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Primary Pulmonary Hypertension as a Manifestation of Adult Multi-System Mitochondrial Disorder

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Pulmonary artery hypertension (PAH) is characterized by increased blood pressure in the pulmonary arteries either due to heart or pulmonary disease (secondary PAH) or without any detectable cause (primary PAH).[1] In single cases, primary PAH occurred in young patients with a mitochondrial disorder (MID).[1-5] So far, primary PAH has not been described in an adult patient with a MID.

A 70 years-old Caucasian female, height 163 cm, was admitted for paresthesias in both lower legs since three weeks and muscle cramps in the thighs after exercise. Her history revealed primary PAH since age 66 years, treated with continuous remodulin infusions intravenously via a Port-a-Cath system (44 lambda/h), chronic obstructive pulmonary disease (Gold IV), emphysema, tricuspid insufficiency, mitral insufficiency grade,[2-3] paroxysmal atrial fibrillation, incomplete right bundle branch block, recurrent episodes of heart failure, cataract surgery bilaterally, hyponatriemia, hypokaliemia, hyperuricemia, hyperlipidemia, chronic venous insufficiency, and peripheral occlusive vascular disease 2a. Her family history was positive for myocardial infarction (uncle, brother), but negative for MID.

Clinical neurologic investigation revealed weakness for head anteflexion (M5-), sicca-syndrome, diffuse weakness of the upper limbs with right-sided and distal predominance (M4 to M5-), diffuse weakness of the lower limbs with distal predominance (M4+ to M5-), diffuse wasting, brisk tendon reflexes, left-sided bradydiadochokinesia, drum stick fingers, left-sided lower limb ataxia, and stocking type hypesthesia. Serum creatine-kinase and lactate were normal. The cerebral CT scan showed atrophy and non-specific hypodensities. Nerve conduction studies revealed sensori-motor polyneuropathy and needle-electromyography was myogenic.

MID was assumed upon the combination of short stature, cataract, sicca syndrome, hypothyroidism, tetraparesis, tetraspasticity, hyponatriemia, hypokaliemia, polyneuropathy, and myopathy. Peripheral artery obstructive disease was excluded as the cause of her complaints since Doppler investigations were not indicative of severe proximal or distal arterial stenosis or occlusion. Cervical or lumbar disc stenosis was excluded as causes of the described clinical features since weakness included also the head ante-flexors.

Primary PAH has been reported to be associated with mutations in the bone morphogenetic protein type II receptor (BMPR2), actin A receptor type II-like 1 (ACVRL1) or endoglin genes and occasionally in young MIDs.[1-5] In a 3 year-old boy, PAH was diagnosed at age 3 years, because of dyspnea, pedal edema, intolerance to oral intake, somnolence and irritability. Additionally, mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome due to the m.3243A > G mutation was diagnosed, manifesting as mild language delay, microcephaly, lactacidosis, myopathy (delayed walking, hypotonia, ragged-red muscle fibers, increased succinate dehydrogenase (SDH) staining in blood vessel walls), epilepsy, and stroke-like episodes.[1] PAH was also

diagnosed in a newborn and a 7 months-old boy with severe hepatopathy from MID, based on biochemical studies,[2] in a 6 weeks-old child with myopathy and cardiomyopathy due to the m.14709T > C mutation,[3] in two 6 and 4 months-old girls with stroke-like episodes and epilepsy,[4] and in a newborn with COX-deficiency.[5] A causal relation between PAH and MID could be explained by widespread membrane depolarization, calcium influx, cellular proliferation, vasoconstriction from mitochondrial dysfunction and decreased production of reactive oxygen species.[6]

The present case shows that PAH may occur also in adults together with a MID. Whether there is a causal relation between PAH and MID remains to be elucidated.

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