Clonidine Treatment in Paroxysmal Localized Hyperhidrosis

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• **We report two cases of paroxysmal localized hyperhidrosis (PLH), a rare disorder usually of undetermined origin. The patients were treated with clonidine hydrochloride on the assumption that this paroxysmal phenomenon is of CNS origin, probably hypothalamic. Both patients responded favorably to treatment. In treating PLH, clonidine may serve as an alternative approach to local or surgical treatment.**

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Sweating is an important part of thermoregulation and is probably dependent on dual control of a central receptor mechanism and reflex activity from skin.[1] The eccrine sweat glands are innervated by postganglionic fibers that, though sympathetic, are cholinergic and gave a roughly segmental distribution.[1]

Symmetric idiopathic hyperhidrosis affecting either the palms, soles, face, or axillae is not uncommon; however, occasionally the hyperhidrosis is paroxysmal and localized. Treatment of this unpleasant situation is usually local[2] or surgical, ie, partial sympathectomy.[3]

We present two cases with paroxysmal idiopathic localized hyperhidrosis (PLH) that showed the patients' excellent response to treatment with clonidine hydrochloride.

REPORT OF CASES

CASE 1.—A 65-year-old woman who suffered from mild diabetes mellitus, well controlled by glyburide, and hypertension treated with diuretics, complained throughout the previous 12 months of paroxysms of sweating on the right side of her face involving the eyebrow, the temple, and upper part of the cheek. The sweating was associated with a sensation of local coldness and paresthesia. Paroxysms occurred several times daily and lasted from 15 to 30 minutes. They were not associated with food ingestion, physical activity, or any known stress situation.

Results of the physical and neurologic examinations were normal. Blood counts, urea and electrolyte values, and urinalysis findings were all normal. The VDRL was negative. The blood glucose level was 144 mg/dL, and the EEG and the chest and skull roentgenograms were normal. A sweat test with iodine and starch resulted in localized sweating on the right side of the face in reaction to heat. Perspiration was induced with prolonged heating over the entire body but was much more pronounced over the right side of the face.

The patient was administered clonidine hydrochloride (0.25 mg three times daily) after three days, the PLH episodes almost disappeared. The patient has been followed up for more than 12 months and has shown an excellent response to treatment.

CASE 2.—A 52-year-old woman complained of numerous attacks (15 to 20) of sweating, sometimes associated with flushing, in the upper part of the body; these attacks lasted for about ten minutes. The patient had been suffering for 20 years from headaches compatible with basilar artery migraine and for the last two years from a left-sided Horner's syndrome. The results of the physical examination were normal. Although the neurologic examination showed a left mild ptosis and miosis compatible with Horner's syndrome, the rest of the results were normal. Pharmacologic tests (cocaine, phenylephrine hydrochloride, and hydroxyamphatemine hydrobromide [Paredrine]) confirmed a third nerve lesion. The paroxysms of sweating were not associated with elevation of BP or tachycardia and were not caused by any food ingestion, physical activity, or any stress situation. A sweat test triggered by heat, using iodine and starch, showed sweating in the right side of the face and the upper part of the body with a sharp demarcation zone at about T-12. Skull roentgenograms, EEGs, and a computed tomographic scan of the head were all normal. Urinary serotonin 5-hydroxyindoleacetic acid and urinary vanillylmandelic acid levels were normal.

The patient was treated with clonidine hydrochloride (0.25 mg three times daily). The paroxysms of sweating were reduced to about one or two a day. An increase in the dose of clonidine hydrochloride to 0.25 mg five times daily resulted in the disappearance of the attacks. The attacks have not occurred in the 12 months since treatment.

COMMENT

Although PLH is a rare condition, it may occur as a nervous system disease symptom, such as syringomyelia, tabes dorsalis, or pressure on a nerve root.[4] It may be a manifestation of gustatory sweating, either idiopathic[5] or associated with diabetes mellitus.[6] It may also result from surgical removal of the stellate ganglion,[5] or it may simply be idiopathic.[7,8]

Patient 1 suffered from diabetes mellitus but showed no other nervous system impairment. Patient 2 suffered from migraine headaches and a peripheral Horner's syndrome but had no other impairment of the nervous system. Because both patients' attacks are paroxysmal, were influenced only by heat, and were not associated with any gustatory or emotional stimuli, thermoregulatory mechanism, probably hypothalamic, seemed to be involved. These paroxysms, well-demonstrated zones of hyperhidrosis, suggest some impulse discharge analogous to the paroxysmal phenomenon observed in multiple sclerosis.[9]

The mild flushing associated with the paroxysmal sweating may also support a hypothalamic origin, as central hypothalamic catecholamines have been linked to hypothalamic temperature regulation and to the originating of hot flushes.[10] Clonidine is a CNS α_2-noradrenergic receptor agonist, thus it suppresses norepinephrine release and therefore inhibits central noradrenergic activity. Both of our patients responded favor-

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ably, after a short time, to clonidine therapy with no obvious side effects, thus strengthening the hypothesis that PLH is a CNS phenomenon, probably associated with noradrenergic activity. Clonidine is also known to be quite a successful treatment of menopausal flushing, thus indicating a possible common mechanism between these two phenomena. Clonidine treatment was also found to be effective in gustatory sweating associated with diabetes mellitus.[11]

We suggest that clonidine may provide effective therapy in cases of PLH, thus offering an alternative to local or surgical treatment.

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Hyperammonemic Encephalopathy Related to Ureterosigmoidostomy

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• Urinary diversion to the colon may produce a metabolic encephalopathy with elevated blood ammonia levels. The condition resembles hepatic encephalopathy but can occur without obvious liver disease. The patient described herein also had a computed tomographic scan showing diffuse brain swelling and superficial contrast enhancement. The condition responds rapidly to lowering of the blood ammonia level and requires a high level of suspicion for diagnosis in the patient who has undergone urinary diversion and has an unexplained metabolic encephalopathy.

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Hepatic encephalopathy usually occurs in the setting of overt liver disease. However, certain disorders produce an altered mental state and elevated blood ammonia level without obvious liver dysfunction. Among these, hereditary urea cycle defects become symptomatic early in life, with seizures, episodic stupor and coma, and mental retardation. In adults, congenital intrahepatic and extrahepatic shunts have been known to cause intermittent ataxia and confusion.[1,2] Urinary diversion may also, rarely, lead to hyperammonemic encephalopathy.[3-6] Because this complication of certain urologic procedures is not widely appreciated, and the disturbance is entirely treatable, I wish to report another such case with an unusual head computed tomographic (CT) scan.

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REPORT OF A CASE

A 33-year-old woman was referred to this hospital with headache of two weeks' duration and progressive obtundation. Urinary incontinence of unclear origin had been treated previously with several diversionary procedures, the most recent being reimplantation of the ureters from her skin into her sigmoid colon seven months before entry.

On admission, the patient appeared cachectic, had a temperature of 38.5 °C, and had no stigmata of liver disease. She was fully oriented but lethargic and had amnesia, nuchal rigidity, asterixis, bilateral papilledema, a mild left hemiparesis, and bilateral Babinski's signs. Initial blood studies were remarkable for the following: chloride, 118 mEq/L; carbon dioxide, 13 mEq/L; SGOT, 44 IU/L; and normal potassium, glucose, alkaline phosphatase, and total bilirubin levels. The CSF was under an increased pressure of 430 mm H_2O and contained 15 WBCs per cubic millimeter, 430 RBCs per cubic millimeter; the glucose level was 67 mg/dL, and the protein level, 22 mg/dL. Head CT scan showed diffuse brain swelling with small ventricles and pronounced, superficial contrast enhancement (Fig 1).

The patient's mental status improved over the next week. The CSF continued to have a markedly increased opening pressure and mild pleocytosis (Table). With a tentative diagnosis of meningoencephalitis, all cultures, as well as cryptococcal antigen and coccidioidomycosis titer, returned negative. In the second week the patient became more lethargic, and a nasogastric tube was placed to aid feeding. She then became deeply comatose, responding only to deep pain with extensor posturing. Because the arterial blood gas analysis showed a profound respiratory alkalosis, an arterial ammonia sample was drawn and showed a level of 275 μmole/L. The patient was treated with lactulose per rectum and within one day her mental status improved dramatically and her blood ammonia level had fallen to 112 μmole/L. Her hospital course was complicated by hypernatremia related to tube feedings, and by pneumatosis coli leading to resection of the right colon and colostomy formation. Further evaluation of the patient's liver included a normal liver-spleen scan, an initially positive but subsequently negative (three times) test for hepatitis B surface antigen (HBsAg) in the serum, and negative tests for antibodies to HBsAg and hepatitis B core antigen. The patient's mental status returned to normal, and repeated CT scan was greatly improved (Fig 2).

COMMENT

The diagnosis of hyperammonemic encephalopathy rests mostly on the clear correlation between blood ammonia level and clinical status. Thus, the patient became more alert as the initially elevated ammonia level declined with treatment. Although no CSF glutamine or blood ammonia level was obtained in the first days of hospitalization here, the patient's mental status declined precipitously