Alteration of Extracellular Nucleotide Metabolism in Pseudoxanthoma Elasticum

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Résumé en anglais	Pseudoxanthoma elasticum (PXE) is a rare genetic condition primarily caused by hepatic ABCC6 transporter dysfunction. Most clinical manifestations of PXE are due to premature calcification of elastic fibers. However, the vascular impact of PXE is pleiotropic and remains ill defined. ABCC6 expression has recently been associated with cellular nucleotide export. We studied the impact of ABCC6 deficiency on blood levels of adenosine triphosphate and related metabolites and on soluble nucleotidase activities in PXE patients and Abcc6 mice. In addition, we investigated the expression of genes encoding ectocellular purinergic signaling proteins in mouse liver and aorta. Plasma adenosine triphosphate and pyrophosphate levels were significantly reduced in PXE patients and in Abcc6 mice, whereas adenosine concentration was not modified. Moreover, 5'-nucleotidase/CD73 activity was increased in the serum of PXE patients and Abcc6 mice. Consistent with alterations of purinergic signaling, the expression of genes involved in purine and phosphate transport/metabolism was dramatically modified in Abcc6 mouse aorta, with much less impact on the liver. ABCC6 deficiency causes impaired vascular homeostasis and tissue perfusion. Our findings suggest that these alterations are linked to changes in extracellular nucleotide metabolism that are remote from the liver. This opens new perspectives for the understanding of PXE pathophysiology.
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