Sensory Radicular Neuropathy of the Hereditary Type

A Case Report

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A case of sensory radicular neuropathy of the hereditary type is reported. This disease was described as "hereditary perforating ulcer of the foot" by Hicks in 1922, as "acropathie ulcero-mutilante familiale" by Thevenard in 1942, and as "hereditary sensory radicular neuropathy" by Denny-Brown in 1951. The patient has the striking and characteristic indolent, ulcerative, mutilatory acropathy of the feet with the underlying dissociated sensory neuropathy. A chart of the differential diagnosis of ulcerative mutilatory acropathy is presented.

SENSORY radicular neuropathy of the hereditary type (Denny-Brown)[1] can cause an ulcerative mutilatory acropathy which is characterized clinically by severe and relapsing ulcerations of the skin of the feet and hands, and dissociated sensory deficit and osteolysis of the bones in the involved sites. This clinical picture may also be seen in leprosy, syringomyelia, diabetes mellitus (pseudotabes diabetica), tabes dorsalis, primary amyloidosis (especially the familial type), and chronic interstitial neural hypertrophy (Dejerine-Sottas disease).

We report below a case of sensory radicular neuropathy of the hereditary type.

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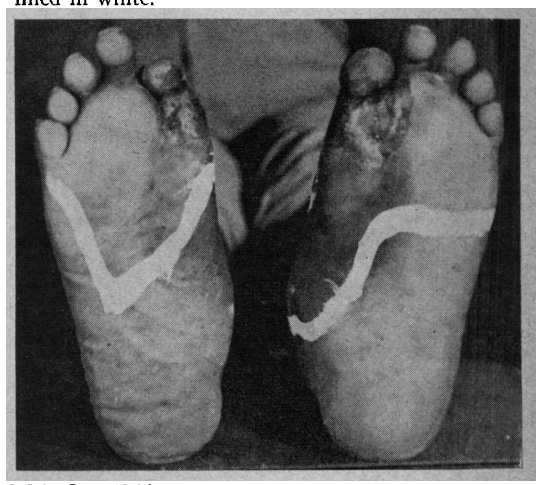
Report of a Case

This 38-year-old Negro man was perfectly well until 12 years ago when he developed painful calluses in the areas of the heads of the first metatarsal bones. Four years later, he noted that his calluses became painless. Later, his stockings began to "stick" to his feet. On investigating this problem, he noted ulcers beneath his great toes. These ulcers healed if he remained off his feet, but recurred on resuming ambulation. During his three hospitalizations for this condition, the ulcers almost completely healed. In spite of being a poor historian, he did recall that his father had a similar condition which resulted in the amputation of his great toes. He has been a heavy beer drinker for the past six years.

On physical examination at the time of his third admission in March 1966, he was an obese, well-nourished, Negro man. His pupils were of equal size and reacted to light. His eyegrounds were normal. There were no oral mucous membrane or tongue changes suggestive of any nutritional deficiencies. On auscultation and percussion of the

Fig 1.—The ulcers in the areas of the heads of the first metatarsal bones. The boundary of the hypesthesia of the anterior parts of the feet is outlined in white.



chest, no pulmonary abnormalities were observed. His heart was not enlarged by percussion, no murmurs were audible, and his blood pressure was 135/90 mm Hg. The edge of the liver was palpable at the right costal margin. No other organs or masses were palpable in the abdomen or the costovertebral areas. There was no significant lymphadenopathy. Peripheral pulses were palpable. There were no changes of the skin or its appendages consistent with arteriolar insufficiency. No ankle edema was present.

Two large ulcers were present in the areas of the heads of the first metatarsal bones (Fig 1). The adjacent great toes were atrophic and shrunken. The skin (Fig 2) approximating the L_5 and S_1 dermatomes, that is the dorsa of the feet, the lateral aspect of the lower tibiae, and the area about the ulcer, was hypesthetic to light touch, pain, and temperature, and was hyperpigmented; there was no sensory loss of vibration, position, or pressure in these areas. In the areas of sensory changes, the patient experienced hyperhidrosis when psychically stimulated; the histamine skin test in these areas was abnormal because no erythematous flare about the induced wheal was evident. Deep tendon reflexes were intact and brisk. The plantar responses were characterized by flexion of toes. There was no evidence of muscular weakness, fasciculation, or atrophy. No peripheral nerves were tender or enlarged.

The following laboratory tests were within normal limits: urinalysis, complete blood count, hemoglobin, hematocrit, two-hour postprandial blood glucose test, a glucose tolerance test, BUN, serological and spinal fluid VDRL, complete spinal fluid analysis and dynamics, SGOT, alkaline phosphatase, cholesterol, bleeding and clotting time, platelet count, hemoglobin electrophoresis, and liver scan. Two LE preparations were normal. Laboratory studies revealed the following values: total serum proteins, 8.5 gm/100 cc; serum albumin, 3.7 gm/100 cc; γ-globulin by serum electrophoresis, 2.36 gm/100 cc (normal=0.5-1.99 gm/100 cc). A liver biopsy was read as fatty liver; his sulfobromophthalein (BSP) revealed an abnormal retention of dye (24% at the end of three fourths hour). Audiograms were normal. Rectal and gingival biopsy results were negative for amyloid.

The radiologist reported: "X-ray of his feet reveals gross disintegration of phalanges and distal metacarpal bones of the great toes bilaterally. There is marked shortening of the great toes. The destructive changes are not those of erosion, demineralization, or osteomyelitis, but of neuropathic degeneration such as may be seen in diabetes mellitus, syphilis, and leprosy. The symmetry suggests the possibility of a spinal cord lesion. X-rays of the lumbosacral area are normal."

The histopathologic report of a biopsy of the ulcer of the right foot was a nonspecific ulcer of skin with no evidence of malignancy.

The patient was treated by hexachlorophene (pHisoHex) washes of the ulcers, debridement of the ulcers, and reduction of ambulation. He was instructed in foot hygiene and had metatarsal bars put on his shoes by the orthopedic service. There has been no significant change in his clinical status or therapeutic program.

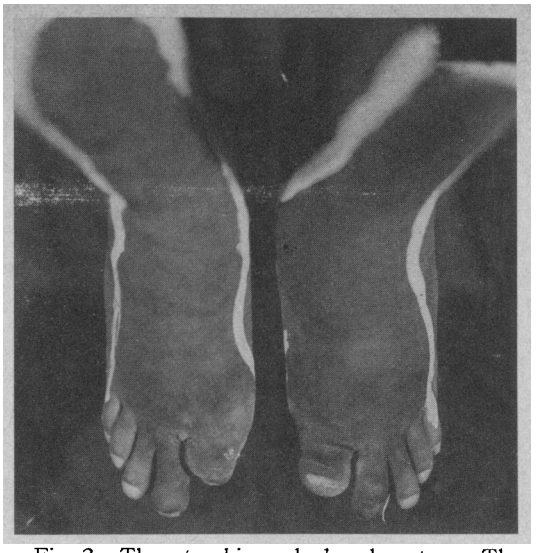


Fig 2.—The atrophic and shrunken toes. The areas of hypesthesia are outlined in white.

Comment

A persistent nonhealing ulcer, particularly when associated with a callus, should alert the physician to the possibility of sensory denervation. The selective degeneration of nerve fibers is not unusual in familial or hereditary diseases of the nervous system. The lesion which causes sensory neurone derangement, yet spares motor and autonomic fibers, is most reasonably placed in the dorsal root ganglia.

The earliest cases which are similar to the above reported one have been described in the British and continental literature as "familial syringomyelia" (Schultze 1917),[2] "hereditary perforating ulcer of the foot" (Hicks 1922),[3] "familial trophoneurosis" (Weitz 1924),[4] "status dysraphicus" (Enderle 1933),[5] "acropathie ulcero-mutilante familiale" (Thevenard 1942),[6] and "hereditary sensory radicular neuropathy" (Denny-Brown 1951).[1]

In 1922, Hicks studied 34 members in four generations of a family and described ten members who suffered from a disease which was characterized by perforating

ulcers of the feet, shooting pains about the body, and deafness. He felt that this disease differed clinically from syringomyelia in the rarity of amyotrophy or other motor accompaniments and the severity of the trophic disturbance which invariably starts in the lower extremities. In 1942, Thevenard coined the descriptive name, "Acropathie ulcero-mutilante familiale," for this entity. In 1951, Denny-Brown did a postmortem examination of one of the members of the third generation of the family described by Hicks as having hereditary perforating ulcer of the foot. He described degeneration of the dorsal root ganglia, dorsal roots, and peripheral nerve trunks, and the secondary deposition of amyloid in the most severely affected ganglia. He coined the descriptive name "hereditary sensory radicular neuropathy" and reported three sporadic cases with features identical to the hereditary cases. In 1953, Van Bogaert [7] reported that sporadic cases occurred more commonly than the familial but the symptomatology was not as typical or striking.

The disease is relatively unusual in children. Heller and Robb [8] reported two children who were 9 and 12 years of age and had the familial type of radicular sensory neuropathy without lightning pains or deafness. Walker [9] described a child with the sporadic type and another possibly with the familial type; both had dissociated sensory deficit, lightning pains, and deafness. However, the child with the sporadic type had the characteristic ulcero-mutilatory acropathy while the other child had not developed it.

The reported clinical features observed in the hereditary or sporadic cases of sensory radicular neuropathy are the following:

Trophic Ulceration.—Trophic ulceration, which is almost always present on the feet, is initially relapsing and is the most striking feature of this disease. It is related to the loss of pain sensation in the feet and, in some cases, the hands. On the feet, a callus appears beneath the small joints, which are subjected to undue pressure, especially the head of the first metatarsal. A hemorrhagic blister forms beneath this callus. The blister ruptures and a necrotic undermined ulcer, which may reveal the underlying joint and bone structure and yield bone sequestra, forms. The ulcer is painless, but may become infected. As a result of a complicating infection, the nonanesthetic area surrounding the painless ulcer may become painful. Osteolysis of the phalanges and metatarsal bones may precede the cutaneous ulceration by months. Progressive destruction of tarsal and ankle joints may result in the formation of Charcot's joints. Particularly interesting, but rare, are the cases in which the bones of the toes and fingers become shortened and covered by loose, folded skin; this deformity has been called "main en lorgnette" because the fingers appear as if they were telescoped like opera glasses.

Sensory Changes.—Dissociated sensory deficit, which is the loss or diminution of one or more types of sensation with the retention of others, is prominent in this entity. One is struck by the peripheral and relatively symmetrical sensory loss. The dorsal roots and ganglia of L_5 and S_1 vertebrae are often the first to be involved.[3] Sensory loss of pain and temperature is greater than that of touch and usually begins on the feet. Vibratory and position sensations are not usually lost. The sensory dissociation becomes less as the disease progresses. In many cases, the sensory changes extend to the middle of the leg and, infrequently, above the knee. Thevenard reported that the sensory disturbances in the upper limbs have been recorded more frequently since 1942 and pointed out that their spread is similar to that in the lower extremities. The sensory changes can ultimately result in a stocking and glove type of anesthesia.

Lightning Pains.—Lightning pains, which resemble clinically those of tabes dorsalis, result from the sensory radicular involvement. They usually appear in the lower extremities and later in the trunk, upper extremities, and head. The onset of these pains is usually months or years after the appearance of the ulcers of the feet. They have been reported in the familial and sporadic types of sensory radicular neuropathy.[2,3,10]

Deafness.—Neurogenic deafness has been described in cases of familial and sporadic sensory radicular neuropathy. Its

*Differential Diagnosis of Ulcerative Mutilatory Acropathy**

Diseases	Familial or Hereditary	Dissociated Sensory Deficit	Deafness	Lightning Pains	Deep Reflex Changes: Myotatic	Deep Reflex Changes: Pupillary	Bladder and Rectal Sphincters	Motor Disturbance	Ataxia	Palpably Enlarged Nerves	Diagnostic Laboratory Studies
Hereditary sensory radicular neuropathy	+++	+++	+	+	+	0	Rare	0	0	0	Dorsal root biopsy
Diabetes mellitus[15] (pseudotabes diabetica)	0	0	0	0	+++	+	+	0	0	0	Blood and urine sugar determination
Syringomyelia (familial lumbosacral type)	+	+++	0	+	+++	+	Rare	+++	+	0	Myelography
Leprosy	0	+++	0	0	0	0	0	+++	0	+++	Skin smears for lepra bacilli; biopsy of skin and nerve
Primary amyloidosis[16] (esp familial)	+	++	0	+	++	+	+	++	0	++	Biopsy of involved sites
Hypertrophic[17] interstitial neuritis (Dejerine-Sottas)	++	++	+	0	++	+	0	++	+	+++	Biopsy of nerve
Tabes dorsalis	0	0	+	++	+++	+++	++	+	++	0	STS of serum and spinal fluid. Spinal fluid analysis

* Scale of incidence, in the order of increasing frequency: 0, rare, +, ++, +++.

onset follows that of the peripheral neuropathy. The deafness is usually bilateral, progressive, and unassociated with tinnitus. Deafness is not a specific symptom of this disease because it may occur in other familial or hereditary neuritidies, such as hypertrophic interstitial polyneuritis (Dejerine-Sottas), Charcot-Marie-Tooth peroneal muscular atrophy, and familial amyloidosis, as well as in the acquired sensory neuropathies of hypothyroidism and malnutrition.[11]

Reflexes.—The tendon reflexes are usually absent in the lower extremities and may be depressed later in the upper extremities. The abdominal reflexes are preserved. The pupils are of equal size, accommodate, and react to light. The cutaneous sensory axon reflex is usually disturbed in the involved areas and this can be demonstrated by the histamine skin test. The autonomic axon reflex is intact, and the patients sweat normally.

Miscellaneous Features.—The hereditary sensory radicular neuropathy is transmitted by a dominant gene with reduced penetrance and variable expressivity. Sensory radicular neuropathy has no striking sex incidence and usually affects people in their third or fourth decades. There is characteristically an absence of muscle weakness, fasciculation, and atrophy. Ataxia has been reported, presumably due to a deficit in proprioception. Urinary and rectal sphincter incontinence is rare, and, if it occurs, appears late in the disease. The disease tends to be progressive; however, Ogden et al[12] have described a nonprogressive type which is sporadic, has its onset at birth, and has more scattered and asymmetrical clinical features than the progressive type.

A chart of the differential diagnosis of ulcerative mutilatory acropathy is presented in the Table.

In the current dermatologic literature, Tappeiner [13] reports a 36-year-old woman, who had plantar ulcers and osteolysis of her toes and hands, and called attention to two of her sisters who had a similar disease. On physical examination of the patient, he did not observe any sensory changes or other clinical evidence of syringomyelia. Tappeiner reported the patient as a case of familial acro-osteolysis with trophic ulcers. His case resembled clinically those of hereditary sensory radicular neuropathy. The lack of demonstrable sensory changes may be due to the patient's inability to interpret the results of the tests for the evaluation of sensation. Gobell and Runge [14] described a family which in two generations had nine members with perforating ulcers of the feet. Two of these members had a doubtful loss of sensation and a retention of the deep tendon reflexes.

In this case report, the patient has a slowly progressive ulcerative acropathy of feet. There was a family history of this disease. Although the patient has a fatty liver and a history of alcoholism, the clinical history and picture are not consistent with that of the neuropathy of chronic alcoholism. The patient did not have lightning pains or deafness. The sensory dissociation in this case was in the dermatomes innervated by sensory nerve roots of I_5 and S_1. The histamine skin test revealed an impaired axon reflex in the involved areas. Psychic stress resulted in hyperhidrosis in the hyperpigmented anesthetic areas. Biopsy of neural tissue for laboratory confirmation of the clinical diagnosis was deferred because of the potential aggravation of a chronic progressive irreversible condition.

Lt Cdr Neil H. Raskin, MC, USNR, saw the reported patient in consultation and made the diagnosis of hereditary sensory radicular neuropathy (Denny-Brown).

Generic and Trade Names of Drug

Hexachlorophene—*Gamophen, pHisoHex, Surgicen, Surofene.*

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