Severe Paroxysmal Hypertension (Pseudopheochromocytoma)

Understanding the Cause and Treatment

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Severe, symptomatic paroxysmal hypertension always generates suspicion of a pheochromocytoma, a catecholamine-secreting tumor. However, most patients with this disorder do not have this tumor and their condition remains undiagnosed and ineffectively treated. This case series, summarizing the course of 21 such patients, suggests a cause and an effective treatment approach. All 21 patients insisted that the paroxysms were not related to stress or emotional distress, initially discouraging consideration of a link to emotions. Nevertheless, with careful psychosocial interviewing, the disorder could be attributed to emotions patients were not aware of, and, therefore, unable to report. Such emotions were related either to previous severe emotional trauma or to a general tendency to keep distressful emotions out of awareness. With treatment based on this understanding, further paroxysms were eliminated in 13 (62%) of 21 patients. α- plus β-blockade was used, combined, when necessary, with an antidepressant agent, with or without an anxiolytic agent. In 3 cases, the disorder was cured with psychotherapy alone. Because the presenting symptoms are physical rather than emotional, patients present to internists and primary care physicians rather than to psychotherapists. For this reason, more awareness of this disorder in the medical community is needed.

The clinical syndrome of severe and symptomatic paroxysmal hypertension always generates suspicion of a catecholamine-secreting pheochromocytoma. However, most patients with this disorder do not have this tumor and, once it is ruled out, diagnostic investigation rarely uncovers a cause. Most remain ineffectively treated, and many experience chronic disability. Despite this, paroxysmal hypertension, which has been referred to as “pseudopheochromocytoma” by Kuchel and others, has been the subject of far fewer studies or reports than the much less common pheochromocytoma.

The purpose of this article is to present the clinical characteristics of the disorder in a series of 21 cases, and to describe a treatment approach that has been successful in most patients. Five case histories will be briefly presented to illustrate both the clinical flavor and the treatment of the disorder.

METHODS

The records of 700 consecutive new patients seen by the author between January 1990 and December 1997 for evaluation of hypertension were reviewed, and cases of paroxysmal hypertension were identified. Patients were considered to have paroxysmal hypertension if they had been experiencing documented hypertensive paroxysms characterized by 3 features: (1) abrupt elevation of blood pressure, (2) equally abrupt onset of distressful physical symptoms, and (3) absence of reported fear or panic at the onset of attacks. Blood pressure elevation during episodes was documented by a physician on at least one occasion. Twenty-one cases met this description. A pheochromocytoma was diagnosed in none, after appropriate assessment of plasma or urinary catecholamine levels, and, if indicated, radiological studies. In many cases, prior extensive diagnostic investigations had been conducted, including imaging procedures of the adrenal gland in 8 patients and of the brain in 7 and radionuclide or...
angiographic studies to exclude ischemic coronary disease in 6.

Treatment and treatment outcome were also assessed. Treatment was considered successful if hypertensive episodes ceased occurring.

**RESULTS**

The clinical characteristics of the disorder are summarized in the Table. Hypertensive episodes were accompanied by severe physical symptoms, such as headache, chest pain, dizziness, nausea, palpitations, flushing, and diaphoresis. All patients described the episodes as abrupt in onset, and insisted they were not provoked by stress, emotional distress, fear, or panic. Episodes persisted from a half hour to many hours and were usually followed by profound exhaustion for up to 1 or 2 days. The frequency of attacks ranged from once every few months to once or twice a day. The peak blood pressure exceeded 200/110 mm Hg in most patients. Between episodes, blood pressure was normal or more mildly elevated.

Most had failed treatment with various antihypertensive medications, alone and in combination. Thirteen (62%) of the 21 patients had been hospitalized at least once because of the disorder. Because of the unpredictable occurrence of the paroxysms and the severity of the symptoms, the disorder significantly impaired the quality of life of most of the patients.

**PSYCHOSOMATIC BASIS**

The insistence by all the patients that the episodes were not related to emotional distress initially discouraged consideration of a psychosomatic basis. However, details of the psychosocial history, and the subsequent rapid response to psychotherapeutic or psychopharmacological intervention, uncovered the disorder’s relationship to emotions kept from conscious awareness.

Fourteen (67%) of the 21 patients acknowledged a history of severe emotional trauma, such as the Holocaust or prolonged physical or emotional abuse. Their uniform and striking insistence that they harbored no distressing trauma-related emotions was strongly suggestive of emotional defenses such as repression or dissociation. The other 7 did not report a history of overt trauma or abuse, but careful clinical interviewing suggested a lifelong pattern of coping with distressful emotions by both minimizing awareness of them and confiding in no one.

**TREATMENT OUTCOME**

A successful outcome was achieved in 13 patients (62%), with a mean follow-up of 9 months (range, 4-60 months). The follow-up exceeded 9 months in 11 of the 13 patients.

Three of the 13 responded to psychotherapeutic intervention, without pharmacological intervention. Three others responded to antihypertensive drug therapy with combined α- plus β-blockade. The remaining 7 responded to α- plus β-blockade combined with either a tricyclic antidepressant or a selective serotonin reuptake inhibitor. Four of these 7 were also prescribed an anxiolytic agent.

Of the 7 patients in whom a successful outcome was not observed, 2 were treatment failures, 2 died before treatment could be assessed (1 died of cancer; 1 died of aspiration [autopsy revealed no pheochromocytoma]); 1 was lost to follow-up; 1 refused treatment; and
was intolerant of medication. In 1 additional patient, episodes ceased without specific intervention.

Report of Cases

The case histories of 5 patients, in whom this disorder was successfully treated, help to demonstrate the origin, clinical severity, and treatment of paroxysmal hypertension.

Patient 1

A 33-year-old Hispanic man had been hospitalized many times during 5 years and was medically disabled with severe hypertensive paroxysms, with blood pressure readings reaching 220/140 mm Hg, associated with diaphoresis, chest pain, nausea, dizziness, palpitations, headache, and back and neck pain. Repeated urine catecholamine assays, renal and abdominal computed tomographic scans, metaiodobenzylguanidine scans, and renal angiography were unrevealing. Antihypertensive regimens had been ineffective or poorly tolerated.

The patient reported no stressors other than his illness. However, as a child, he had been physically abused by his father, frequently and without provocation. Yet, he reported feeling strong love and no anger toward his father. A psychiatric consultant diagnosed the patient as having an “anxiety disorder, not otherwise specified.” Treated with alprazolam and amitriptyline, the patient’s hypertensive episodes ceased completely, with no recurrence during 3 years of follow-up.

Patient 2

A 35-year-old foreign-born physician presented with a 4-year history of muscle weakness, for which extensive investigation had revealed no cause or objective findings; a 3-year history of labile hypertension; and a 6-month history of daily symptomatic hypertensive paroxysms, associated with chest pressure, unilateral flushing, dizziness, weakness, tachycardia, and polyuria. Her self-monitored blood pressure rose as high as 200 to 210/130 mm Hg, with a heart rate of up to 120 beats per minute. The episodes could last for hours, followed by extreme exhaustion. At other times, her blood pressure was roughly 160/100 mm Hg.

Plasma and urine catecholamine levels, renal scan, and an echocardiogram were normal. Because of hypotension during previous tilt-table testing, the diagnosis of chronic fatigue syndrome had been considered, but salt tablets had not worked. Regimens including atenolol, clonidine, enalapril maleate, and diltiazem had been ineffective.

Because of the paroxysmal nature of her hypertension and the prior unrevealing medical investigation, the patient’s psychosocial history was carefully explored. Her childhood home life had been pleasant. She was currently married with no marital strife. She had 1 child. The only possibly traumatic event, mentioned almost incidentally, was a 1-month imprisonment for political activism while in college in her native country. Further questions, however, revealed that during that month she was blindfolded, tortured, and repeatedly threatened with execution. Several of her friends were executed. She claimed she had suffered no emotional repercussions and never talked about that experience.

A β-blocker, atenolol, 25 mg twice daily, combined with a vasodilator, amlodipine, 5 mg daily, a selective serotonin receptor antagonist, paroxetine, 20 mg, and anxiolytic clonazepam, were prescribed. Her blood pressure quickly stabilized at 140/80 mm Hg, and the attacks ceased completely. She was not interested in seeking psychotherapy.

Patient 3

A 66-year-old man with a 5-year history of mild hypertension began to experience hour-long episodes of sweats and facial redness, with blood pressure elevation to 190/110 mm Hg or higher, followed by exhaustion. Between episodes, his blood pressure was normal. Treatment with nifedipine, atenolol, hydrochlorothiazide, and enalapril had not helped, and he could no longer operate his business. He was hospitalized once. Urine catecholamine levels, magnetic resonance imaging of the brain and abdomen, and urinary 5-hydroxyindoleacetic acid determination were all normal.

The patient, who described his parents as emotionally distant, considered himself independent, never needing or seeking emotional support and having a very even temperament. Typical of this, he shed no tears 7 years earlier when his son became paraplegic after a nearly fatal automobile crash.

The patient was treated with α-plus β-blockade (atenolol, 25 mg twice daily, plus terazosin, 2 mg twice daily) and a combination of desipramine (ultimately 50 mg daily) and lorazepam. The hypertensive episodes promptly ceased and the patient resumed operating his business.

Patient 4

A 52-year-old white woman with a long history of anxiety began to experience unprovoked and debilitating 2-hour episodes of dizziness, weakness, flushing, and nausea, with blood pressure elevation to 165 to 170/100 mm Hg. Attacks had been occurring every 1 to 2 days for 4 months. Plasma catecholamine levels were normal.

She described a stress-free affluent life and did not believe that this disorder was related to emotional stress. She insisted that she was happy, but, in further conversation, came to acknowledge that the opposite was true and realized and confided painfully that she felt useless and ashamed of herself.

Her attacks ceased completely within a month of this emotional disclosure, without any psychotherapeutic intervention. She has remained free of attacks for 3 years. She has been intermittently depressed but is making changes in her life.

Patient 5

A 56-year-old white woman reported suffering hypertensive paroxysms during a 7-year period, with blood pressure elevation to 200/120 mm Hg accompanied by ocipital throbbing, diaphoresis, dizziness, and weakness. Episodes occurred 1 to several weeks apart and persisted for half an hour to 12
hours, resolving with or without treatment. Her blood pressure between episodes was 145/90 mm Hg. She had to stop working because of her many unpredictable absences. Repeated random determinations of plasma and urinary catecholamine and urine samples collected following episodes were normal. By her estimation, she had been to 39 physicians. Various antihypertensive regimens had been ineffective.

Aware of no major stressors or emotional distress in her life, she reacted angrily to the suggestion of an emotional cause. However, in the absence of any alternative explanation, she reluctantly began to see a psychotherapist. Within months, a pattern of emotional denial in dealing with stress was uncovered and traced back to a childhood characterized by emotionally unavailable parenting. As she learned to recognize her distressful emotions, her attacks came to a halt. She had 1 attack 18 months later, and none in the 5 years since then.

COMMENT

DIFFERENTIAL DIAGNOSIS

The diagnoses most likely to be considered in patients with this disorder are pheochromocytoma, labile hypertension, and panic disorder. The diagnosis of pheochromocytoma should be excluded in all patients with unprovoked paroxysmal hypertension. Usually, plasma or urinary catecholamine studies are sufficient to serve this purpose.

In most patients with pheochromocytoma, plasma and urinary catecholamine levels are persistently and markedly elevated. Normal levels, particularly when obtained during an episode, virtually exclude a pheochromocytoma. In contrast, in patients with paroxysmal hypertension who do not have a pheochromocytoma, catecholamine levels are normal between episodes and are either normal or only mildly elevated during paroxysms. If elevated, further efforts to exclude the possibility of a pheochromocytoma may be indicated.

Labile hypertension differs starkly from paroxysmal hyperten-
ment of the sympathoadrenal system. Preventive treatment with adrenergic blockade seems more logical and appears far more effective than treatment with agents such as angiotensin-converting enzyme inhibitors and diuretics, which are directed more at nephrogenic mechanisms of essential hypertension. Central α-agonists (eg, clonidine) can be effective, but fatigue and somnolence usually preclude adequate dosage.

Even with these agents, treatment can be difficult, because of the severity of blood pressure elevation during paroxysms and the lower or even normal blood pressure level at other times, which often limits the prescribed dose. If severe paroxysms recur despite antihypertensive treatment, acute intervention may also be necessary, administered either intravenously (labetolol) or orally (labetolol, prazosin, terazosin, clonidine). An extra dose of a β-blocker might be useful if attacks are accompanied by tachycardia.

If α- plus β-blockade does not control the disorder, adding a psychopharmacological agent can be dramatically effective in eliminating paroxysms and restoring a normal quality of life.

Psychopharmacological Intervention

Even when patients reject the possibility of an emotional basis, treatment with antidepressant agents, possibly combined with an anxiolytic agent, can eliminate attacks, as illustrated in patients 1, 2, and 3. Treatment may have to be initiated by the primary care physician if the patient is unwilling to consult a psychiatrist.

Tricyclic antidepressants, such as desipramine, and selective serotonin-reuptake inhibitors, such as paroxetine, used at their usual recommended doses, have been effective. There is inadequate data to suggest that one type of agent is more effective than any other. The efficacy of these agents in the absence of concomitant administration of adrenergic-blocking agents has not been evaluated.

Psychotherapeutic Intervention

Antihypertensive and psychopharmacological agents can control the disorder but cannot cure it. The responses in patients 4 and 5 indicate that in some cases psychotherapeutic intervention can provide a cure, and an alternative to unending pharmacological treatment. Further studies are needed to determine the type or types of psychotherapy best suited for this disorder.

OBSTACLES TO SUCCESSFUL TREATMENT

Because the manifestations of this disorder are physical, its emotional basis is rarely suspected by either patient or physician. Attacks are not linked to perceived emotional distress and, consequently, even psychosocially oriented physicians are unlikely to consider an emotional basis, even when a diagnosis or effective treatment has been elusive. Instead, the emphasis on diagnostic testing, which is wholeheartedly supported by patients, dominates.

In the absence of conscious emotional distress, it is difficult for people to believe that emotions underlie the disorder, even in the absence of any other explanation or effective treatment. In addition, the pertinent emotions are extremely painful ones, which is why patients have battled to keep them out of awareness in the first place. For some, those emotions may still be too overwhelming to face. In this setting, a psychopharmacological rather than psychotherapeutic approach is usually more realistic.

Many patients will refuse psychotherapeutic or psychopharmacological intervention no matter how sensitively the psychosomatic link is suggested. However, the severity of the symptoms and the disruption caused by the disorder will ultimately motivate many patients to accept a therapeutic trial of a psychopharmacological agent.

In conclusion, the syndrome of unexplained paroxysmal hypertension is not uncommon and can cause severe and chronic disability. Yet, its origin and treatment are destined to remain a mystery unless the mind-body link is considered. Understanding its origin in emotions kept from awareness opens the door to a logical and successful treatment approach that uses adrenergic-blocking agents, antidepressant and anxiolytic agents, and/or psychotherapy. Further studies are needed to confirm these observations, to better understand the link between this disorder and panic disorder, and to better delineate treatment options.

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