by CT. Exclusion criteria included non-atherosclerotic causes, and patients on oral anticoagulants. Controls (n=271) were age -and sex-matched, without a history of stroke. Genotyping was done by PCR-SSP (4G/5G) or PCR-RFLP using Xho I (G[-844]A); PAI-1 and t-PA levels were assayed by ELISA. *Results*. Higher frequencies of the 5G allele (p=0.024; RR=1.72) and the -844 A/A genotype (p=0.032; OR=1.71; 95% CI=1.07-2.73) was seen in patients, while higher frequencies of the -844G allele (p=0.023; RR=0.584) and the 4G/4G genotype (p=0.03; OR=0.58; 95% CI=0.36-0.94) were found among control subjects. Complete linkage disequilibrium was seen between the 4G and -844G alleles, and between the 5G and -844A alleles in patients (p=0.022). While *PAI-1* antigen levels were increased in 4G/4G, more than -844 A/A carriers, and were associated with reduced t-PA levels, significant increases in *PAI-1* levels were seen between cases and controls, irrespective of the genotype. Summary/Conclusion. Whereas significant differences were seen in the distribution of some PAI-1 4G/4G and G[-844]A variants between cases and controls, yet their modest influence on *PAI-1* levels and activity (t-PA) suggests the contribution of other stroke-associated factors in modulating PAI-1 levels and activity.

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VASCULAR AND SINUSOIDAL ENDOTHELIAL ACTIVATION, PROLIFERATION, DIFFERENTIATION AND ERYTHROPHAGOCYTOSIS: ULTRASTRUCTURAL FINDINGS ON A CASE OF AUTOIMMUNE LYMPHOPROLIFERATIVE SYNDROME (ALPS)

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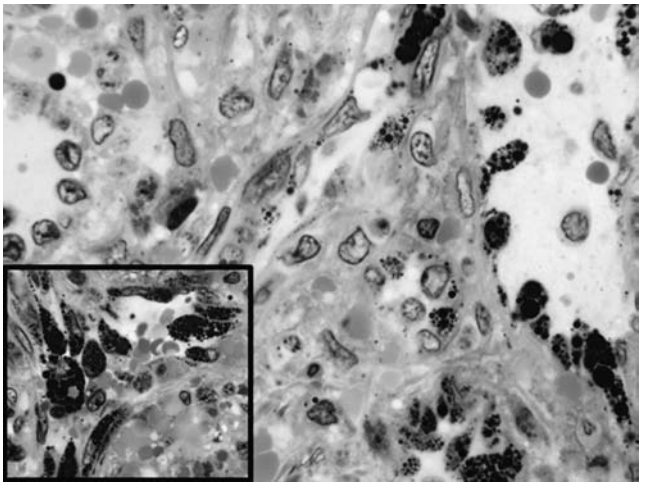
Backgrounds. Since 1991, one of us (Sencer H) has reported that; 'vascular endothelial cells have reserved the capacity of stem cell and can activate, proliferate, and differentiate to other stromal and hemapoietic cells in health and diseases. Activated endothelial cells can migrate to the stroma or circulate in the vascular lumen as 'circulating progenitor endothelial cells (CEC/CPEC)' after plumping and detaching from basal lamina. Besides, viral replications and damages on erytrocytes were clearly demonstrated ultrastructurally by Sencer H in 1995. Aims. The aim is to provide morphological basis of functional modifications occurring in the disease. This is the first ultrastructural study on ALPS, to our knowledge. *Case Report and Methods.* The patient was healthy until the age of 6 months when he presented with disseminated vesicular skin lesions, generalized lymphadenopathy, hepatosplemegaly, tachycardia and was diagnosed with severe varicella zoster virus (VZV) infection. Coombs positive(IgG) hemolytic anemia, thrombocytopenia, elevated immunoglobulin levels and severe proteinuria were detected. CMV IgM and IgG were also found to be positive. At the age of 10-month CMV IgM and whole blood polimerase chain reactions analysis for CMV were negative. He presented with Evans syndrome symptoms and he was diagosed as ALPS after the detection of increased percentage of double negative T cell population in the peripheral blood. The patient underwent splenectomy at the age of 20 months because of refractory thrombocytopenia. Material for this study were obtained during splenectomy and performed EM preparation. Semi-thin sections were stained with toluidine blue-borax. Thin sections were contrasted with uranyl acetate/lead citrate and observed with JEOL100BEM.



Results. Red pulp was widespread, but white pulp wasn't distinctive with increased follicular hyperplasia and prominant marginal zone in the spleen. Increased fibrotic elements some of which related several arteries in plane of sections and plasmacytes were seen. Virus-like particles were observed. Activation and proliferation of vascular and sinusoidal (littoral) endothelial cells had occured. Some of them were committed to erythrophagocytosis which were became large and shuttle shape. Their cytoplasms were full with erytrocytes, erytrocyte fragments and/or phagocytic end-products. Erytrocytes probably damaged with viruses- were internalized by endothelial cells, but could not been digested totally. Both of the activated and phagocytic endothelial cells could detach from their original sites and move to the sinusoidal and/or vascular lumen. These could functionally be named circulating endothelial progenitor cells (CPEC) and circulating erythro-phagocytic endothelial cells (CEPEC) respectively. These were neither sinusoidal histiocytes, nor cordal macrophages classical. *Conclusions.* We suggest that the splenic endothelial cells have erythrophagocytic activity in ALPS. Viral replication on erythrocytes and/or endothelium may be causative agent. Endothelium should be most important key system in the health and diseases. Electron microscopy is useful to avoid misinterpretation.

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ENDOTHELIAL MICROPARTICLES AND MARKERS OF COPPER METABOLISM AS NOVEL INDICATORS OF ANGIOGENESIS IN B-CELL CHRONIC LYMPHOCYTIC LEUKEMIA

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Backgrounds. Angiogenesis is currently considered an important process in biology of B-cell chronic lymphocytic leukemia (B-CLL). Copper is an important cofactor for some angiogenic factors. Elevated serum levels of copper (Cu) and its transport protein coeruloplasmin (CP) have been reported in patients with advanced cancers. Endothelial microparticles (EMPs) are fragments of endothelial cells which are produced during endothelial proliferation or damage and circulate in peripheral blood. Neither parameters of copper metabolism nor EMPs have been used so far to assess angiogenesis in B-CLL. *Aims.* To analyze serum concentrations of Cu and CP and quantitate EMPs in patients with B-CLL. Methods. We measured serum Cu and CP in 19 patients with B-CLL diagnosed according to NCI-WG criteria. Cu was measured using chromatography and CP by immunoturbidimetry. EMPs were analyzed in 20 B-CLL patients and 10 healthy donors using two-colour flow cytometry of platelet-poor plasma. CD105 (endoglin) and CD144 (VE-cadherin). CD41 was used as a platelet marker. *Results.* Cu and CP were detectable in all B-CLL patients. Both markers were in normal range (Cu: mean ± SD [standard deviation], 18.13±3.98 μmol/l, 95% CI [confidence interval] of mean, 16.21-20.05 μmol/l; CP: mean±SD, 0.294±0.062 g/L, 95% CI of mean, 0.264-0.324 g/L). Neither Cu nor CP were significantly different between B-CLL patients with stable (n=7) and progressive (n=12) disease (p=0.77 and 0.54, respectively). There was a statistically significant increase of CD41+/105+ microparticles (mean ± SD 142.8 ± 22.4/ul, 95% CI of mean, 95.8-189.7/μL) in B-CLL patients when compared to control group (mean ± SD [standard deviation], 60.8 ± 32.4 /ul, 95% CI of mean, 37.6-84.0 /ul; p=0.003). There was no significant difference between patients with. *Conclusions.* Our study is the first one to report measurement of endothelial microparticles and markers of copper metabolism as angiogenesis indicators in CLL. However, neither serum Cu nor CP were significantly elevated in B-CLL patients over controls. In addition, we did not observe differences in Cu or CP levels between patients with stable vs progressive disease. Furthemore, we found elevated numbers of CD41+/105+ (aggregates of platelets and EMPs) but not CD144+ or CD105+ EMPs in B-CLL patients. Larger study is clearly warranted to confirm these findings and perform a detailed statistical analysis including comparison with other angiogenic markers.

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