Anti-neutrophil cytoplasmic antibody (ANCA) and viral infection

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Anti-neutrophil cytoplasmic antibodies (ANCA) are a group of autoantibodies targeted at a variety of cytoplasmic constituents of neutrophils and monocytes. Established target antigens are proteinase 3 (PR3), myeloperoxidase (MPO), lactoferrin (LF), lysozyme (LZ), elastase (HLE), cathepsin G (CG), and azurocidin. ANCA have been extensively described as a sensitive marker for systemic vasculitis including Wegener's granulomatosis (WG), rapidly progressive glomerulonephritis (RPGN), and microscopic polyangiitis (MAP). Two major types of ANCA can be distinguished on indirect immunofluoresence (IIF): one is shown a characteristic cytoplasmic or classic fluorescence pattern (cANCA), which corresponds to anti-PR3 antibodies; and the other is a perinuclear pattern (pANCA), which is mostly directed to MPO and other positively charged granule proteins, such as LF, LZ, HLE, etc. c-ANCA and p-ANCA are thought to be associated with Wegener's granulomatosis and necrotizing glomerulonephritis, respectively. Recently, ANCA has been detected in patients with a variety of rheumatic autoimmune diseases, including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and others. A total of 160 serum samples from the reference laboratory of Chung Shan Medical and Dental College Hospital collected from different clinics for testing ANCA and 40 normal serum samples for control were tested for c-ANCA and p-ANCA by indirect immunofluorescence (IIF). All available sera were further tested by enzyme-linked immunosorbent assay (ELISA) for antibodies to PR3, MPO, LF, and LZ. In addition, the sera from 110 patients with SLE and 51 patients with RA were also tested by ELISA for antibodies to PR3, MPO, LF, and LZ. ANCA was detected in 81 of the 160 sera by IIF. Of the 81 serum samples with ANCA, 21 (26%) were found to be c-ANCA and 60 (74%) were defined as p-ANCA. P-ANCA was more commonly found in sera with ANA-positive than those with ANA-negative ($p < 0.01$). By ELISA testing, of the 21 sera with c-ANCA, 12 sera were reacted to PR3, 4 to LF, 4 to LZ, and 3 to MPO. Of the 60 sera with p-ANCA, 15 sera were reacted to MPO, 13 to PR3, 8 to LF, and 4 to LZ. Of the 110 sera from patients with SLE, only one serum contained c-ANCA and five sera had p-ANCA. None of the sera from patients with RA contained c-ANCA or p-ANCA. ANCA were not commonly detected in sera from patients with SLE and RA.

The human vasculitides are idiopathic syndromes for which both autoimmune and infectious etiologies have been proposed. The strongest viral candidates for human vascular disease are ones that establish long-term persistent infections such as

hepatitis B and hepatitis C viruses, human cytomegalovirus, Epstein-Barr virus, herpes simplex virus, human immunodeficiency virus (HIV) and human parvovirus B19. We described four patients who had clinical diagnosis of erythema infectiosum and presented with skin rash, polyarthralgia, polyarthritis, and mild fever. Anti-parvovirus B19 IgM and IgG antibodies were found in all four patients and parvovirus B19 DNA was detected in three of the four patients by polymerase chain reaction (PCR) in sera using standard methods. Anti-neutrophil cytoplasmic antibody (ANCA) included three p-ANCA and one c-ANCA was detected in all four patients by indirect immunofluoresence (IIF). Both anti-PR3 and anti-MPO antibodies were found in two patients whom had polyarthritis for more than 6 months. These data indicate parvovirus B19 may be linked to the induction of an autoimmune response. Hepatitis C virus (HCV) infection is an important infection worldwide. The association of HCV infection, vasculitis and autoimmunity has been reported. Several studies have suggested that chronic HCV may act as a trigger factor for the development of vasculitis and autoimmune rheumatic diseases. The role of HCV in these disorders has not been established. HCV is a linear, single-stranded RNA virus of the Flaviviridae family, with extensive genomic variability associated with different autoimmune manifestations. ANCA, anti-dihydrolipoamide dehydrogenase (anti-E3), rheumatoid factor (RF), anti-dihydrolipoamide acetyltransferase (anti-E2), anti-SS-A/Ro (60 kD), anti-SS-A/Ro (52 kD), anti-SS-B/La, anti-topoisomerase II (anti-topo II), anti-cardiolipin (aCL), anti-dsDNA, anti-ssDNA, antinuclear antibodies (ANA), anti-PR3 and anti-MPO were determined in sera from 516 patients with HCV infection, 11 primary biliary cirrhosis (PBC) and 44 healthy controls by indirect immunofluoresence assay, particle latex agglutination test, enzyme-linked immunosorbent assay (ELISA), and immunoblotting.

ANCA, anti-E3 antibody, and RF were positive in 278/516 (55.6%), 276/516 (53.3 %), and 288/516 (56%) patients with HCV infection, respectively. Positivity for ANA was present in 15.8%, anti-ssDNA in 15.6%, anti-dsDNA in 8.5%, aCL in 5%, anti-SS-B/La in 4.1%, anti-SS-A/Ro (60 kD) in 3.9%, anti-E2 in 3.3% and anti-SSA/Ro (52 kD) in 1.2 %, anti-MPO in 4.8%, anti-Topo II and anti-actinin in 0%. All sera with ANCA showed c-ANCA pattern and contained anti-PR3 specificity. HCV patients with ANCA showed a higher prevalence of skin involvement, anemia, abnormal liver functions and α-Fetoprotein (α-FP). In conclusion, autoantibodies are commonly found in patients with HCV infection. There is a high prevalence of anti-E3, ANCA, and RF in these patients. Proteinase 3 is the major target antigens in HCV infection.