MAS is a life-threatening complication of Still's disease

MAS is a subtype of secondary HLH that occurs in the setting of rheumatic disease.[1,2] MAS is a life-threatening condition that significantly increases the risk of death for patients with Still's disease[3–5]

Incidence

sJIA | 0.3–0.8/100,000[a,6]
AOSD | 0.16–0.62/100,000[a,7]

Subclinical MAS may be present in 31–53% of people with known or suspected sJIA[b,12,13]

Diagnosed with MAS

sJIA | 10–25%[8,9]
AOSD | 8–23%[4,7,10,11]

MAS may occur

- At the onset of Still's disease
  In a study of 362 patients with MAS in sJIA, MAS occurred at sJIA onset for 22% of patients[8]
- MAS is also known to be recurrent in sJIA, but information on the frequency of recurrence is lacking[14]

Time to diagnosis may differ depending on prior diagnosis of underlying Still's disease[15]

Mortality

sJIA | 8–23%[2,16]
AOSD | 20–56%[2,4,17]

MAS in Still's disease is a severe burden on patients and healthcare resources

Intensive care

In a study of 362 patients with MAS in sJIA:[8]

35%
were admitted to the ICU

In a multi-institutional retrospective study of 71 confirmed adult patients with HLH/MAS who required ICU admission:[c,18]

- 72% required mechanical ventilation
- 71% required norepinephrine

In a study of 8 patients with MAS in AOSD:[19]

Long hospital stay — Median 45 days (range 20–180 days)

Further relapses — ~25% of patients have multiple relapses

[a]Estimation based on limited available published literature. [b]Patients with subclinical MAS have mild MAS disease activity, with presence of activated macrophages or hemophagocytosis, but do not meet the criteria for a full clinical diagnosis.[12] [c]All-cause HLH/MAS.[18]

AOSD, adult-onset Still's disease; HLH, hemophagocytic lymphohistiocytosis; ICU, intensive care unit; MAS, macrophage activation syndrome; sJIA, systemic juvenile idiopathic arthritis.

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Clinical diagnosis of MAS in Still's disease

Clinical and laboratory features of MAS include:[1,2]

- High fever
- Hepatosplenomegaly
- Hyperferritinema
- Lymphadenopathy
- Hypertriglyceridemia
- Cytopenias

MAS can occur at the onset of Still's disease or later in disease course[3]

Compared with late-onset MAS, patients with MAS at the onset of Still's disease:[3]

- Are younger
- Have less CNS involvement
- Have higher ESR

Other than ESR, laboratory parameters are comparable in patients with early or late onset of MAS[3]

Diagnosing MAS is challenging because of the clinical overlap with other conditions[1,2,4]

- Infection[a,5–7]
- Sepsis[2,6]
- Rheumatoid disorders[2,7]
- Malignancy[2,6,7]
- Liver failure[1,6]
- Immune disorders[1,6]

The MAS/sJIA (MS) score and EULAR/ACR/PRINTO classification criteria have been developed specifically for patients with sJIA[8,9]

MAS in sJIA (2016 EULAR/ACR/PRINTO) classification criteria[9]

- ✓ Fever
- ✓ Ferritin ≥684 ng/mL
- ⊕ Any 2 of:
  - ✓ Platelet count ≤181 × 10^9/L
  - ✓ AST >48 U/L
  - ✓ Triglycerides >156 mg/dL
  - ✓ Fibrinogen ≤360 mg/dL

Laboratory and biomarker patterns may help differentiate MAS from other conditions[4]

Increased

- CXCL9
- IL-18
- Ferritin
- sCD25
- ALT
- AST
- Bilirubin
- Triglycerides
- D-dimer
- PT/INR/PTT
- CRP
- LDH
- CSF studies

Decreased

- Fibrinogen
- Neutrophils
- Lymphocytes
- Hemoglobin
- Platelets
- Albumin

Other

- ESR may increase or decrease
- Brain imaging may be abnormal

[a]Infection is estimated to trigger MAS in one-third of patients with sJIA.[3]

ACR, American College of Rheumatology; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CNS, central nervous system; CSF, cerebrospinal fluid; CRP, C-reactive protein; CXCL9, chemokine C-X-C motif ligand 9; ESR, erythrocyte sedimentation rate; EULAR, European Alliance of Associations for Rheumatology; IL, interleukin; LDH, lactate dehydrogenase; MAS, macrophage activation syndrome; PRINTO, Paediatric Rheumatology International Trials Organisation; PT/INR/PTT, prothrombin time/international normalized ratio/partial thromboplastin time; sCD25, soluble CD25 (also known as soluble interleukin-2 receptor α [sIL-2Rα]); sJIA, systemic juvenile idiopathic arthritis.

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