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Idiopathic orthostatic hypotension

Report of a Case

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NORMAL persons have adaptive mechanisms that help to maintain a constant cerebral blood flow. Changes from the recumbent to the upright position may cause pooling of fluid in the lower extremities, which leads to decreases in venous return and in cardiac output. This results in increased action in sympathetic output, which leads to increases in heart rate, in peripheral resistance, in plasma norepinephrine content, in urinary catecholamine concentration, and to venous constriction. Adequate cerebral circulation is maintained by a rise in the diastolic arterial pressure as a consequence of the sympathetic action and a dilatation of the cerebral blood vessels.

Postural hypotension may result from the use of hypotensive drugs, blood volume depletion from blood loss or sodium depletion, and conditions associated with low blood volume such as Addison's disease. Neurologic diseases including diabetic peripheral neuropathy, tabes dorsalis, multiple sclerosis, syringomyelia, and cerebral arteriosclerosis, have been associated with postural hypotension.

In some cases of postural hypotension there is no recognized disease. Idiopathic orthostatic hypotension was clearly described by Bradbury and Eggleston[1] in 1925. The pathognomonic feature is the orthostatic hypotension. Other evidences of autonomic dysfunction are anhidrosis, impotence, and sphincter and especially bladder dysfunction. In a few patients there are, in addition to the autonomic dysfunction, evidences of motor disturbance with a parkinsonian-like syndrome, general muscle weakness, ataxia, increased tendon reflexes, positive Babinski responses, fasciculation, and ptosis.[2-4] This report concerns a patient with such impairment.

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Report of a case

A 51-year-old Caucasian housewife was first examined at the Cleveland Clinic on April 3, 1964, because of recurrent syncope during the previous six months. Initial symptoms were a feeling of heat and pressure in the head, hazy vision, and palpitations. These effects could be relieved when the patient sat down, but several times the patient had fainted for a short period. For about one year there had been increasing difficulty in urinating, and attacks of dysuria occurred several times. The patient had also noted loss of her ability to write legibly.

For 17 years the patient had been subject to episodes of depression, and for this she had been hospitalized twice, in 1949 and in 1962. During the last hospitalization she was treated with electroshock therapy. Depression continued to recur. Two weeks before examination at the Cleveland Clinic, the patient had begun treatment with imipramine hydrochloride, 25-mg doses three times daily.

On physical examination the patient's systolic blood pressure was 105 mm Hg and the diastolic 85 mm Hg, and the pulse rate was 120 in the sitting position; in the standing position the systolic blood pressure was 90 mm Hg, with no definite diastolic end point. The other significant findings were related to the neurologic examination. The right side of the face was slightly flattened. There was some rigidity in all limbs with cogwheel effect, but not associated with loss of arm swing or with static tremor.

The patient was then hospitalized because of syncope and depression. The blood count, urinalysis, serologic tests for syphilis, glucose tolerance test, urinary 17-hydroxycorticoids and ketosteroids, gonadotropins, and a metapyrone stimulation test were all normal. An electroencephalogram was normal except for mild theta activity in the temporal lobes, mostly in the left temporal area. Urologic examination disclosed a bladder of large capacity and no lesions in the urethra. Treatment consisted of adherence to a voiding schedule, and bethanechol chloride, 40-mg doses taken orally four times a day. The imipramine hydrochloride therapy was discontinued, but orthostatic hypotension persisted. The patient continued to feel depressed, and psychiatric consultation was obtained. The clinical impression was that she exhibited some features of an involutional depression and conversion reaction.

The patient was discharged from the hospital and was advised to follow a course of medication—tranquilizers and antidepressants—but there was little improvement. On November 17, 1964, because of continuing and progressive symptoms, with difficulty in using the hands in fine movements, staggering gait, and difficult urination, she was readmitted to the hospital.

Orthostatic hypotension persisted with the patient in the recumbent position, the systolic blood pressure being 130 mm Hg, and the diastolic 90 mm Hg, and the standing blood pressure ranging from 90 mm Hg systolic with no definite end point, to levels of 70 mm Hg systolic and 60 mm Hg diastolic. The neurologic examination continued to show bilateral cogwheel rigidity, bradykinesia, and gait disorder, with decreased arm swing consistent with Parkinson's disease. An electroencephalogram showed decreased left temporal delta activity. A scintigram of the brain was normal, as were roentgenograms of the skull. A lumbar puncture yielded a specimen of normal fluid. The patient was discharged from the hospital and was advised to follow a course of medication—dextroamphetamine sulfate, 5-mg doses twice daily; diphenhydramine hydrochloride, 25-mg doses four times daily; and trihexyphenidyl hydrochloride, 2-mg doses twice daily—and to wear elastic hose.

On December 26, 1965, the patient was readmitted to the hospital because of persistent orthostatic hypotension. At that time, studies were done to define better the extent and degree of her autonomic impairment. A sweat test showed generalized decrease in sweat production. Hemodynamic studies confirmed the presence of orthostatic hypotension. The blood pressure progressively declined with increments in upright tilt. Associated with the hypotension were compensatory increases in heart rate. The other evidence of sympathetic reflexes was not clear cut. The Valsalva overshoot and associated bradycardia were not normal. The blood pressure and increase in heart rate with cold stimulation were subnormal, and the reflex bradycardia associated with the norepinephrine pressor response was absent. There was evidence of normal catecholamine stores, provided by a response in blood pressure and increase in heart rate to injection of tyramine. After the infusion of 1 liter of dextran, no orthostatic hypotension was demonstrated, and there was no significant decrease in cardiac output with the patient in various degrees of upright tilt.

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From these studies we concluded that the orthostatic hypotension could be explained in part by impaired sympathetic responsiveness as well as a relative decrease in effective circulating blood volume in the upright position. Further studies showed an impaired aldosterone response to sodium restriction. While the patient was receiving a regular hospital diet, a 24-hour urine specimen contained 5 mg of aldosterone. The patient then received a 200-mg sodium diet for three days. On the third day of this program a 24-hour urine specimen was collected which contained 72 meq per liter of sodium and 14 meq per liter of potassium. On the following day the patient received an injection of 2 ml of meralluride. On the following day a 24-hour urine collection contained 6 μg of aldosterone and demonstrated the patient's inability to increase aldosterone excretion in the presence of sodium deprivation and the administration of a potent diuretic.

The patient was discharged from the hospital and was advised to take fludrocortisone acetate, 0.5-mg doses three times daily, and sodium chloride, 5 g daily, and to wear elastic hose to prevent the hypotension. The symptoms of hypotension were well controlled; however, urinary incontinence increased, and for control required that the patient have an indwelling catheter. The patient and her family then moved from this region in October 1966, and the only follow-up report was a letter from her local physician stating that she had died in June 1968 from a progressive generalized muscular weakness and respiratory failure.

Discussion

The patient whose case we report had many of the abnormalities characteristic of the syndrome of idiopathic orthostatic hypotension. It has been suggested by studies of Thomas and Schirger[2] and Schatz, Podolsky and Frame[3] that the impairment of the autonomic nervous system may be but an early stage of a more generalized neurologic disorder. These studies indicate that the autonomic dysfunction may be followed by corticobulbar, corticospinal, basal ganglionic, and cerebellar dysfunction.

A severe form of idiopathic orthostatic hypotension was described by Shy and Drager[4] as part of a central nervous system degeneration that, in addition to the autonomic impairment, included external ocular palsies, muscle rigidity and tremor, atrophy of the iris, and biopsy evidence of changes of a neuropathic lesion and degeneration of the anterior horn cell. The patients had normal plasma norepinephrine contents and normal responses to parenteral injections of norepinephrine.

In the case we report it is of interest that both the parkinsonian-like features and the orthostatic hypotension were evident in association with the chief symptom of syncope. This would confirm the theory that both these processes are related to the primary neurologic disorder rather than that the hypotensive episodes are responsible for cerebral ischemia and injury to the central nervous system.

It has been noted previously that patients with autonomic insufficiency may fail to have a normal response of aldosterone production to sodium restriction and to upright posture.[5-8] In addition it has been shown that some patients with idiopathic orthostatic hypotension may have renal salt wasting.[9] The sympathetic nervous system may be involved in the normal response to stimuli of upright posture and to sodium depletion, which result in increases in urinary catecholamines, in plasma renin action and in urinary aldosterone content.

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Studies of a patient with severe autonomic insufficiency demonstrated that the upright posture and sodium deprivation did not produce the normal increases in urinary catecholamines, plasma renin action, or in urinary aldosterone content.[7] That patient did respond to infusion of catecholamines, which produced increases in plasma renin action and in aldosterone excretion. The studies led to the conclusion that both the upright posture and sodium depletion resulted in decreases in effective plasma volume and to increases in sympathetic nervous system action. This sympathetic response then resulted in the sequence of increase in renal arteriolar constriction, in renin secretion, and in aldosterone secretion. In the patient with idiopathic orthostatic hypotension, such a sympathetic response is absent, thereby failing to trigger this sequence of events.

The treatment of this form of orthostatic hypotension may be by (a) sympathomimetic drugs, (b) mechanical vasoconstrictors, or (c) sodium-retaining steroids and salt. The most frequently used medication is ephedrine, with the usual dose of ephedrine sulfate being 50-mg doses by mouth at intervals determined according to the response to treatment. Sodium-retaining steroids in combination with sodium chloride may be used to produce hypervolemia. Fludrocortisone acetate, from 0.1 to 0.4 mg daily, together with extra sodium chloride added to the diet has been used to good effect. This program of medication requires careful observation, since hypokalemia and excessive hypertension in the recumbent position may ensue. The use of elastic garments from the waist down while the patient is ambulatory is helpful in preventing the venous distension and pooling of the blood in the lower extremities. In severe cases an antigravity suit has been effectively employed. By such measures the patient's symptoms may often be temporarily relieved; however, in most patients the disease is slowly progressive over a period of years.

Summary

The data of a patient with a neurologic disorder resulting in severe autonomic deficiency and a parkinsonian-like syndrome are presented. The patient had a reduced response of aldosterone formation to sodium depletion, with no other evidence of adrenal deficiency. The features of this neurologic disorder and the relationship of autonomic disease to aldosterone production are discussed.

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