

Pure autonomic failure: the first report in Poland?

Małgorzata Dec-Ćwiek, Karolina Porębska, Magdalena Witkowska,
Jakub Antczak, Magdalena Bosak, Marcin Tutaj

Department of Neurology, Jagiellonian University Medical College, Kraków, Poland

A 70-year-old man was referred to the Department of Neurology due to a 5-year history of episodes of unpredictable weakness followed by dizziness, mainly when rising. The patient reported anosmia, recurrent diarrhea, and complained of “cold feet” and sleep disturbances (violent moving during nightmares; sometimes he had accidentally injured his wife during such episodes). Medical history of the patient included chronic ischemic heart disease, hypercholesterolemia, impaired fasting glycemia, gout, intestinal diverticulosis, and sleep apnea.

During the initial diagnostic work-up, performed by endocrinologists and cardiologists, orthostatic hypotension (OH) was diagnosed, along with a slightly impaired baroreflex function during the tilt test. Holter monitoring, echocardiography, and diagnostic coronary angiography did not reveal any abnormalities.

Upon admission to the Department of Neurology, no abnormalities were found on neurological examination. Magnetic resonance imaging of the head (T2-weighted image) showed limited, bilateral, subcortical white matter hyperintensities, presumably of vascular origin. Neuropsychological tests were unremarkable, while laboratory tests only revealed normocytic anemia (hemoglobin level, 12.2 g/dl; reference range, 14.0–18.0 g/dl; hematocrit, 36.4%; reference range, 40%–54%; mean corpuscular volume, 87.9 fl; reference range, 80.0–96.0 fl).

Given the dysautonomic nature of the chief symptoms, we performed a comprehensive autonomic system evaluation, including standard cardiovascular autonomic tests (deep breathing, Valsalva maneuver, head-up tilt) with continuous R-R interval and blood pressure monitoring (TaskForce Monitor; CNSystems Medizintechnik GmbH, Graz, Austria), and sympathetic skin response assessment (VikingQuest; Natus, San Carlos, California, United States).¹ The results showed severe autonomic, primarily

sympathetic dysfunction (FIGURE 1A–1D).¹ Peripheral neuropathy and myopathies were excluded, as was transthyretin-related familial amyloid polyneuropathy.

In light of all the findings, pure autonomic failure (PAF) was suspected. A liquid diet high in sodium was introduced together with midodrine (5 mg twice daily), fludrocortisone (0.1 mg/d), and pyridostigmine (20 mg thrice daily to avoid supine hypertension) treatment, which led to improvement of the patient's condition. In addition, physical counter-maneuvers were applied (FIGURE 1E–1F).²

PAF is a rare, sporadic neurodegenerative disorder with noradrenergic nerve fiber loss that gives rise to a postganglionic pattern of autonomic denervation due to cytoplasmic inclusions of α -synucleins termed Lewy bodies in the neurons. The disease is more prevalent in men. The diagnosis is based on the presence of OH, usually with the evidence of widespread failure; approximately half of patients have concomitant supine hypertension. Autonomic failure may lead to genitourinary, bowel, and thermoregulatory dysfunctions.³ More than 80% of patients have anosmia.⁴ There is no evidence of central nervous system dysfunction, although REM sleep behavior disorder occurs in 72% of cases.⁴ Subtle parkinsonian syndrome may be found and is indicative of a possible subsequent neurodegenerative conversion.⁵ Systemic involvement, for example, anemia, arterial hypertension, increased arterial stiffness, and renal dysfunction with mild proteinuria may be encountered.⁴

PAF should be considered in patients presenting with subacute to chronic OH without parkinsonism, dementia, neuropathy, or valvular heart disease, congestive heart failure, and chronic kidney disease. The diagnosis may be supported by imaging studies, that is, cardiac functional imaging with ¹²³I-metaiodobenzylguanidine myocardial single-photon emission computed tomography

Correspondence to:
Małgorzata Dec-Ćwiek MD, PhD,
Department of Neurology,
Jagiellonian University Medical
College, ul. Botaniczna 3,
31-503 Kraków, Poland,
phone: +48 12 424 86 00, email:
malgorzata.dec-cwiek@uj.edu.pl
Received: December 12, 2021.
Revision accepted:
December 12, 2021.
Published online:
December 15, 2021.
Pol Arch Intern Med. 2022;
132(3): 16175
doi:10.20452/pamw.16175
Copyright by the Author(s), 2022

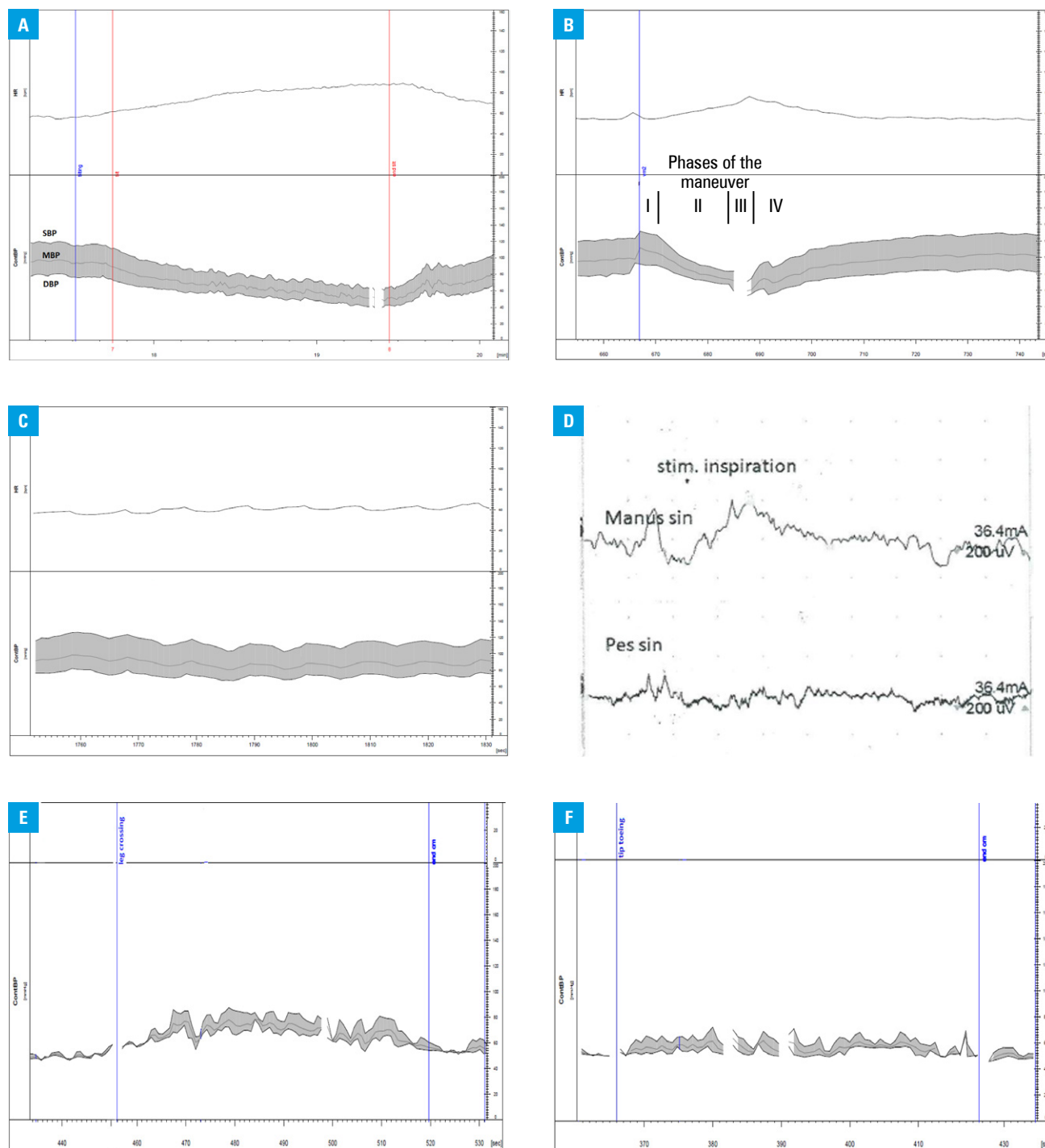


FIGURE 1 Comprehensive autonomic system evaluation (deep breathing [DB], Valsalva maneuver [VM], head-up tilt [HUT]) with continuous heart rate (HR) and blood pressure (BP) monitoring (TaskForce Monitor, CNSystems)^a, and sympathetic skin response (SSR) assessment (EMG, VikingQuest, Natus);¹ **A** – severe orthostatic hypotension (systolic and diastolic BP falls by 61 and 40 mm Hg, respectively) during HUT accompanied by presyncope and requiring tilting the patient back to the supine position; **B** – severe sympathetic failure demonstrated using VM, which resulted in a continuous unopposed fall in BP during the whole phase II, without BP overshoot in phase IV, thus showing both alpha- and beta-adrenergic dysfunction; **C** – six-per-minute DB resulted in typical, mechanically-induced oscillations in BP but reduced reflex vagal responses, as demonstrated by decreased HR changes (I/E ratio = 1.06, age-adjusted normal value: ≥ 1.10).¹ **D** – SSR induced by inspiratory gasp had reduced amplitude and prolonged latency in the upper extremities and was absent in the lower extremities. **E, F** – subsequent HUT was performed and—upon the fall in BP and occurrence of presyncope—the patient was taught to apply physical counter-manuevers. Marked BP increases were induced by leg crossing (**E**) and tip-toeing (**F**), involving repetitive standing on the toes. Both manuevers were proven effective in preventing syncope in this patient.

a Gaps in the shaded areas of BP curves (showing systolic, mean, and diastolic BP) visible in panels **A, B, E**, and **F** indicate periods of temporary signal loss from the finger cuffs due to very low BP values.

and 6-[¹⁸F]-fluorodopamine positron emission tomography, usually demonstrating decreased cardiac sympathetic innervation. Laboratory

data may include low supine norepinephrine levels with minimal to no increase on standing.³ In the absence of neurologic symptoms, patients

initially present to cardiologists, endocrinologists, gastroenterologists, or urologists, warranting multidisciplinary approaches. To date, PAF is incurable; clinical improvement may be achieved with nonpharmacologic and pharmacologic measures to control blood pressure fluctuations ([FIGURE 1E–1F](#)).²

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

OPEN ACCESS This is an Open Access article distributed under the terms of the Creative Commons AttributionNonCommercialShareAlike 4.0 International License ([CC BY-NC-SA 4.0](#)), allowing third parties to copy and redistribute the material in any medium or format and to remix, transform, and build upon the material, provided the original work is properly cited, distributed under the same license, and used for noncommercial purposes only. For commercial use, please contact the journal office at pamw@mp.pl.

HOW TO CITE Dec-Ćwiek M, Porębska K, Witkowska M, et al. Pure autonomic failure: the first report in Poland? *Pol Arch Intern Med.* 2022; 132: 16175. doi: 10.20452/pamw.16175

REFERENCES

- 1 Ziegler D, Laux G, Dannehl K, et al. Assessment of cardiovascular autonomic function: age-related normal ranges and reproducibility of spectral analysis, vector analysis, and standard tests of heart rate variation and blood pressure responses. *Diabet Med.* 1992; 9: 166-175. [↗](#)
- 2 Wieling W, Colman N, Krediet CT, Freeman R. Nonpharmacological treatment of reflex syncope. *Clin Auton Res.* 2004; 14 (Suppl 1): 62-70. [↗](#)
- 3 Coon EA, Singer W, Low PA. Pure autonomic failure. *Mayo Clin Proc.* 2019; 94: 2087-2098. [↗](#)
- 4 Kaufmann H, Norcliffe-Kaufmann L, Palma JA, et al. Natural history of pure autonomic failure: a United States prospective cohort. Autonomic Disorders Consortium. *Ann Neurol.* 2017; 81: 287-297. [↗](#)
- 5 Coon EA, Mandrekar JN, Berini SE, et al. Predicting phenocconversion in pure autonomic failure. *Neurology.* 2020; 95: e889-e897. [↗](#)