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RAPID-ONSET SEVERE ORTHOSTATIC HYPOTENSION AS THE PRESENTING FEATURE OF PURE AUTONOMIC FAILURE: A CASE REPORT

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ABSTRACT

Background: Pure autonomic failure (PAF) is an uncommon, sporadic neurodegenerative synucleinopathy in which sympathetic and parasympathetic failure occurs in isolation, without accompanying central or peripheral motor involvement. Because its dominant feature—orthostatic hypotension—overlaps with far more common causes of dysautonomia, PAF is easily overlooked, particularly in patients with an existing predisposing illness such as diabetes mellitus. **Case Presentation:** We describe a 55-year-old woman with a six-year history of type 2 diabetes mellitus who developed rapidly progressive orthostatic intolerance, culminating in near-instantaneous lightheadedness on standing. Cardiovascular autonomic testing demonstrated combined sympathetic and parasympathetic failure, while cognitive, extrapyramidal, cerebellar, sensory, and motor examinations were unremarkable. The clinical picture supported a diagnosis of PAF. Treatment with fludrocortisone and midodrine achieved satisfactory blood pressure control and restored independent ambulation. **Conclusion:** PAF should be considered in patients with disproportionately severe or rapidly evolving orthostatic hypotension even when a plausible alternative cause, such as diabetes, is present. Given the substantial long-term risk of phenoconversion to a central synucleinopathy, such patients warrant sustained longitudinal follow-up.

INTRODUCTION

Pure autonomic failure (PAF) belongs to the group of neurodegenerative disorders known as synucleinopathies and, unlike its central counterparts, spares cognition and voluntary motor control for years after onset [1]. It is rare, with an estimated prevalence below 1 per 100,000 people, and the true burden of disease is likely underestimated because of frequent misattribution to more common causes of dysautonomia [2]. Onset typically occurs in the sixth or seventh decade of life, and although the conditionis somewhat more common in men, a substantial proportion of patients are women [3]. We report a case in which severe, rapidly progressive orthostatic hypotension in a middle-aged woman with pre-existing diabetes was ultimately attributed to PAF rather than to diabetic autonomic neuropathy, illustrating the clinical features that help distinguish the two conditions.

Case Presentation

A 55-year-old woman presented with a several-month history of gradually worsening orthostatic intolerance. She initially noticed brief episodes of near-fainting brought on by walking, which settled promptly once she sat down; these spells were accompanied by transient visual blurring that likewise resolved with rest. Her symptoms progressed steadily, and by the time she sought hospital evaluation she was becoming markedly lightheaded within seconds of rising to stand.

A systematic review of autonomic function was otherwise unremarkable: sweating, appetite, satiety, lacrimation, salivation, and bowel and bladder control were all preserved. Her medical history was notable only for type 2 diabetes mellitus, diagnosed six years earlier and managed on standard therapy; she reported no family history of comparable neurological or autonomic disease.

Examination confirmed pronounced orthostatic hypotension. Formal autonomic testing showed clear cardiovascular dysautonomia: heart rate variability with deep breathing was blunted, and the expected blood pressure overshoot during phase IV of the Valsalva maneuver was absent. Sympathetic reactivity was similarly impaired, as demonstrated by abnormal responses to both cold-pressor and mental-arithmetic stress testing.

Importantly, a comprehensive neurological assessment found no cognitive decline, extrapyramidal signs, or cerebellar dysfunction, and sensory and motor testing of the limbs was entirely normal. Given the combination of severe, isolated sympathetic and parasympathetic failure with objectively confirmed orthostatic hypotension and no evidence of central nervous system or extrapyramidal disease, a clinical diagnosis of PAF was made [4].

Treatment was initiated with the mineralocorticoid fludrocortisone at 0.1 mg daily, up-titrated to 0.2 mg daily; the alpha-1 agonist midodrine was subsequently added to further support blood pressure [5]. With this regimen her orthostatic symptoms improved sufficiently for her to walk unaided and without assistance.

She continues to be followed as an outpatient. Ongoing care is directed at fine-tuning her antihypotensive therapy while guarding against supine hypertension at night, along with regular clinical reassessment forany new motor, cognitive, or multisystem autonomic features that might signal evolution toward a central synucleinopathy [5,6].

DISCUSSION

A diagnosis of PAF requires that autonomic failure remain isolated—unaccompanied by motor or cognitive deficits—over an extended observation period [4]. Long-term follow-up studies show, however, that this isolation is not always permanent: roughly one-quarter to one-third of patients initially labeled with PAF go on, over five to ten years, to develop a central synucleinopathy such as multiple system atrophy, dementia with Lewy bodies, or Parkinson's disease [7,8].

The principal differential diagnosis in this patient was diabetic autonomic neuropathy. Diabetic peripheral neuropathy classically follows a length-dependent, dying-back pattern [9], and severe orthostatic hypotension caused by diabetes typically emerges only after many years of disease and is accompanied by prominent distal sensory loss and renal impairment [10]. Neither feature was present here, and her diabetes history of only six years made an advanced diabetic autonomic process an unlikely explanation for such profound dysautonomia.

Several features of this case argue against diabetic autonomic neuropathy and in favor of PAF: the rapidity and severity of orthostatic symptoms were disproportionate to a relatively short diabetes duration; autonomic testing revealed combined parasympathetic and postganglionic sympathetic failure, reflected in the absent Valsalva phase IV overshoot and abnormal sympathetic stress responses [4,6]; and, unlike the typical mixed sensory and gastrointestinal pattern of diabetic autonomic neuropathy, her deficits were confined to the cardiovascular autonomic system, with entirely normal sensory and motor findings. Together, these observations support a diagnosis of PAF rather than an atypically advanced diabetic neuropathy [4,10].

CONCLUSION

This case highlights that severe, rapidly progressive orthostatic hypotension in a patient with diabetes need not be attributed reflexively to diabetic autonomic neuropathy, particularly when the clinical tempo and pattern of autonomic testing are atypical for that diagnosis. Recognizing PAF as a distinct entity has direct implications for management and prognosis, and given the meaningful risk of later conversion to a central synucleinopathy, affected patients require careful, sustained longitudinal follow-up.

DECLARATIONS

Consent for Publication: Written informed consent was obtained from the patient for publication of this case report.

Conflict of Interest: The authors declare no conflict of interest.

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