LETTER TO THE EDITOR

Bone marrow evaluation in leprosy: clinical implications

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We read with great interest the first case report of hemophagocytic lymphohistiocytosis (HLH) in association with leprosy by Høyvoll et al.\textsuperscript{1} They described a young female with multibacillary leprosy (MBL) and erythema nodosum leprosum (ENL). After 3 weeks of instituting multidrug therapy (MDT) with rifampin, dapsone, clofazimine, and prednisolone, she developed high-grade fever and other systemic symptoms which led to the diagnosis of HLH. The patient satisfied six of eight HLH-2004 criteria such as fever, splenomegaly, pancytopenia, marked hyperferritinemia, hypertriglyceridemia, and histiocytic hemophagocytosis in bone marrow (BM).\textsuperscript{2} In addition, \textit{Mycobacterium leprae} (\textit{M. leprae}) was also demonstrated in the BM. However, in spite of immunosuppressive therapy, antibacterial and antifungal treatment, and renal and respiratory support, the patient succumbed to fulminant bacterial and fungal sepsis. The authors attributed HLH in association with leprosy; however, the patient was diagnosed with systemic lupus erythematosus (SLE) 1 year prior to her current presentation. Therefore, a repeat of antibody titers (antinuclear antibodies, anti dsDNA, and/or anti Smith) would have been very informative in the patient because HLH is known to be associated with autoimmune diseases, such as SLE.

HLH has a well known association with disseminated tuberculous \textit{Mycobacterial} infections; and even reported to occur following initiation of first line antituberculous drugs such as rifampin and isoniazid.\textsuperscript{3} Although leprosy and tuberculosis have been the scourge of mankind for centuries, surprisingly, the association of HLH with leprosy was described only recently in a middle aged Tunisian man with MBL following the initiation of MDT with dapsone and rifampin; but responded well to corticosteroid.\textsuperscript{4} Another report from China described a case of suspected HLH with low natural killer cell activity and high CD25 levels which preceded the histological diagnosis of MBL.\textsuperscript{5} Dapsone, an integral component of MDT

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for leprosy, has been reported to cause HLH in a patient with Sézary syndrome. Moreover, dapsone is known to cause a hypersensitivity syndrome (dapsone syndrome) characterised by fever, skin rash, hepatosplenomegaly, hepatitis, and generalised lymphadenopathy. To make matters more intriguing, ENL (a Type II reaction in leprosy) presents with a similar clinical picture. In such a scenario, BM evaluation can be of great help to differentiate HLH from dapsone syndrome and Type II reaction.

Bone marrow evaluation in leprosy has been infrequently reported in the literature and in the majority of those cases, BM examination was performed either prior to or after establishing the diagnosis of leprosy for evaluation of cytopenia(s) and fever of unknown origin. Suster et al. demonstrated viable Lepra bacilli in BM aspirate smears by using modified Fite stain; and suggested that bone marrow may act as a reservoir for viable organisms in the absence of a host response in treated and untreated patients with MBL. The persistence of viable organisms in the BM in patients with MBL may account for the high rate of relapse and/or recrudescence of the disease following cessation of specific therapy. Bone marrow examination with the Fite modification of the acid-fast stain is therefore indicated in such patients to evaluate marrow involvement and the efficacy of treatment. This may have a great clinical implication similar to the cutting edge discovery by Das et al. a few years ago, of hidden M. tuberculosis in the bone marrow stem cells.

Considering the ethical issues involved in carrying out BM evaluation and with the available literature from the past, it is still a matter of debate whether marrow evaluation in leprosy should be done in all cases or restricted to specific clinical settings. The present report of HLH in MBL by Høyvoll et al. definitely adds a new dimension to the hematological aspect of this old disease.

References