Online supplement to Hemophagocytic Lymphohistiocytosis: Prevalence, Risk Factors, Outcome, and Outcome-related Factors in Adult Idiopathic Inflammatory Myopathies, *The Journal of Rheumatology,* doi:10.3899/jrheum.190542

Supplementary Table 1: Revised diagnostic guidelines for HLH [11]

HLH: Hemophagocytic lymphohistiocytosis; NK cell: Natural killer cell; IL-2: Interleukin-2.

The diagnosis HLH can be established if one of either (1) or (2) below is fulfilled
(1) A molecular diagnosis consistent with HLH
(2) Diagnostic criteria for HLH fulfilled (five out of the eight criteria below)
(A) Initial diagnostic criteria (to be evaluated in all patients with HLH)
Fever (≥38.5°C for ≥7 days)
Splenomegaly
Cytopenias (affecting 2 of 3 lineages in the peripheral blood)
Hemoglobin <90 g/L (in infants <4 weeks: hemoglobin <100 g/L)
Platelets <100*10^9/L
Neutrophils <1.0*10^9/L
Hypertriglyceridemia and/or hypofibrinogenemia:
Fasting triglycerides≥3.0 mmol/L (i.e., 265 mg/dl)
Fibrinogen≤1.5 g/L
Hemophagocytosis in bone marrow or spleen or lymph nodes (No evidence of malignancy)
(B) New diagnostic criteria
Low or absent NK cell activity (according to local laboratory reference)
Ferritin≥500 mg/L
Soluble CD25 (i.e., soluble IL-2 receptor)≥2,400 U/ml

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Supplementary Table 2: P value, P-adjusted, OR value and 95% Cl for factors in univariate logistic regression analysis.

OR value: Odds ratio value; 95%Cl: 95% Confidence interval; P-adjusted: adjusted p value after false discovery rate (FDR) correction; y: years; m: months; ILD: Interstitial lung disease; AE-ILD: Acute exacerbation of interstitial lung disease; CK: Creatine kinase; LDH: Lactate dehydrogenase; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; On-admission hyperferritinemia: on-adimission serum ferritin≥500ng/ml; ANA: Antinuclear *antibody; ACA:* Anti-centromere antibody; *MMF:* Mycophenolate mofetil; DMARDs: disease-modifying anti-rheumatic drugs; DST-based antibiotics: antibiotics based on drug resistant testing; Prophylactic SMZ: Prophylactic application of sulfamethoxazole; DM: dermatomyositis; PM: Polymyositis; CADM: Clinically amyopathic dermatomyositis.

Factors	P value	OR value	95%Cl	P-adjusted
Age(y)	**0.990**	**1.000**	**0.962~1.040**	**1.000**
Sex(male/female)	**1.000**	**1.000**	**0.316~3.168**	**1.000**
Course of disease(m)	**0.947**	**0.999**	**0.982~1.017**	**1.000**
Duration of diagnosis delay(m)	**0.652**	**1.010**	**0.968~1.053**	**1.000**
Disease activity				
On-admission disease activity	**0.001**	**1.350**	**1.139~1.600**	**0.020**
Clinical manifestations or complications				
Heliotrope rash	**0.524**	**1.400**	**0.497~3.945**	**0.999**
Gottron's sign	**0.524**	**1.400**	**0.497~3.945**	**0.999**
Periungual erythema	**0.872**	**0.875**	**0.172~4.455**	**1.000**
Mechanic's hands	**0.352**	**0.365**	**0.044~3.052**	**0.859**
Raynaud's phenomenon	**0.999**	**<0.001**	**0.000~**	**1.000**
Muscle pain	**0.394**	**1.571**	**0.556~4.439**	**0.887**
Muscle weekness	**0.258**	**2.473**	**0.516~11.854**	**0.743**
Joint pain	**0.713**	**1.244**	**0.388~3.993**	**1.000**
Joint swelling	**1.000**	**1.000**	**0.250~3.998**	**1.000**
Dysphagia	**0.195**	**2.059**	**0.690~6.140**	**0.681**
Dysarthria	**0.833**	**0.788**	**0.086~7.200**	**1.000**
Respiratory muscle involvement	**0.999**	**<0.001**	**0.000~**	**1.000**

ILD	**0.999**	**>100.000**	**0.000~**	**1.000**
AE-ILD	**<0.001**	**10.771**	**3.293~35.233**	**<0.001**
Gastrointestinal hemorrhage	**0.005**	**5.909**	**1.732~20.159**	**0.061**
Cardiac involvement	**0.301**	**2.200**	**0.493~9.811**	**0.798**
Infection	**<0.001**	**12.143**	**3.180~46.361**	**<0.001**
Carcinoma	**1.000**	**1.000**	**0.193~5.173**	**1.000**
On-admission laboratory findings				
CK(U/L)	**0.201**	**1.000**	**1.000~1.000**	**0.681**
LDH(U/L)	**0.845**	**1.000**	**0.999~1.002**	**1.000**
ESR(mm/h)	**0.499**	**1.008**	**0.985~1.032**	**0.999**
CRP(mg/L)	**0.226**	**1.008**	**0.995~1.021**	**0.726**
Hepatic insufficiency	**0.049**	**3.780**	**1.005~14.215**	**0.329**
Renal insufficiency	**0.106**	**3.143**	**0.782~12.623**	**0.497**
On-admission hyperferritinemia	**0.009**	**16.081**	**2.031~127.320**	**0.092**
ANA	**0.099**	**0.412**	**0.143~1.182**	**0.497**
ANA titer	**0.153**	**0.993**	**0.983~1.003**	**0.630**
Anti-SSA	**0.484**	**0.567**	**0.116~2.776**	**0.999**
Anti-SSA52	**0.396**	**0.625**	**0.211~1.849**	**0.887**
Anti-SSB	**0.999**	**<0.001**	**0.000~**	**1.000**
Anti-Ro52	**NA**	**NA**	**NA**	**NA**
Anti-RNP	**0.999**	**<0.001**	**0.000~**	**1.000**
Anti-Jo-1	**0.696**	**0.647**	**0.073~5.742**	**1.000**
ACA	**0.999**	**<0.001**	**0.000~**	**1.000**
Comorbidities/Harmful hobbies				
Smoking	**0.872**	**0.875**	**0.172~4.455**	**1.000**
Alcohol abuse	**0.256**	**0.294**	**0.036~2.426**	**0.743**
Hypertension	**0.004**	**5.084**	**1.705~15.161**	**0.061**
Diabetes	**1.000**	**1.000**	**0.193~5.173**	**1.000**
Allergy	**0.188**	**0.244**	**0.030~1.989**	**0.681**
Medications				
Steroids	**NA**	**NA**	**NA**	**NA**
MMF	**0.024**	**0.092**	**0.012~0.734**	**0.209**
Thalidomide	**0.654**	**0.693**	**0.139~3.447**	**1.000**
Hydroxychloroquine	**1.000**	**1.000**	**0.250~3.998**	**1.000**
Cyclosporine	**0.321**	**4.176**	**0.248~70.200**	**0.816**
Azathioprine	**NA**	**NA**	**NA**	**NA**
Methotrexate	**0.155**	**4.375**	**0.572~33.439**	**0.630**
Immunoglobulin	**0.045**	**3.182**	**1.025~9.873**	**0.329**
Cyclophosphamide	**1.000**	**<0.001**	**0.000~**	**1.000**
Steroid monotherapy	**0.910**	**1.065**	**0.355~3.194**	**1.000**

Steroid+DMARDs	**0.080**	**0.364**	**0.118~1.127**	**0.444**
Steroid+immunoglobulin	**0.054**	**3.571**	**0.980~13.012**	**0.329**
Steroid+DMARDs+immunoglobulin	**0.559**	**1.675**	**0.298~9.430**	**1.000**
DST-based antibiotics	**0.999**	**<0.001**	**0.000~**	**1.000**
Third-line antibiotics	**0.888**	**1.143**	**0.179~7.283**	**1.000**
Intravenous antifungal drugs	**0.999**	**>100.000**	**0.000~**	**1.000**
Prophylactic SMZ	**0.268**	**2.875**	**0.443~18.654**	**0.743**
IIM subtypes				
DM	**0.914**	**1.060**	**0.368~3.054**	**1.000**
PM	**0.577**	**0.723**	**0.231~2.260**	**1.000**
CADM	**0.407**	**2.125**	**0.357~12.634**	**0.887**

Supplementary Data 1: Details about infection and anti-bacterial/anti-fungal therapy within case group and control group.

EBV: Epstein-Barr virus; CMV: Cytomegalo virus.

In case group, 6 had bacterial infection, 5 had fungal infection, one was diagnosed with tuberculosis, one was found to have EBV and bacterial infection, and 2 suffered from both bacterial and fungal infection. The 9 cases with bacterial infection included 3 cases with positive blood culture results (one with Stenotrophomonas maltophilia and 2 with Acinetobacter baumannii), 5 cases with positive findings in sputum culture (one with Escherichia coli, one with Acinetobacter baumannii, one with Staphylococcus haemolyticus and two with Stenotrophomonas maltophilia) and one case with positive finding in blood and sputum culture (Klebsiella pneumoniae). 7 cases with fungal infection were identified based on one blood culture positive finding of Candida albicans and 6 positive results of sputum culture (one with Aspergillus fumigatus, one with Cryptococcus, and 4 with medium to large amount of Candida albicans). Mycobacterium tuberculosis was found in sputum culture of one patient. Serum IgM and DNA of EBV were detected in one patient and confirmed his EBV infection.

In control group, the 11 cases with bacterial infection included 3 cases with positive blood culture results (one with Stenotrophomonas maltophilia and 2 with Escherichia coli), 8 cases with positive findings in sputum (one with Stenotrophomonas maltophilia, one with Streptococcus viridans, one with Staphylococcus aureus, one with Escherichia coli, two with Pseudomonas aeruginosa and two with Enterobacter cloacae). 13 cases with fungal infection were identified based on positive results of sputum culture (one with Pneumocystis carinii, one with Cryptococcus, 2 with Aspergillus fumigatus and 9 with medium to large amount of Candida albicans). Mycobacterium

tuberculosis was found in sputum culture of one patient. Serum IgM and DNA of CMV were detected in one patient and confirmed her CMV infection.

In case group, 66.7% of secondary HLH patients with bacterial infection received intravenous third-line antibiotics with vancomycin in 2 cases, meropenem in 3 cases, imipenem in 3 cases and linezolid in one case. Most of the antibiotics therapies (66.7%) were reasonably based on the result of drug susceptibility testing, meanwhile 33.3% of them were merely empirical. In addition, in secondary HLH patients with fungal infection, 100% of them received potent intravenous antifungal therapies. Prophylactic use of SMZ was only seen in 2 HLH patients (11.1%).

In control group, 63.6% of patients with bacterial infection received intravenous third-line antibiotics with meropenem in 3 cases, imipenem in 3 cases and linezolid in 2 cases. For all the patients with bacterial infection, antibiotics therapies were reasonably based on the result of drug susceptibility testing. In addition, in patients with confirmed fungal infection, 69.2% of them received potent intravenous antifungal therapies. Prophylactic use of SMZ was only seen in 3 patients (4.2%).

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Supplementary Figure 1: Hemophagocytosis on bone marrow smear of 3 patients with HLH in this study (from a to c).

HLH: Hemophagocytic lymphohistiocytosis.