China (Xiang ST, Wang SS, Zhou JF, Gan S and Chen ZQ)
Correspondence to: Dr. XIANG Song-tao, Department of Urology, Guangdong Provincial Hospital of Chinese Medicine, Guangzhou University of Chinese Medicine, Guangzhou, Guangdong 510105, China (Email: tonyxst@163.com)

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Letter

Bone marrow biopsy findings in brucellosis patients with hematologic abnormalities: useful remarks

To the editor: We found very interesting the paper by Demir et al[1] about bone marrow biopsy findings in brucellosis patients. Although brucellosis remains the world's most common bacterial zoonosis, with over half a million new cases annually and prevalence rates in some countries exceeding ten cases per 100 000 population and can result in serious clinical complications, scientific and public health interest and funding for these diseases remain relatively minor and inadequate.[2] In the paper by Demir et al,[1] forty-eight brucellosis cases were prospectively investigated. Anemia, leukopenia, thrombocytopenia and pancytopenia were found in 39 (81%), 28 (58%), 22 (46%) and 10 patients (21%), respectively. In addition, hemophagocytosis was observed in 15 (31%) patients. The clinical characteristics of these 15 patients did not significantly differ from those of the other patients. As it is known, the identification of hemophagocytosis in marrow biopsy aspirate (BMA) represents one of the diagnostic criteria for the diagnosis of the hemophagocytic lymphohistiocytosis (HLH) syndrome developed by the HLH Study Group of the Histiocyte Society.[3] HLH is a potentially fatal hyperinflammatory syndrome characterized by histiocyte proliferation and hemophagocytosis. HLH may be inherited (primary, familial, generally occurring in infants) or secondary to infection, malignancy or rheumatologic disease and occurring at any age. The diagnosis of HLH is established by fulfilling one of the following criteria: (1) A molecular diagnosis consistent with primary HLH (e.g. PRF mutations, SAP mutations, MUNC13-4 mutations); (2) Having five out of eight of the following: fever; splenomegaly; cytopenia (affecting more than two cell lineages, ≤9 g haemoglobin per dl, ≤100 000 platelets per ml, ≤1000 neutrophils per ml); hypertriglyceridaemia (≥265 mg triglycerides per dl) and/or hypofibrinogenaemia (≤150 mg fibrinogen per dl); haemophagocytosis in the bone marrow, spleen, or lymph nodes without evidence of malignancy; low or absent natural killer (NK) cell cytotoxicity; hyperferritinaemia (≥500 ng ferritin per ml); elevated soluble CD25 (≥2400 IU interleukin-2Ra chain per ml).[3] Two points should be stressed: (1) the identification of hemophagocytosis in BMA represents only one of 5/8 criteria needed for the diagnosis of HLH; (2) a diagnosis of primary HLH should always be excluded. In fact, with improved molecular diagnostics it is recognized that cases of adult onset HLH that had previously been considered secondary may represent a primary HLH with underlying mutation in the *PFR1* gene.

In conclusion, we think that HLH should be considered in severe cases of brucellosis especially if associated with pancytopenia, and the finding of hemophagocytosis in BMA of patients with brucellosis is not necessarily associated with a severe disease. Further studies are needed to understand whether an immunosuppressive treatment could be beneficial in those cases that do not respond promptly to antibiotic therapy.

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Antonio Cascio, Giovanni Pellicanò, Lucia Maria Pernice, Antonio David and Chiara Iaria
Department of Human Pathology (Cascio A, Pellicanò G and Pernice LM), Department of Neurosciences, Psichiatric and Anesthesiological Sciences (David A), University of Messina, Messina, Italy
Infectious Diseases Unit - Azienda Ospedaliera Piemonte-Papardo, Messina, Italy (Iaria C)
Correspondence to: Prof. Antonio Cascio, Programma di Infettivologia Speciale, Medicina Tropicale e delle Migrazioni e Parassitologia, Policlinico "G. Martino", Via Consolare Valeria n. 1, 98125 Messina, Italy (Tel: 39-90-2213680. Fax: 39-90-692610. Email: acascio@unime.it)

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