Hereditary Spastic Paraplegia in Association with Sensory Neuropathy in a Saudi Family

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A case report of three siblings from a Saudi Arabian family with spastic paraplegia and painless ulcerations. The cases were characterized by a degenerative disorder with a slowly progressive spasticity of the lower limbs. The cases were classified into two forms: a pure form and a complicated form. The pure form showed pyramidal tract dysfunctions in the lower limbs, with findings such as mental retardation, dysarthria, epilepsy, atrophy, retinal degeneration, and pigmentary abnormalities. Rarely, an associated sensory neuropathy was reported.

We describe aSaudi family with autosomal recessive spastic paraplegia and sensory neuropathy occurring in early childhood.

Case Reports

Case 1

M.H. was an 8-year-old Saudi girl, product of a full-term pregnancy and spontaneous vaginal delivery who had been developing normally until 2 years previously, when she developed an abnormal spastic gait. About 1 year previously, a painless ulcer appeared at the base of the big toe of her left foot. The ulcer started as a small nodule which then ulcerated and persisted in spite of proper treatment. There were no clear precipitating factors like trauma or a febrile illness. Her spastic gait also persisted, but did not get worse. She had no history of incontinence for urine or stool, hearing difficulty or visual disturbance and her school performance was satisfactory. Her parents were distantly related and her five siblings suffered from spastic gait. The father died at an advanced age because of a chest problem. The mother was clinically well but deaf, and had two daughters from a previous husband, one of whom was also deaf.

On examination, the patient was found to be intelligent and in no obvious distress. Her temperature was 37.5°C, pulse 98/min and regular, respiratory rate 22/min, and blood pressure 105/62 mmHg. Her height was 119 cm at 10th percentile and her weight was 22.1 kg just above the 10th centile. She had no dysmorphic features and/or neurocutaneous lesions. Neurological examination revealed a slight stiffness, but she was able to walk without support. Her muscle tone was normal in the upper limbs but increased in the lower limbs, and the power was normal in all limbs. Deep tendon reflexes were normal in the upper limbs but markedly exaggerated in the lower limbs, with sustained ankle clonus bilaterally. Plantar reflexes were extensor, and the abdominal reflexes were present. Examination of
disease research laboratory) test. Urine for
neurometabolic screen was negative. Cerebrospinal fluid
(CSF) analysis was also within normal. Biopsy of skin
tissue surrounding the ulcer revealed hyperkeratotic
tissue including parakeratosis and thick layer of
anucleated orthokeratin, consistent with a cutaneous
horn. Culture of a swab from the foot ulcer yielded
heavy growth of mixed organisms namely: Proteus
mirabilis, Pseudomonas aerogenosa, and Staphylococcus
aureus. A Mantoux test with 10 unit PPD was negative.
Serum immunoglobulins assay showed mild IgG
elevation but normal IgA and IgM levels. Nerve
conduction study revealed normal motor conduction
velocity but delayed sural nerve conduction velocity with
reduced sensory action potential amplitude. Auditory
evoked potentials were normal. A myelogram as well
as CT scans of the spinal cord and brain revealed normal
findings. A magnetic resonance imaging (MRI) scan of
thoracic and lumbar spines revealed no abnormalities
of the spinal cord or the surrounding structures.

Case 2

A.H. was a brother of the patient in Case 1 who was
19 years old, with a history of abnormally stiff gait and
recurrent feet ulcers since the age of 7 years. The ulcers
responded poorly to treatment, and led to a partial
amputation of the right big toe. Later, this affected the
sole of his left foot causing progressive deformity.
Examination of his lower limbs showed a huge deep
ulcer in the middle of the sole of his left foot with an
amputated right big toe and deformity of other toes (Fig.
2). Neurologically he had spastic paraplegia with
moderate weakness and exaggerated deep tendon
reflexes in both lower extremities. All sensory modalities
were diminished in both lower limbs and the feet were

Figure 1. A deep painless ulcer at the base of the left big toe
in Case 1.

touch, pinprick, temperature and vibration using
standard methods revealed mild impairment in the distal
part of the lower extremities especially in the feet.
Pinprick sensation was extensively lost around the ulcer
edge (Fig. 1). Her coordination was intact.
Laboratory investigations revealed a normal
haemogram, renal profile, liver function tests, bone
profile, brucella titre and negative VDRL (venereal

Figure 2a. Deep painless ulcers in sole of left foot with deformity of toes and feet (Case 2).
severely involved. Plantar responses were dilaterally extensor. His baseline investigations including haemogram, serum electrolytes, urea, creatinine, blood sugar and liver function tests were normal. The X-ray of his feet was as shown in Fig. 3. A swab from his left foot ulcer grew a mixture of Proteus mirabilis, Morganella morganii and Staphylococcus aureus. A nerve conduction study revealed mild slowing in motor conduction velocity of the common peroneal nerve (39.2 m/s in the left) but severe reduction of amplitude of compound muscle action potential (0.34 mV). Sural nerve action potential was absent on both sides.

**Case 3**

B.H. was another brother of the patient in Case 1 who was 16 years old with an abnormal gait of long standing. Neurologically, he had spasticity and hyperreflexia in the lower limbs but no ulcers in the feet. His plantar responses were extensor and all sensory modalities were mildly diminished bilaterally in the lower extremities.

**Discussion**

The literature of HSP has been extensively reviewed by various authors. The essential clinical feature of HSP is a slowly progressive spastic weakness of the lower extremities without demonstrable cause.

The age of onset varies from early childhood to old age. Symptoms of progressive dysfunction of the pyramidal tracts begin in the lower limbs, with difficulty in walking or an abnormal gait. The lower limbs are spastic, with exaggerated muscle stretch reflexes and extensor plantar responses; weakness of the lower limbs is surprisingly uncommon and, if present, tends to be mild. Subsequently the upper limbs, and occasionally the bulbar muscles, become involved, the latter resulting in spastic dysarthria and dysphagia. Harding distinguished a 'pure' form of hereditary spastic paraplegia from 'complicated' forms by the absence of associated neurological or non-neurological features. Dementia, seizures, ataxia, optic atrophy, cutaneous lesions and peripheral neuropathy have been described in complicated HSP. The mode of inheritance of HSP is usually autosomal dominant in the pure variety, while autosomal recessive inheritance is seen in most of the complicated forms. Sex-linked recessive inheritance is extremely rare, but has been reported in both the pure and complicated forms.

Clinically, our patients conformed to the complicated type of HSP. The early onset of symptoms in our patients was consistent with this
form, in contrast with the ‘pure’ form of HSP in which onset is usually during adulthood and early middle age. In our patients, HSP was associated with a sensory neuropathy which led to the ulcer formation in two of them. This entity was also studied and classified. Thomas has classified the hereditary sensory neuropathies into five main groups. Our family was considered as a subgroup within the second congenital sensory neuropathy. The onset of such cases is in infancy or early childhood, and the inheritance is commonly autosomal recessive. Association between this type and HSP is only rarely described. Cavanagh et al. described five such cases from three families. All had their symptom in early childhood starting with gait abnormalities and later on manifesting sensory disturbances affecting mainly the lower limbs with development of painless ulcers like our cases. The mode of inheritance in those cases was thought to be probably autosomal recessive. Genetically, our patients also conformed to the autosomal recessive form of inheritance. Although the parents were not close relatives, they were from the same tribe and likely to have some autosomal recessive genes in common. Deafness was also reported in association with HSP and hereditary sensory neuropathy. However, none of our patients had deafness; evidenced in one of them by normal auditory evoked potentials; its occurrence in the mother and another half-sister may have been a manifestation of an associated genetic abnormality. We postulate therefore that our patients represented a unique presentation of HSP. This accords with the well known clinical and genetic heterogeneity of HSP.

References