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Reply to the article of C.Markello et al. entitled "Vascular pathology of medial arterial calcifications in NT5E deficiency: Implications for the role of adenosine in pseudoxanthoma elasticum"

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Dear Editor

We have read with great interest the article of C. Markello et al. entitled "Vascular pathology of medial arterial calcifications in NT5E deficiency: Implications for the role of adenosine in pseudoxanthoma elasticum" [1]. The reported case raises a new hypothesis about another rare inherited tissular calcifiying disease known as pseudo xanthoma elasticum (PXE) characterized by a deficiency in the ABCC6 transporters. Although their hypothesis is seductive, several crucial clinical signs that characterize PXE are lacking in the NT5E patient's phenotype. Based on the literature and our own comprehensive cohorts (>100 patients) with documented ultrasound imaging and CT scans, there are major differences to the NT5E case. Uni or bilateral arteriomegaly, an aneurismal-like lesion, in the distal femoral and popliteal arteries has never reported in PXE cohorts [2] (see Fig. 1) and in the *Abcc6*-null mice, an animal model that closely mimic the human PXE condition [3–5]. Very importantly, the basic ophthalmologic findings (angioid streaks and peau d'orange) and skin lesions that characterize the PXE phenotype [2] are lacking (or not mentioned) in the present case and others recently published [6]. Rare aneurismal lesions in PXE are restricted to the cerebral vasculature which differs histologically from the lower-limb vasculature. In addition, a reduction of the diameter of the peripheral arteries (rather than an increase), with thickening of the medial layer, and fragmentation of elastic fibers occurs in PXE, illustrate further the divergence with the present case [3–5]. Therefore, we believe that the proposed hypothesis that adenosine (or AMP) is the ABCC6 substrate responsible for the vascular manifestation in PXE is certainly premature and would require careful demonstration in

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large cohorts. Although it cannot be excluded that some amount of extracellular adenosine could be transported via ABCC6, other important mechanisms intervene to explain the phenotypic differences that remain unanswered.

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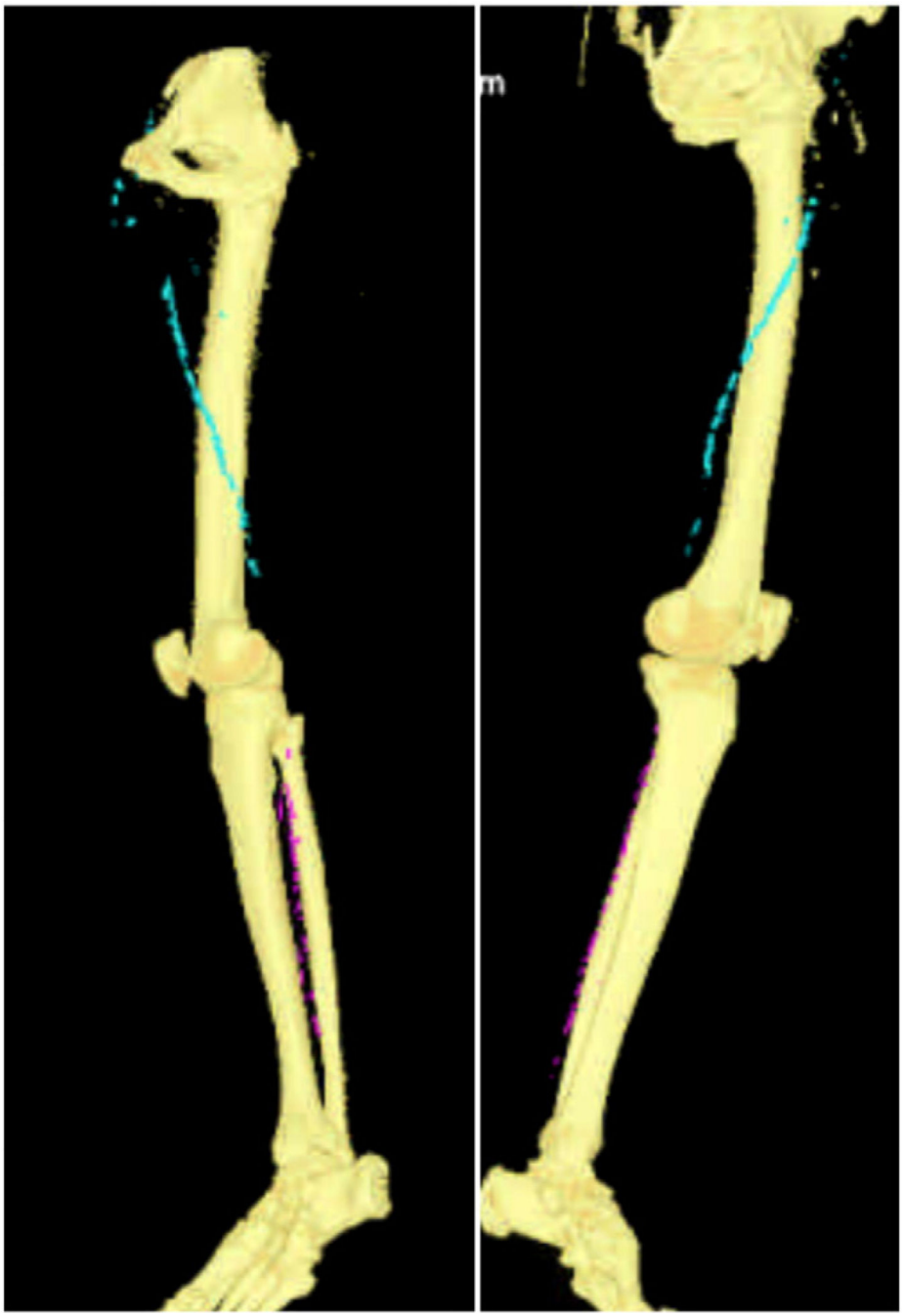

Fig. 1.

Non-opacified CT-scan of the lower legs in a patient with PXE disease (male, 59 years) showing the typical calcified proximal (blue) and distal (cyan) arteries. Note the absence of arteriomegaly. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)