orphanaesthesia

Anesthesia recommendations for patients suffering from

# Macrophage activation syndrome

**Disease name:** Macrophage activation syndrome

**ICD 10:** D76.2

**Synonyms:** haemophagocytic lymphohistiocytosis, reactive haemophagocytic syndrome, hemophagocytic syndrome

Macrophage activation syndrome (MAS) is a life-threatening complication of rheumatic disease that, for unknown reasons, occurs much more frequently in individuals with systemic juvenile idiopathic arthritis (SJIA) and in those with adult-onset Still disease. Macrophage activation syndrome is characterized by pancytopenia, liver insufficiency, coagulopathy, and neurologic symptoms and is thought to be caused by the activation and uncontrolled proliferation of T lymphocytes and well-differentiated macrophages, leading to widespread hemophagocytosis and cytokine overproduction.

The incidence of MAS is unknown as there is a wide spectrum of clinical manifestations, and episodes may remain unrecognized.

Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

**Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net**

## Disease summary

Recent findings in hemophagocytic lymphohistiocytosis, a disease that is clinically similar to MAS, highlight the possible pathogenetic role of a defective function of perforin, a protein involved in the cytolytic processes and control of lymphocyte proliferation.

Primary MAS is the most typical manifestation of rare autosomal-recessively inherited disorders due to several genetic defects involved in granule-mediated cytotoxicity, killing of infected cells and termination of immunologic responses. It has been shown that mutations of the perforin gene (PRF-1,10q21) can explain 20-40% of primary forms of MAS.

Secondary or acquired forms of MAS can break out at any time during the course of a primitive disease and occasionally it might be its presenting manifestation. In cases of acquired MAS no underlying immunologic deficiency can be identified. Acquired forms of MAS are most frequent in children with systemic onset-juvenile idiopathic arthritis: some authors suggest an association rate of 5-10% and MAS is believed to contribute significantly to mortality rate in this category of juvenile idiopathic arthritis.

Both primary and acquired forms of MAS can be triggered by viral, bacterial, fungal infections, parasitic infestations or specific drug administrations

Although the clinical features of MAS have been well documented, early diagnosis can be difficult. Measurement of the serum ferritin level may assist in the diagnosis and may be a useful indicator of disease activity, therapy response, and prognosis. The recognition that MAS belongs to the secondary or reactive hemophagocytic syndromes has led to the proposal to rename it according to the contemporary classification of histiocytic disorders.

The principle challenge for treating patients with HLH is making a timely diagnosis. It is also critical to search for and treat underlying triggers of HLH, and institute specific antimicrobial therapy.

Although HLH appears to be a disease of excessive immune activation, the ideal form of immune suppression/anti-inflammatory therapy remains unknown. Although somewhat responsive to corticosteroids and clearly responsive to etoposide or anti-T-cell serotherapy (ATG or alemtuzumab), HLH remains difficult to treat. Generally, HCT is recommended in the case of documented familial HLH, recurrent or progressive disease despite intensive therapy, and CNS involvement

## Typical surgery

Bone marrow aspirate, long term central venous catheter positioning, pleuric tube positioning, abdominal tube positioning, liver biopsy.

Other incidental surgeries apart from disease or for diagnosis may also be required in such children.

## Type of anaesthesia

There is no definite recommendation for either general or regional anaesthesia, notwithstanding macrophage activation syndrome starts often with very low platelet count

and reduced coagulation activity due to liver failure. In order to perform safe anesthesia, regional anesthesia should be avoided.

The main concerns in patient with MAS are its perioperative risk of flare and thus avoidance of trigger factors. The role of anesthetic drugs as trigger factor for MAS has not been reported in literature.

In SoJIA, MAS is a life-threatening complication and accounts for a significant proportion of the morbidity and mortality (8–22%). It is triggered by viral infections, drugs [Non-steroidal anti-inflammatory agent (NSAID), disease-modifying agents such as gold salts, sulphasalazine and penicillamine] and external stresses such as exposure to cold.

The anaesthetic drugs that are histamine releasers such as morphine and atracurium needs to be avoided.

Various trigger factors (NSAIDs, drugs releasing histamine and cold) that may lead to MAS need to be avoided in the perioperative period. Elective procedures should be scheduled during remission phase of disease.

## Necessary additional diagnostic procedures (preoperative)

Cardiac function tests like electrocardiography and echocardiography.

Blood examinations, enlarged metabolic or coagulation tests, Lactate blood level, kidney function exams.

BNP blood level is useful to monitor cardiac failure.

X-ray of the thorax, lung ultrasound, blood gas analyzes to focus on atelectasis, pleural fluid effusion and PaO2/FiO2.

Consultation of a specialist to document for juridical reasons already existent deficits, e.g. of neurological nature.

## Particular preparation for airway management

There are not reported particular difficulties in airway management.

## Particular preparation for transfusion or administration of blood products

Assure availability of fresh frozen plasma, platelet and concentrated red cells, tranexamic acid and coagulation factors may be necessary.

## Particular preparation for anticoagulation

There is no evidence to support the need of particular anticoagulation. But the impaired mobility of severe clinical presentation may suggest a higher risk of postoperative thrombosis.

## Particular precautions for positioning, transport or mobilisation

Not reported, related to haemodinamic instability.

## Probable interaction between anaesthetic agents and patient's long term medication

Not reported.

## Anaesthesiologic procedure

In case of present cardiac failure and /or pericardiac effusion avoid nitrous oxide because of cardio-depressant effects.

Inotropic drug support is required usually.

Opiates, propofol and local anaesthetics have been used without any complication. Patients may require a lower dose of propofol or opiates.

Hoffman's reaction dependent drugs such Remifentanil and Cis-Atracurium are suggested to facilitate drugs' metabolism and elimination.

Mechanical ventilation or non invasive ventilation are reccomended to limit atelectasis development.

## Particular or additional monitoring

Monitor body temperature to avoid hypertermia and increased oxygen demand.

Due to MAS life threatening nature, arterial cannulation for invasive blood pressure measurement and central venous line placement is recommended. In case of cardiac failure, transesophageal echocardiography and SviO2 catheter are very useful.

## Possible complications

Patients with MAS are at risk for acute cardiac, respiratory and renal failure so far it is known as multi organ failure syndrome.

Sedative drugs (benzodiazepines) can worsen respiratory insufficiency.

## Postoperative care

Degree of postoperative monitoring is depending on surgical procedure and preoperative condition of the patient. Intensive care is mandatory.

## Information about emergency-like situations / Differential diagnostics

caused by the illness to give a tool to distinguish between a side effect of the anaesthetic procedure and a manifestation of the diseases, e.g.:

Not reported.

## Ambulatory anaesthesia

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## Obstetrical anaesthesia

Is requested to follow general anaesthesia recommendations.

## Literature and internet-links


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**Last date of modification: October 2013**

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