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Hereditary Sensory Radicular Neuropathy (HSN)*

(Clinical, Biochemical, Neurophysiological, and Laboratory Investigation)

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A hereditary disease which was later described as acropathic ulcero mutilante, hereditary perforating ulcer of the foot has been known since the middle of the last century.[1] The clinical findings were erroneously related to lumbo-sacral syringomyelia,[2] myelodysplasia[3] or status dysraphicus[4] until descrition of histologic appearance by Denny-Brown[5] and later by Jedrzejowska and Milczarek.[6]

This group of disease were divided into four types according to inheritance and clinical findings.[7]

Type I: Dominantly inherited HSN commonly called hereditary sensory radicular neuropathy.[5]

Type II: Recessively inherited HSN. The term congenital sensory neuropathy applies to this form of HSN.[8-10]

Type III: Recessively inherited, referred to as familial dysautonomia.[11]

Type IV: Recessively inherited and known as the congenital insensitivity to pain with defect in temperature sensation and absence of sweating.[12]

The purpose of this paper is to present a rather rare case of recessive from of HSN with clinical, biochemical, neuropathological, and laboratory investigations.

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Case Report

D. A., a 14 year old boy, was admitted to the Hacettepe Children's Hospital with chief complaints of disability to walk due to ulcers as well as deformity of the feet, partial loss of sensation and spontaneous amputation of the tips of the fingers and toes. Family history revealed that the parents were first cousins and healthy. His older brother who had had similar complaints following severe burns of both hands and feet had died at the age of 20 from an unknown disease. His 20 year old sister and 16 year old brother were reported healthy. The fifth pregnancy of the mother had ended in stillbirth (Figure 1).

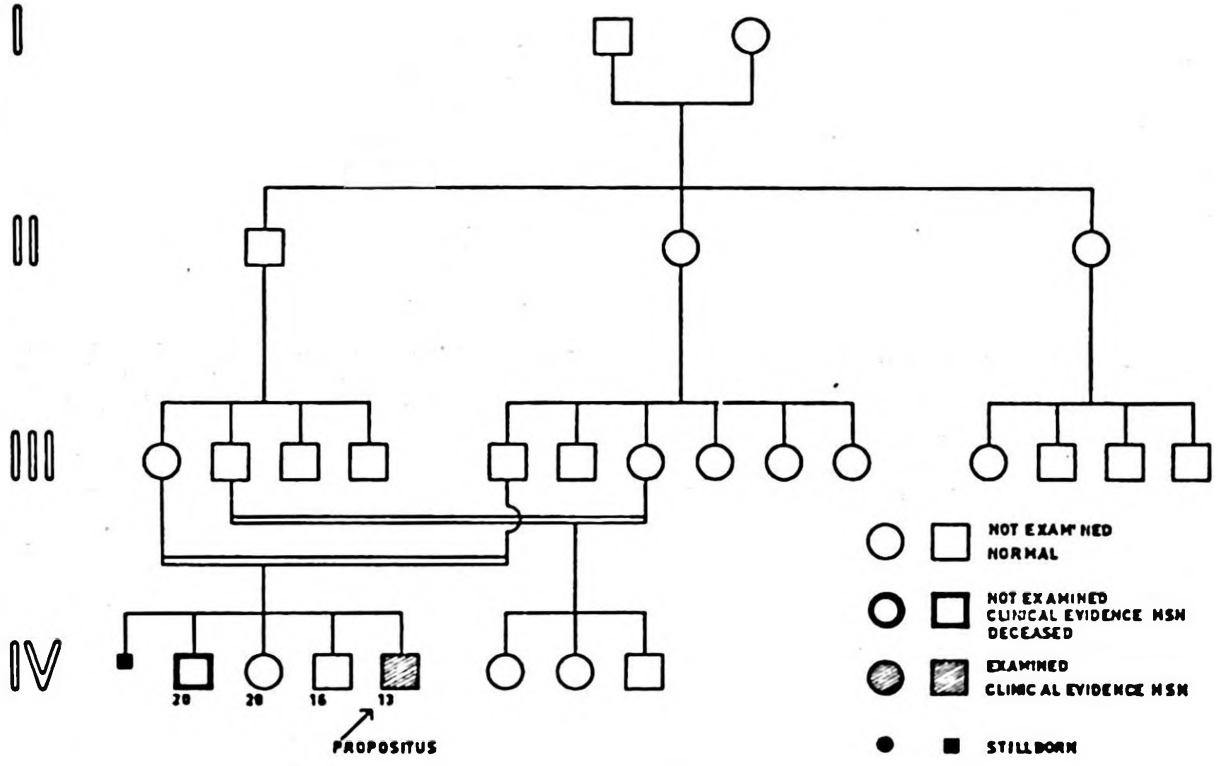

Figure 1
Family tree of the patient with HSN type II

Past history revealed that he was the fourth child, born after normal pregnancy and delivery. His motor and mental development were considered normal. The first complaint was numbness of the right big toe which had started at the age of ten. He began to have difficulties in walking following the swelling and redness of the toe in an interval at one month. Drainage of the yellowish purulent material was described as the confronting event. Incurvation of the toes developed following shortening of the distal portion of the extremities. There was no sensory alteration or weakness of the lower extremities.

The patient had also started to have sensory loss in the hands and delay in the healing of the ulcers and spontaneous amputation of the tips of the fingers. He described some pain and numbness with minimal

weakness of the extremities. No mental deterioration nor urinary incontinance were described. His school performance was good. He had lost 5 kg. during the past year. (Figures 2 and 3).

Physical examination revealed that the last phalanges of both index fingers were missing and that right knee and left ankle were swollen. There was a 5x4 cm ulceration of the left planter region, acute swelling and hyperemia were observed on the left tibia. Liver was 2 cm below the right costal margin. All further results of the physical examination were within normal limits.

Neurological examination revealed that he was alert and intelligent. Cranial nerves were intact, the eye ground examination was usual. No weakness or distortion of the upper extremities was observed. The lower extremities could not be examined adequately due to ulcers and DTR 1 + and abdominal reflexes were obtainable. Sensory examination showed slight impairment in pain sensation, light touch and thermal perception up to the elbow and the mid tigh. Vibration was diminished at the finger tips.

Laboratory findings were as follows: Hb: 10.5-13.35 g %, WBC: 5400-9800/mm^3, sedimentation rate 145/h, total protein: 5.2-5.6 g %, albumin: 2.8-3.4 g %, uric acid 2.5 mg %, creatinine 0.6 mg %, BUN: 15 mg %. CSF protein was 30 mg %, sugar 72 mg %, blood sugar 62 mg % Ig electrophoresis was normal, lipid electrophoresis: 9.6 %, pre 40.3 %, 49 %. LE, FANA, VDRL and Coombs test were all negative. Urinalysis: Density 1009-1026, protein + (325 mg % in 1200 cc).

X-rays of the hands showed severe acroosteolysis with complete distruction of several of the distal phalanges, evidence of loss of soft tissue at the tips of the fingers and fragmentation of the left patella. X-rays of the feet showed severe degenerative changes in both ankle joints and all the tarsal joints. The disorganization of the joint surfaces with cystic and in places sclerotic changes appears to be typical of neuropathic arthropathy. Bilateral equinus deformity was present and there was subperiostal new bone formation in distal fibula and several of the metatarsal bones adjacent to areas of soft tissue loss. Acroosteolysis was also present in several of the toes.

Audiogram was normal.

Sural nerve biopsy. There was marked loss of myeline and degenerative changes, only few myelinated fibers were observed. The appearance of the arterioles was normal. At muscle biopsy, scattered area of neuropathic atrophy with increased amount of interstitial lipid were reported.

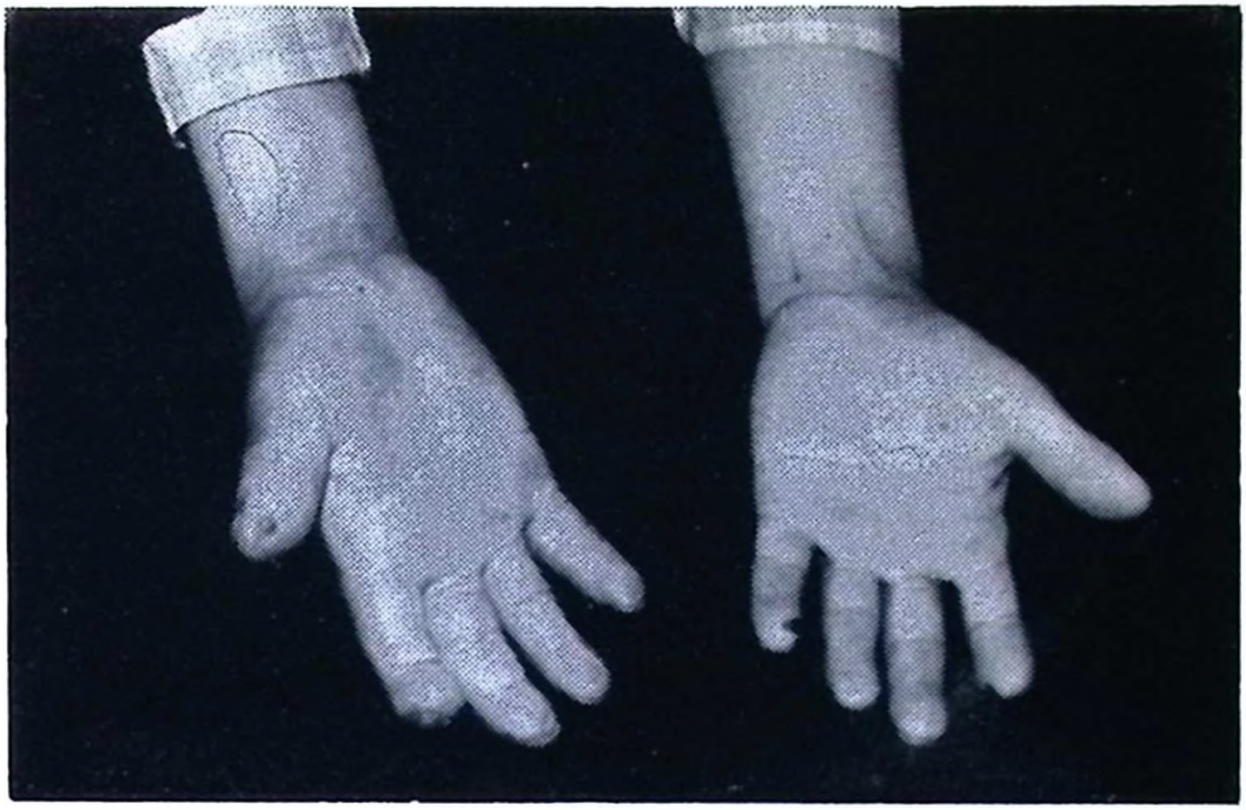

Figure 2
Deformity of the hands due to misuse of the phalanges

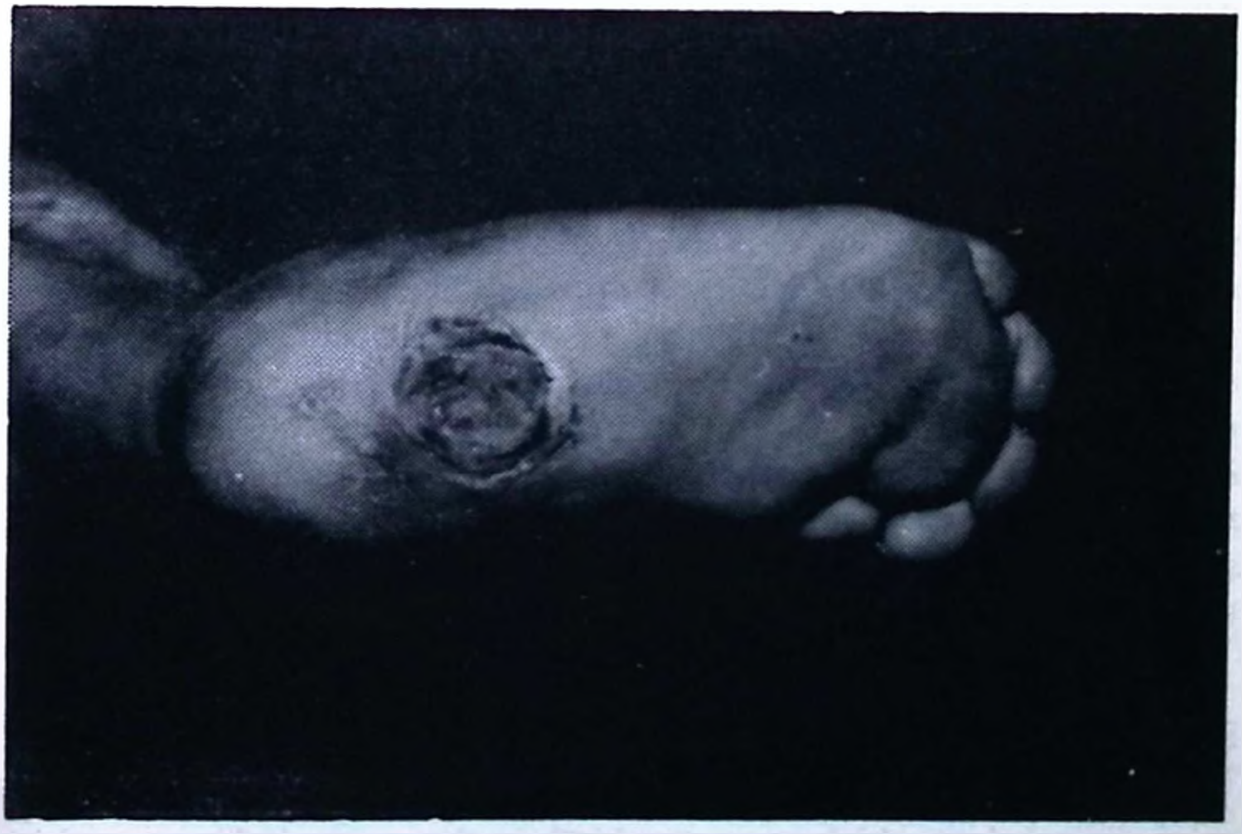

Figure 3
Ulceration and deformity of the left foot

Total bone survey with $Tc^{99\text{-}m}$ pyrophosphate demonstrated increased activity at the distal portion of the right femur and right knee, and increased activity at the left ankle. These findings were interpreted as increased osteoblastic activity of those areas.

Bone biopsy from clinically osteomyelitic areas was normal.

Electromyographic studies were carried out on the M. Opponens Pollicis, M. Tibialis Anterior and M. Extensor Digitorum Brevis of the right side. The M. Opponens Pollicis exhibited normal insertion potential. there were no signs of denervation such as fibrillations, fasciculations or positive sharp waves. During voluntary contraction, there were polyphasic motor unit action potentials from time to time.

On the Anterior Tibial and Extensor Digitorum Brevis muscles normal insertion potential was found with + 1 fibrillation potential and + 1 positive sharp wave. Voluntary contraction did not bring out any signs of motor unit action potential.

The motor nerve conduction velocity of the right median nerve was found to be 30.9 m/sec. Distal latency was 6.1 m/sec, proximal latency was 11.6 m/sec.

The same nerve did not exhibit any sign of sensorial conduction. These findings suggest a form of neuropathy which mostly affects the sensory branches.

Discussion

Congenital sensory neuropathy or HSN type II is an autosomal recessive disease, usually characterized by an onset in infancy or early childhood with distincly clinical features.[13] The neurologic deficiency may not be apparent until the end of the first decade, The symptoms are impaired pain sensation resulting in repeated injuries, ulceration, painless bone fractures, mutilating athropathies, and acroosteolysis. It is evident from the descriptions of various authors that sensory abnormalities in this form of the disease may vary in their character and extensiveness. Involvement of touch-pressure-sensation more than pain and temperature is common.

Recessively inherited HSN is distinguished from congenital nonprogressive sensory neuropathy and progressive sensory neuropathy.[9]

The clinical and pathological features of both diseases, in the presence of clinical signs which appear at birth in the congenital type, and in the early years of the life in the progressive type. Some of the authors

claim that only one type of the disease exists, namely congenital sensory neuropathy which is non-progressive.[8] It is difficult to share this opinion because of the occurrence of the recessive cases with definitely a progressive course of the disease. According to Ohta et al (1973) there is also one type of recessively transmitted HSN, but these authors assume that its course may either be static or slowly progressive.[7]

The histological findings in the sural nerve biopsy suggested progressive nature of the pathological process in one of the recently reported cases.[6]

In conclusion probably two different types exist in the autosomal recessive from of HSN II, 1. Congenital non-progressive neuropathy with onset in the early childhood, and 2. Progressive sensory neuropathy with its onset in childhood. In our patient the clinical course was suggestive of the progressive type of the disease. The impairment of the cutaneous sensation was more extensive than could be shown by conventional neurological methods of examination, this was shown by the poor healing of the ulcers in skin areas where no sensory abnormalities were detected.

Summary

A case of autosomal recessive hereditary sensory neuropathy (HSN Type II), with an onset at the end of the first decade of life is presented. Family history revealed that the parents were first cousins and the patient's brother who had had similar clinical findings had died at the age of 20 years from an unknown disease. The symptoms of which had been impaired pain sensation resulting in repeated injuries, ulceration, painless bone fractures, mutilating arthropathies, and acroosteolysis. On the basis of the clinical course and the laboratory investigation of the present case it can be said that in autosomal recessive hereditary sensory neuropathy type II, progressive as well as non-progressive types exist.

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