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P32. VACUOLATED PAS-POSITIVE LYMPHOCYTES: A SCREENING TEST FOR POMPE DISEASE AND OTHER AUTOPHAGIC MYOPATHIES

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Pompe disease is an autosomal recessive lysosomal disorder caused by mutations of the acid-α-glucosidase (GAA) gene. Deficiency of GAA enzyme leads to glycogen accumulation and autophagy impairment in cardiac and skeletal muscles, but also in lymphocytes. Since an effective therapy is available, a rapid, sensitive and specific test is crucial to early identify affected subjects. Number of lymphocytes containing Periodic-acid-Schiff (PAS)-positive vacuoles were evaluated on blood smears from 78 adult patients with hyperckemia and/or muscle weakness, 13 Late-onset-Pompe-disease (LOPD) and 13 symptomatic LOPD offspring. More than 4 PAS-positive lymphocytes were found in all LOPD patients and in all LOPD offspring resulted to have only a single GAA mutation but low GAA levels. PAS-positive lymphocytes were also found in 17 out of the 78 patients: 6 new diagnosis of LOPD, 3 different glycogen storage myopathies, 1 glucose-6-phosphate-dehydrogenase deficiency, 1 caveolinopathy and 6 myopathies with glycogen deposition and autophagic vacuoles in muscles biopsies, in which mutations for Pompe disease was subsequently ruled out. Immunostaining with the autophagy marker LC3 confirmed the autophagic nature of vacuoles in all positive lymphocytes. ROC curve assessment of PAS-positive lymphocytes disclosed a 100% sensitivity and a 90% specificity in recognizing both homozygous and heterozygous GAA mutations carriers. The other myopathies with more than 4 PAS-positive lymphocytes appeared to be all related to impaired autophagy, that seems to be responsible of PAS-positive vacuolated lymphocytes formation. Quantification of PAS-positive lymphocytes in blood smears should be routinely used as first level test for Pompe disease and other autophagic vacuolar myopathies.