Antinuclear and Antiphospholipid Autoantibodies in Patients with peripheral Arterial Occlusive disease

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Referring to the Chapel Hill Consensus Conference, large peripheral arteries are only affected by giant cell vasculitis and in rare cases by polyarteritis nodosa (4,5). Vasculitis manifest via involvement of typical organs (lung, kindney, skin) or elevated C-reactive protein (CRP) level or erythrocyte sedimentation rate (ESR). Thus, a specific diagnostic effort to exclude vasculitis as an underlying disease in peripheral arterial occlusive disease (PAOD) patients might be unnecessary. On the other hand, there is increasing evidence that humoral immunity may play a role in the pathogenesis of atherosclerosis (1,2,9). Antinuclear antibodies were reported in 70 % of patients with severe coronary heart disease (CHD), compared to only 17 % in the control group (3). Thus, we prospectively studied the importance of autoantibody determination in patients symptomatic with PAOD.

695 patients (mean age ± SD: 68 ± 10 years) referred for interventional treatment of PAOD from 1998 to 1999 were included. In 118 PAOD-patients (61 ± 12 years) with a low atherosclerotic risk profile, or with rarefied distal arteries without media calcinosis, or with elevated ESR or CRP independent from local infections, the following autoantibodies were determined: antinuclear antibodies (ANA) by indirect immunofluorescence technique; antibodies against extractable nuclear antigens (ENA: SCL 70, RNP, SS-A, SS-B, Jo1, SM) by Western-blot; double-stranded DNA antibodies (ds-DNA), antineutrophil cytoplasmatic antibodies (c- and p-ANCA), antiphospholipid antibodies [cardiolipin, phosphatidylserine (APSA) and beta-2-glykoprotein] by enzyme linked immunoassay. In order to stratify the importance of autoantibody determination all patients with increased autoantibody concentration were clinically and sonographically followed up (24 ± 6 months) for evidence of vasculitides or collagen disease. A multivariate logistic regression analysis was performed to evaluate the importance of CRP and ESR in patients with autoantibody concentrations above the appropriate reference value.

38 out of the 121 patients had increased autoantibody concentrations (Tab. 1). ANA were the most frequent autoantibodies detected in 14 patients followed by APSA in 11, and anti-beta-2-glycoprotein antibodies in 12. Patients with increased autoantibody concentration were not different in PAOD stages and affected segments, but in patients with increased autoantibody concentrations the rate of elevated ESR was higher ($p = 0.0043$). Increased 2 hours ESR was associated with an odds ratio of 7.1 (95%-CI: 1.49 – 33.81) in determination of increased

autoantibody concentrations. During follow-up of 24 ± 6 months no vasculitides or collagen diseases could be detected by clinical examination and in part by nail fold capillary microscopy, pulmonary or gastrointestinal imaging in the 38 patients.

The analysed population of 121 PAOD patients is an individually selected group out of all PAOD patients, but represent those patients in whom we are confronted with the question for vasculitis. Elevated concentrations of autoantibodies were not a rare finding in the investigated patients. Increased autoantibody concentrations significantly correlated with elevated ESR. Our data are the first to report the results of autoantibody determination in a larger population of patients suffering from PAOD. In contrast to the high rate of ANA in patients with coronary atherosclerosis (3,7,8), the prevalence of ANA in our PAOD patients was much lower. Whether this different prevalence of ANA was due to different extensions of atherosclerosis, or due to specific differences in coronary and peripheral manifestations can only be speculated. In aggreement with the coronary studies, no association of the determined autoantibodies with the classical risk factors was found. The higher rate of elevated ESR in the patients with increased autoantibody concentrations might be associated with a higher degree of inflammatory activity of the atherosclerosis. Antiphospholipid and beta-2-glykoprotein antibodies which are most relevant in association to atherosclerosis did not seem to be of prognostic impact (6,7,8), but antibody determination in larger groups of non-selected patients is desirable.

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	No Autoantibody Determination	Autoantibody Determination	
		No Increased Autoantibodies	Increased Autoantibodies
Number	577	83	38
Age (mean ± SD)	68 ± 10 years	61 ± 12 years	59 ± 14 years
PAOD stage II	74 %	63 %	58 %
Stage III	5 %	4%	9 %
Stage IV	21 %	33 %	33 %
Segment of vascular lesions:			
Crural	8 %	22 %	24 %
Femoral	41 %	30 %	31 %
Iliacal	9 %	5 %	8 %
Combined	42 %	43 %	37 %
Risk factors:			
Diabetes mellitus	37 %	26 %	10 %
Hypertension	50 %	39 %	30 %
Dyslipoproteinemia	66 %	41 %	28 %
Nicotine abuse	75 %	27 %	35 %
Markers of inflammation			
1. h BSR > 20 mm	31 %	29 %	61 %*
2. h BSR > 40 mm	32 %	30 %	61 %*
CRP > 1 mg/dl	20 %	37 %	50 %
History of CHD	47 %	17 %	16 %

Tab. 1: Given are the characteristics of those patients no autoantibodies were determined in, those patients autoantibodies were determined in, but not increased, and those with increased autoantibodies.
Frequencies of variables are expressed in per cent of the number of patients in each group. * p = 0.0043 versus “no measured autoantibodies”