

reduction in the density of neurons within sympathetic ganglia results in low supine plasma NE levels and noradrenergic supersensitivity. Some patients who are initially labeled with this diagnosis subsequently go on to develop AAG, but more often a neurodegenerative disease supervenes, typically Lewy body dementia, PD, or MSA. In one recent series, more than one-third of patients initially diagnosed with PAF developed a CNS synucleinopathy within 4 years, and the presence of rapid eye movement sleep behavior disorder (RBD; [Chap. 31](#)) was predictive of subsequent CNS disease. Skin biopsies and autopsy studies demonstrate phosphorylated α -synuclein inclusions in postganglionic sympathetic adrenergic and cholinergic nerve fibers, distinguishing PAF from AAG and indicating that PAF is a synucleinopathy; notably, patients with PD also have alpha synuclein inclusions in sympathetic nerve biopsies.

■ POSTURAL ORTHOSTATIC TACHYCARDIA SYNDROME (POTS)

This syndrome is characterized by symptomatic orthostatic intolerance without OH, accompanied by either an increase in heart rate to >120 beats/min or an increase of 30 beats/min with standing that subsides on sitting or lying down. Women are affected approximately five times more often than men, and most develop the syndrome between the ages of 15 and 50. Presyncopal symptoms (light-headedness, weakness, blurred vision) combined with symptoms of autonomic overactivity (palpitations, tremulousness, nausea) are common. The pathogenesis is typically multifactorial, which frequently confounds the clinical picture. A number of potential causes have been reported, including sympathetic denervation distally in the legs with preserved cardiovascular function or reduced cardiac function due to deconditioning. Hypovolemia, venous pooling, impaired brainstem baroreceptor regulation, or increased sympathetic activity may also play a role. No standardized approach to diagnosis has been established, and therapy typically has included symptomatic relief with a focus on cardiovascular rehabilitation, including a sustained exercise program. Expansion of fluid volume with water, salt, and fludrocortisone can be helpful as an