

Application of MS score in macrophage activation syndrome patients associated with adult onset Still's disease

We read with great interest the article by Minoia *et al* which named development and initial validation of the macrophage activation syndrome (MAS)/systemic juvenile idiopathic arthritis (sJIA) (MS) score for diagnosis of MAS in sJIA.

MAS is a life-threatening complication of rheumatic disorders, including sJIA, adult-onset Still's disease (AOSD) and lupus.¹⁻⁴ Timely diagnosis and appropriate treatment of MAS are particularly important to improve the prognosis of MAS patients. At present, hemophagocytic lymphohistiocytosis (HLH)-2004 and HLH-2009 criteria are widely used to identify MAS associated with AOSD. Hemophagocytic syndrome diagnostic (HS) score was developed previously to facilitate MAS recognition, but still requires validation.⁵ In 2019, Francesca Minoia *et al* reported a MS score for classification of sJIA-associated MAS patients.⁶ Considering that sJIA and AOSD are thought to constitute the same disease entity occurring at different ages, we intended to evaluate the application of MS score in AOSD-associated MAS patients.

We collected AOSD patients from 1 January 2012 to 31 July 2019 from six centres across China. Patients were included in this study if they were older than 18 years of age, and met the Yamagishi criteria for a diagnosis of AOSD. MAS was diagnosed using the HLH-2004 diagnostic criteria, and the diagnosis was confirmed by the attending rheumatologists. Clinical information was recorded and analysed. MS score was calculated for each patient according to the previous report.

A total of 450 AOSD patients (60 AOSD associated MAS, 390 AOSD without MAS) were included in this study. Clinical features and lab results as the time of MAS diagnosis were shown in table 1. The application of the MS score (≥ -2.1) yielded a sensitivity of 100%, a specificity of 29.85%, a positive predictive rate of 36.15%, a negative predictive rate of 100% in the diagnosis of AOSD-MAS with a Kappa value of 0.320. However, a further receiver operator characteristic curve analysis suggested

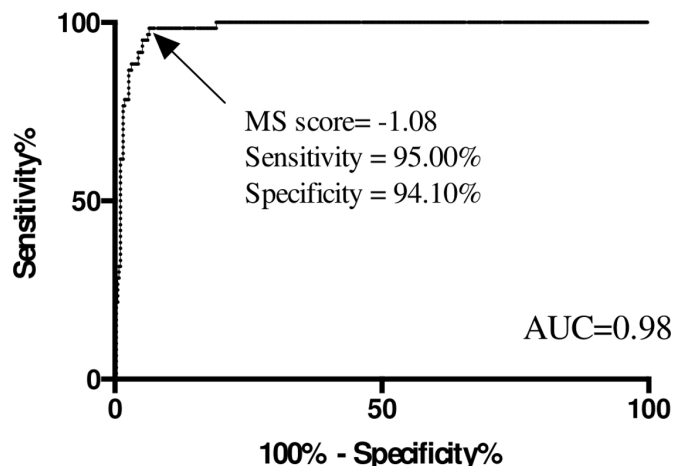


Figure 1 Modified criteria of MS score in the diagnosis of AOSD associated MAS. In a febrile patient with AOSD, the diagnosis of MAS should be considered if the MS score is ≥ -1.08 . The area under the curve (AUC) of the model is 0.98. AOSD, adult-onset Still's disease; MAS, macrophage activation syndrome.

that setting -1.08 as the score cut-off could provide the best discrimination between AOSD with and without MAS (figure 1). MS score ≥ -1.08 yielded a sensitivity of 94.10%, a specificity of 95.00% in the diagnosis of MAS associated with AOSD. The positive predictive rate was 99.19% and the negative predictive rate of 71.25%, with a Kappa value of 0.781.

The current finding suggested that even though there are many similarities between sJIA and AOSD, adult and young patients have notable differences in terms of clinical manifestations and lab results. For instance, central nervous involvement is quite rare in AOSD-MAS patients, probably because adults usually have much more stable central nervous system. In addition, the levels of platelet count and fibrinogen are usually lower in AOSD-MAS patients as compared with those in sJIA-MAS patients, which could lead to higher MS scores in AOSD patients. Therefore, the items calculated in the reported sJIA-MS score as well as


Table 1 Clinical manifestations of AOSD patients with and without MAS

	AOSD with MAS (60)	AOSD without MAS (390)	P value
Sex (male/female)	18/42	72/318	0.055
Age (years)	29 (22-37)	38 (27-50)	<0.0001
Death (n, %)	13 (21.67%)	8 (2.05%)	<0.0001
Fever (n, %)	60 (100%)	255 (65.38%)	<0.0001
Active arthritis (n, %)	19 (31.67%)	372 (95.38%)	<0.0001
Splenomegaly	50 (83.33%)	52 (13.33%)	<0.0001
Central nervous system disease	1 (1.67%)	0	0.133
Haemorrhagic manifestations	1 (1.67%)	3 (0.77%)	0.437
Platelet count ($\times 10^9/L$)	90 (60-144)	244 (222-485)	<0.0001
Liver dysfunction (n, %)	58 (96.67%)	73 (18.72%)	<0.0001
Lactic dehydrogenase (U/L)	1024 (599-2145)	313 (222-485)	<0.0001
Triglycerides (mmol/L)	2.35 (1.82-3.78)	1.42 (0.97-2.03)	<0.0001
Fibrinogen (mg/dL)	151 (104-219)	306 (52-452)	<0.0001
Ferritin (ng/mL)*	1500 (1500-1500)	1264 (359-1500)	<0.0001
Bone marrow hemophagocytosis (n, %)	39 (65%)	13 (3.33%)	<0.0001
MS score (median)	-0.01 (-0.27 to 0.50)	-2.67 (-3.51 to 1.82)	<0.0001

*The up limit of the detection of ferritin was 1500 ng/mL in our centres.
AOSD, adult-onset Still's disease; MAS, macrophage activation syndrome.

the cut-off for sJIA-MAS diagnosis (> -2.1) should be modified for diagnosis of MAS associated with AOSD. In our cohort, MS score ≥ -1.08 might be a better cut-off for AOSD-MAS diagnosis with an area under the curve of 0.98.

Further prospective and independent validations with larger sample size are needed to evaluate the modified MS score in the diagnosis for the life-threatening MAS condition in AOSD patients.

Ran Wang ¹, Ting Li,² Shuang Ye,² Wenefng Tan,³ Cheng Zhao,⁴ Yisha Li,⁵ Chunde Bao ¹, Qiong Fu¹

¹Department of Rheumatology, Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital, Shanghai, China

²Department of Rheumatology, Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital South Campus, Shanghai, China

³Department of Rheumatology, The First Affiliate Hospital of Nanjing Medical University, Nanjing, China

⁴Department of Rheumatology, The Affiliated Nanjing Drum Tower Hospital of Nanjing University Medical School, Nanjing, China

⁵Department of Rheumatology, Xiangya Hospital of Central South University, Changsha, China

Correspondence to Dr Ran Wang, Department of Rheumatology, Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital South Campus, Shanghai 200025, China; wangran686@126.com

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ORCID iDs

Ran Wang <http://orcid.org/0000-0001-7857-8433>

Chunde Bao <http://orcid.org/0000-0002-0466-1872>

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