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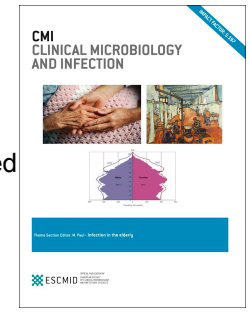

Diversity and combinations of infectious agents in 38 adults with an infection-triggered reactive hemophagocytic syndrome: a multicenter study.

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Introduction

In contrast to familial hemophagocytic syndrome (HS) and other genetic disorders, reactive HS is an acquired, potentially life-threatening disorder than can occur in patients with infections, hematologic malignancies, autoimmune diseases or in a context of acquired immunodeficiencies (for a review, see [1–3]). The cardinal features of HS include fever, hepatosplenomegaly, lymphadenopathy, abnormal laboratory test results (e.g. pancytopenia, liver cytolysis, coagulopathy, hypertriglyceridemia and elevated ferritin), and hemophagocytosis in various organs (especially in bone marrow aspirates). The diagnosis of HS is challenging because none of the associated clinical or biochemical signs are specific, and the bone marrow aspirate is normal in some patients with HS [4]. Treatment of HS is based on supportive care, treatment of the underlying cause, and specific treatments for the most severe conditions (especially corticosteroids and etoposide) [5]. Patients with underlying neoplasia or idiopathic HS usually have a worse outcome [6–9]. The results of pathophysiologic studies suggest that various factors trigger an exaggerated, ineffective immune response because of an underlying inherited or acquired impairment of Natural Killer cells and CD8 T cells cytotoxicity. This results in the uncontrolled activation of antigen-presenting cells and the hypersecretion of proinflammatory cytokines [10].

A variety of infectious agents can trigger HS [1,11]. Viruses (especially Epstein-Barr virus (EBV) and cytomegalovirus (CMV)) are the predominant microbial triggers in HS - either as primary infection in immunocompetent patients or after reactivation in immunocompromised patients. Tuberculosis, several non-mycobacterium bacteria, and some parasites and fungi have also been reported as putative triggers for HS [1].

The nature and frequency of infectious triggers of HS in adults have not been extensively examined as a function of the patient's underlying immune status. Most of the literature data on this topic have been gathered in single-center case series [6–9,12–14]. We have previously described a large, multicenter cohort of 162 patients with HS [4]. The primary objective of the present study was to provide a precise microbiological description of infection-triggered HS in the cohort and compare immunocompetent patients with immunocompromised patients. The secondary objective was to compare patients suffering from infection-triggered HS with those in the cohort suffering from HS triggered by a hematologic malignancy (referred to henceforth as "malignancy-associated HS").

Material and Methods