
27 the most frequent symptoms and are correlated with health-related quality of life in patients with
28 AOSD, the inflammatory changes associated with these symptoms have not been elucidated. We
29 performed musculoskeletal ultrasound (MSKUS) in 11 patients between January 1, 2008 and July
30 31, 2023, seven of whom had abnormalities. MSKUS findings of those cases suggested that some
31 patients with AOSD could present with tenosynovitis, tendonitis/peritendonitis, bursitis, and
32 enthesitis along with synovitis. This case series demonstrate the diversity of inflammatory articular
33 manifestations of AOSD identified by MSKUS.

34

35 **Keywords:** Adult-onset Still’s disease, musculoskeletal ultrasound, tendonitis/peritendonitis,
36 bursitis, enthesitis, synovitis

37

38 **1. Introduction**

39 Adult-onset Still’s disease (AOSD) is a rare systemic inflammatory disorder of unknown
40 etiology characterized by high spiking fever, salmon-like evanescent skin rash, arthritis, sore throat,
41 hepatic dysfunction, lymphadenopathy, splenomegaly, and elevated inflammatory marker and
42 serum ferritin levels (1, 2). Arthralgia is one of the most frequent symptoms observed in > 70% of
43 patients with AOSD (3). Patients with a chronic articular clinical course present with severe osteo-
44 destructive features, which cause ankyloses and functional disability (4, 5). However, few studies
45 have evaluated joint involvements in patients with AOSD by musculoskeletal ultrasound (MSKUS).
46 MSKUS is an increasingly available imaging modality in the rheumatology department and is a
47 reliable tool for detecting tendon and synovial inflammation (6, 7). Herein, we reported seven cases
48 of AOSD that presented with variable abnormalities on MSKUS.

50 **2. Patients and methods**

51 Between January 1, 2008, and July 31, 2023, 85 patients were classified as having AOSD
52 according to the Yamaguchi criteria at the Department of Rheumatology, Kobe University Hospital,
53 a 715-bed hospital in Kobe, Japan. Among them, we performed MSKUS in 11 patients, seven of
54 whom had abnormalities.

56 **3. Case reports**

57 In the following section, seven patients with AOSD with MSKUS abnormalities are presented.

58 Table 1 summarizes detailed patient characteristics.

59 **3.1.Case 1**

60 A 65-year-old woman observed erythema 4 weeks earlier and presented with high fever 2
61 weeks earlier. As she developed polyarthralgia 4 days prior, she was admitted to our hospital. On
62 physical examination, she had high fever, enlarged lymph nodes in the left mandible, and
63 polyarthrititis. Laboratory findings revealed hepatic dysfunction, and moderately elevated serum
64 ferritin level (1,941 ng/mL). Contrast-enhanced computed tomography (CT) revealed enlargement
65 of multiple lymph nodes and hepatosplenomegaly. MSKUS revealed active tendonitis of the right
66 quadriceps femoris tendon and left second finger extensor tendon and tenosynovitis of the left
67 extensor digitorum longus and tibialis anterior tendons (Fig. 1A, B). At the time, we suspected of
68 peripheral spondyloarthritis (SpA) and malignant lymphoma as well as AOSD. Nonsteroidal anti-
69 inflammatory drugs initially resolved the symptoms for 3 weeks, but she again presented with fever,
70 rash, and migrating arthralgia. Follow-up MSKUS showed reduction of tendonitis and
71 tenosynovitis, previously noted (Fig.1 C, D). However, active tendonitis of the right second and
72 fifth finger extensor tendons was observed. One month after the admission, the histopathological
73 findings of the left supraclavicular lymph node biopsy performed after admission, showed no
74 malignancy, and the patient was diagnosed with AOSD. At that point, she had developed
75 macrophage activation syndrome (MAS). We initiated prednisolone (PSL) (1 mg/kg) and

76 tocilizumab (TCZ), which relieved the symptoms after 1 week, and abnormal findings on MSKUS
77 had disappeared.

78

79 **3.2.Case 2**

80 A 41-year-old man presented with spike fever, pharyngalgia, and ankle arthralgia. As he
81 had a persistent high fever after antibiotic use, he was referred to our department 4 weeks after
82 onset. Physical examination revealed fever, salmon-like skin rash, and swelling in the right second
83 PIP joint. Initial laboratory findings revealed hepatic dysfunction, and elevated serum ferritin level
84 (5,268 ng/mL). MSKUS revealed active synovitis of the right second PIP joint, mimicking
85 rheumatoid arthritis (RA). After excluding infections and other rheumatic disorders, the patient was
86 diagnosed with AOSD. The patient received PSL (1 mg/kg) after steroid pulse therapy, and all of
87 his symptoms resolved.

88

89 **3.3.Case 3**

90 A 79-year-old woman developed fever, erythema and polyarthralgiafor a month and was
91 referred to our department. She had fever, erythema, and polyarthralgia. Initial laboratory findings
92 revealed notable elevations in hepatic enzymes and serum ferritin levels (22,004 ng/mL). MSKUS
93 revealed active synovitis of the elbow (Fig. 2A), wrist, and right fourth PIP joint, tenosynovitis of
94 the extensor digitorum and indicis tendon of the right wrist, and bursitis of the subscapularis bursa.
95 We performed skin and lung biopsies; excluded the diagnosis of infection, malignancy, and other

96 rheumatic diseases; and diagnosed the patient with AOSD. Subsequently, we initiated PSL (0.6
97 mg/kg) and tacrolimus (TAC). The patient's symptoms, including arthralgia, resolved.

98

99 **3.4.Case 4**

100 A 46-year-old woman observed swollen and tender lymph nodes in her neck 10 weeks
101 earlier. Nine weeks earlier, she presented with spiked fever, pharyngalgia, and skin rash. She had
102 persistent symptoms for 4 weeks, even after taking antibiotics, and was admitted to the previous
103 hospital 5 weeks earlier. After excluding infections, malignancies, and other rheumatic disorders,
104 the patient was transferred to our department. She had fever, pharyngalgia and erythema and
105 polyarthralgia. Laboratory findings elevated serum ferritin level (7,473 ng/mL). MSKUS revealed
106 active synovitis of the bilateral knees and right interphalangeal joint and tenosynovitis of the
107 extensor digitorum and indicis tendons of the right wrist. We diagnosed the patient with AOSD and
108 initiated PSL (1 mg/kg). As only arthralgia persisted, we added TAC, which relieved the symptoms.

109

110 **3.5.Case 5**

111 A 49-year-old woman with a history of rheumatic fever presented with intermittent fever,
112 pharyngalgia, and polyarthralgia for 4 weeks, and was admitted to the previous hospital. As she had
113 a persistent fever after antibiotic use and was excluded from the diagnosis of infection, malignancy,
114 and other rheumatic diseases by culture, bone marrow examination, and CT scans, she was referred
115 to our hospital. The patient experienced shoulder joint pain. As MSKUS revealed bursitis of the left

116 shoulder (Fig. 2B), we suspected polymyalgia rheumatica (PMR) and RA. He received PSL (10 mg)
117 and methotrexate (MTX) (8 mg), which improved the symptoms. Nine months after the first onset,
118 when she was taking 3 mg of PSL, she developed high fever, pharyngalgia, and shoulder joint pain.
119 Laboratory findings revealed elevated hepatic enzymes. As serum ferritin level subsequently
120 increased and we excluded infection and other rheumatic disorders, we diagnosed her with AOSD
121 and initiated PSL (1 mg/kg). Although symptoms other than joint pain quickly resolved, she
122 presented with persistent arthralgia, and TAC and TCZ were administered.

123

124 **3.6.Case 6**

125 A 62-year-old woman developed arthralgia in both hands, skin rash with fever, and right
126 cervical lymphadenopathy. A local physician administered 20 mg of PSL, and all symptoms
127 improved, and she remained stable for 1 year. However, she developed fever and skin rash and
128 polyarthralgia when she was taking 5 mg of PSL. Even after the administration of 20 mg of PSL and
129 1 mg of TAC, she experienced persistent arthralgia and was referred to our department. Physical
130 examination revealed erythema and multiple arthralgias in the fingers. Hand and knee radiography
131 revealed mild narrowing of the PIP joints. MSKUS revealed active peritendonitis of the right fourth
132 finger extensor digitorum tendon and enthesitis of the left fourth PIP joint (Fig. 2C). Because her
133 differential diagnoses were RA, undifferentiated peripheral SpA, and AOSD, establishing the
134 diagnosis was difficult. She was treated with MTX in addition to PSL and TAC but showed little
135 improvement in joint symptoms. Six months after the admission, she developed fever, skin rash,

136 and sore throat. After several examinations, including skin biopsy, the patient was diagnosed with
137 AOSD. We then increased the PSL dose to 1 mg/kg and administered TCZ. Although the symptoms
138 other than joint pain quickly resolved, the patient presented with persistent arthralgia.

139

140 3.7.Case 7

141 A 30-year-old woman was diagnosed with MAS of unknown cause, and received PSL (1
142 mg/kg) after 4 years and 6 months earlier. The patient has been asymptomatic for 6 months. While
143 taking 15 mg of PSL, she developed persistent fever and polyarthralgia. She was diagnosed with
144 AOSD and was administered 0.5 mg/kg of PSL. After starting MTX, the arthralgia showed mild
145 improvement; however, serum CRP level was elevated, and she received 3 mg/kg infliximab (IFX).
146 IFX was insufficiently effective, and the patient was referred to our department. She presented with
147 high fever, salmon-like skin rash, polyarthralgia, hepatic dysfunction, and elevated serum ferritin
148 level (5,299 ng/mL). We diagnosed the patient with AOSD. Two years after the initial visit to our
149 department, we switched from IFX to TCZ, and the arthralgia improved. Fourteen years after the
150 first visit, the arthralgia recurred. MSKUS revealed tendonitis of the extensor digitorum tendon,
151 synovitis of the right fifth and left third metacarpophalangeal (MCP) joints, tenosynovitis, synovitis
152 and space narrowing of the extensor digitorum and indicis tendons of the right wrist (Fig. 2D).

153

154 4. Discussion

155 Herein, we reported seven cases of AOSD in which abnormalities were detected using
156 MSKUS. Although arthralgia and arthritis are the most common symptoms in patients with AOSD,
157 the inflammatory changes associated with these symptoms have not yet been fully elucidated.
158 Ruscitti et al. reported that magnetic resonance imaging could document the presence of synovitis in
159 approximately 60% of the patients with AOSD (8). Only one study reported that MSKUS was
160 performed in patients with AOSD, which revealed that there were tenosynovitis and synovitis in the
161 affected joints (9). In our cases, synovitis, tenosynovitis, bursitis, tendonitis, and enthesitis were
162 detected. The affected joints were the PIPs or IPs, wrists, shoulders, knees, MCPs, elbow, and ankle.
163 A previous study reported that the clinically affected joints in patients with AOSD were the fingers,
164 wrists, and knees (10), and the trend observed in our study is similar to the report. Our case series
165 shows that the inflamed structures detected using MSKUS vary. In most of our cases, we recalled
166 other diseases, such as RA, peripheral SpA, PMR, and osteoarthritis, as differentials rather than
167 AOSD because other symptoms or results of laboratory findings were atypical for AOSD. Although
168 synovitis is commonly observed in RA (11), other findings such as tenosynovitis,
169 tendonitis/peritendonitis and bursitis are also present (12). In PMR, tenosynovitis of the biceps
170 tendon and bursitis in the shoulder are typical MSKUS findings (13). Recent reports have also noted
171 tendonitis in the popliteus tendon in the knee (14). These reports are highlighting the diverse peri-
172 articular involvement seen in many rheumatic diseases. On the other hand, typical MSKUS findings
173 in AOSD have not been well established, and relying solely on MSKUS may lead to misdiagnosis
174 with other rheumatic diseases. It is important to include AOSD in the differential with other

175 diseases and to make a comprehensive assessment when making the diagnosis because MSKUS
176 findings in patients with AOSD resemble those of various other diseases.

177 In our cases, the timing of MSKUS varied from early to late (4 weeks to 20 years). Arthritis
178 in patients with AOSD initially migrates and stabilizes during the course of the disease (15). The
179 migration of joint involvement was detected using MSKUS in case 1. Although the patients in cases
180 1, 2, and 3 experienced elimination of arthralgia after treatment, the patients in the other cases
181 experienced persistent arthralgia even after treatment. The result indicates the patient might be in
182 the early stage of the disease if abnormal findings on MSKUS disappeared, and the early treatment
183 might lead to a favorable prognosis in patients with arthralgia. However, as the number of cases in
184 our study was small, the association between the clinical stage and the targeted lesion and abnormal
185 findings was unclear.

186 In conclusion, our study provides valuable insights into the use of MSKUS in the
187 evaluation of patients with AOSD. Our cases suggest that some patients with AOSD may present
188 with tenosynovitis, tendonitis/peritendonitis, bursitis, and enthesitis along with synovitis, mimicking
189 other inflammatory rheumatic diseases. Further studies focusing on the association among the
190 clinical stages, targeted lesions, and long-term outcomes of AOSD are essential for refining early
191 diagnostic approaches and enhancing treatment strategies.

192

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195

196 **Author contributions**

197 EKY conducted the case studies. EKY drafted the manuscript. HY and SS supervised the case
198 series. All authors have approved the manuscript for submission.

199

200 **Conflicts of interest**

201 All authors have no conflicts of interest to declare.

202

203 **Consent to publish**

204 We obtained the written informed consent to publish.

205

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254 **Table 1. Patient characteristics and MSKUS findings**

Case	Age at onset and sex	Time from onset to MSKUS	Treatment when MSKUS was performed	Joints	MSKUS findings				
					Synovitis	Tenosynovitis	Bursitis	Tendonitis /Peritendonitis	Enthesitis
1	65, F	4 weeks	None	Finger Knee Ankle	R. PIP2/PIP5 L. PIP2	L. ankle		R. PIP2/PIP5 L. PIP2 R. knee	
2	41, M	5 weeks	None	Finger	R. PIP2				
3	79, F	6 weeks	None	Finger Wrist Elbow Shoulder	R. elbow R. wrist R. PIP4	R. shoulder R. wrist	R. shoulder		
4	46, F	11 weeks	None	Finger Wrist Knee	R. & L. knee R. IP (finger)	R. wrist			
5	49, F	32 weeks	None	Shoulder		L. shoulder	L. shoulder		
6	62, F	2 years	PSL 20 mg/day TAC	Finger				R.PIP4	L. PIP4
7	30, F	20 years	PSL 7.5 mg/day TCZ	Finger Wrist	R. Wrist L. MCP3	R. Wrist		R. MCP5 L. MCP 3	

255 R, right; L, left; PIP, proximal interphalangeal; MCP, metacarpophalangeal; IP, interphalangeal; PSL, prednisolone; TAC, tacrolimus; TCZ,
256 tocilizumab.

257 **Figure legends**

258 Figure 1: (Case 1) The longitudinal scan of the right knee shows the presence of synovial effusion
259 (asterisk), synovial proliferation (arrowheads), thickening of the quadriceps femoris tendon, and
260 active PD (A). The longitudinal scan of the left ankle shows thickening of the TA tendon and
261 peritendinous effusion with PD signals (B). After 3 weeks, MSKUS reveals no evident findings (C,
262 D). (GS, gray scale; PD, power Doppler; Q, quadriceps femoris tendon; TA, tibialis anterior tendon)
263

264 Figure 2: (A: case 3) The longitudinal scan of the right elbow shows synovial effusion (asterisk) and
265 proliferation (arrowheads) with active PD. (B:MSKUS case 5) The transverse scan of the left
266 shoulder shows subdeltoid bursal thickness with PD signals (arrows). (C: case 6) The longitudinal
267 scan of the left PIP4 joint shows the per-enthesal thickening (below arrows) and joint effusion
268 (asterisk) and synovial proliferation (arrowheads) with PD signals. (D: case 7) The dorsal
269 longitudinal scan of the right wrist shows the thickening of the extensor digitorum tendon and
270 tendon sheath effusion (asterisks) and intra-articular synovial proliferation (arrowheads) with PD
271 signals. (GS, gray scale; PD, power Doppler; T, triceps brachii muscle; JSN, joint space narrowing;
272 PIP, proximal interphalangeal)



