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CORRESPONDENCE

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β_2-Glycoprotein I-Dependent Anticardiolipin Antibodies as Risk Factor for Reactions in Borderline Leprosy Patients

TO THE EDITOR:

Leprosy reactions are inflammatory acute episodes that alter the uneventful clinical course of leprosy. Leprosy reactions may be severe and cause irreversible damage to the eye and nerves. Although they represent acute hypersensitivity reactions, their pathogenesis and the predisposing factors are yet to be fully elucidated.

Immune responses to a wide range of antigens, not necessarily specific to *Mycobacterium leprae* ([3]), are often seen in leprosy patients. Anticardiolipin (aCL) antibodies have been reported ([1, 4]), but their relationship to the pathogenesis, clinical course or prognosis of leprosy is not known.

We have monitored patients with active borderline leprosy who were starting antileprosy treatment to determine whether a high titer of aCL found at the time of diagnosis could identify patients at increased risk for leprosy reactions. The study group comprised 24 borderline leprosy patients who had not been treated previously or had active disease after prior therapy had been discontinued for more than 1 year. Leprosy was diagnosed on clinical and bacteriological grounds and confirmed by histopathology in 21 of the 24 cases. The disease was classified according to Ridley-Jopling at the time of initial examination as borderline tuberculoid (BT) in 8 patients, mid-borderline (BB) in 2, and borderline lepromatous (BL) in 14. Patients were followed up for 4 to 6 years with visits after treatment was completed.

Serum from all subjects was assayed for aCL antibodies in the presence of β_2-glycoprotein I (β_2-GPI) using a technique previously described ([2]). Briefly, ELISA plates were coated with cardiolipin and post-coated with β_2-GPI. Sera were tested after 1:100 dilution in 1% bovine serum albumin/phosphate buffered saline (BSA/PBS). Optical density was converted to conventional units (GPL units) using commercial aCL standard sera (Antiphospholipid Associated, Louisville, Kentucky, U.S.A.). The significance of differences in the rates of seropositivity was tested by chi-squared analysis.

During the study period, reactions occurred in 12 of the 24 patients; 9 of them experienced type 1 reaction (3 BT, 1 BB, 5 BL) and 3 (all BL) had type 2 reaction. Leprosy classification was not a risk factor for reactions when BT patients (3 of 8) were compared with BB and BL (9 of 16) patients ($p = 0.333$).

The mean absorbance of serum samples was higher in patients who subsequently manifested reactions than in those who did not. The difference, however, was not significant. Seven patients were aCL-positive,

and all but one of these patients had a leprosy reaction. Among the 17 aCL-negative patients, 6 had one or more reaction episodes during the study period. Of interest, leprosy reactions developed in significantly greater proportion in aCL-positive patients ($p = 0.0343$).

ACL antibodies can occur in several conditions and even in the normal population. Although aCL antibodies are relatively common, they have been more frequently associated with autoimmune disorders ([5]) and should be regarded as a sign of an abnormal autoimmune response.

Polyclonal activation of antibody response is well known in leprosy. Leprosy sera show a range of autoantibodies including rheumatoid factor, anti-DNA, antinuclear, anti-organ and aCL antibodies ([3]). Whether aCL antibodies arise in response to crossreaction to mycobacterial antigens or to tissue damage is not known.

In our study the presence of high levels of aCL antibodies was associated with an increased risk for leprosy reaction. A possible explanation is that aCL-positive patients have a higher susceptibility to hypersensitivity reactions. This immunological condition could predispose leprosy patients to develop reactions whenever trigger factors switch on the hypersensitivity response.

The present series is too small to derive final conclusions on this matter. However, if prospective clinical trials confirm these preliminary findings, aCL-positive leprosy patients could be regarded as subjects at risk for leprosy reactions and monitored for clinical signs of these conditions. This may lead to early detection and treatment of reactional episodes with a resulting reduction in nerve damage and disability.

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REFERENCES

1. Fiallo, P., Cardo, P. P. and Nunzi, E. Higher specificity in the serodiagnosis of leprosy by combined titration of antiphenolic glycolipid-I and antiphospholipid antibodies. Int. J. Lepr. **61** (1993) 464–466.
2. Fiallo, P., Tomasina, C. and Cardo P. P. Beta$_2$-Glycoprotein I-dependent anticardiolipin antibodies in ischemic stroke. Eur. J. Neruol. **4** (1998) 29–34.
3. Garcia-de la Torre, I. Autoimmune phenomena in leprosy, particularly antinuclear antibodies and rheumatoid factor. J. Rheumatol. **20** (1993) 900–903.
4. Hojnik, M., Gilburd, B., Ziporen, L., Blank, M., Tomer, Y., Scheinberg, M. A., Tincani, A., Rozman, B. and Shoenfeld, Y. Anticardiolipin antibodies in infections are heterogeneous in their dependency on β_2-glycopotein I: analysis of anticardiolipin antibodies in leprosy. Lupus **3** (1994) 515–521.
5. McNeil, H. P., Chesterman, C. N. and Krilis, S. A. Immunology and clinical importance of antiphospholipid antibodies. Adv. Immunol. **49** (1991) 193–280.