NEUROARTHROPATHY IN CHARCOT-MARIE-TOOTH DISEASE

BY

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The characteristic feature of the syndrome described by Charcot, Marie, and Tooth in 1886 is a symmetrical wasting, weakness, and sometimes fasciculation of the peripheral muscles which slowly ascends the limbs but rarely progresses above the mid-thigh or forearm (Charcot and Marie, 1886; Tooth, 1886). Tendon reflexes are depressed. An associated congenital pes cavus is common. Sensory loss occurs but is not always demonstrable. Perception of vibration is the sense most commonly impaired (Wilson, 1940), but severe or complete loss of pain perception, resulting in trophic ulceration, is well recognized (Charcot and Marie, 1886; Halliday and Whiting, 1909; England and Denny-Brown, 1952). The onset is usually during the first decade, but has occurred up to the fifth. About two-thirds of the cases are familial, inheritance being usually dominant (Christie, 1960; Herringham, 1888; Lhermitte and Mouzon, 1937; Dawidenkow, 1938). Studies of the morbid anatomy suggest that the primary lesion is in the nerve roots, and nerve conduction velocity is usually markedly slowed, confirmatory evidence of a peripheral demyelination (Dyck, Lambert, and Mulder, 1963; Gilliatt, 1966).

Neuroarthropathy has previously been described in only two patients with Charcot-Marie-Tooth disease. In the first (Alajouanine and Boudin, 1942), the metatarsophalangeal joints and right elbow were affected; in the second (Borsari and Jequier, 1966) the ankles and wrists. Apart from minor impairment of vibration sense in the second case, sensation was said to be normal.

We present five further cases of Charcot-Marie-Tooth disease who had joint disorders of varying severity.

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Case Histories

Case 1, a man aged 58 (reported in detail by Bruckner, 1968a) noticed weakness of the legs and then of the arms starting at the age of 9 and numbness of the legs and hands a few years later; he developed painless ankle swelling at the age of 40. There was no family history of Charcot-Marie-Tooth disease.

Examination.—There was wasting and weakness of the lower limbs and of the hands and forearms. Muscle tone and reflexes were depressed. All modalities of sensation were markedly impaired in all four limbs. Pes cavus was present and there was a trophic ulcer on the left sole. Bony swelling of both ankles limited movement. Movement was pain-free and was accompanied by coarse crepitus.

High ulnar nerve motor conduction velocity was grossly reduced (11 m/sec.). Sensory action potentials were absent in the median and lateral popliteal nerves when measured with the techniques of Gilliatt and Sears (1958), and Gilliatt, Goodman, and Willison (1961).

Case 2, a man aged 58, had suffered from weakness of all four limbs since infancy, and from numbness since early childhood. He would injure himself without knowing it. When he was 11 years old he began to get trophic ulcers on his feet which often became infected. At the age of 23, his feet and toes became deformed and began to "shrink", and 20 years later he developed painless swelling of the fingers and wrists of both hands. When he was 56, he had a right through-knee amputation for the ulceration and sepsis, and since then there has been no further ulceration on the other leg.

There was no relevant family history.

Examination.—There was oedema of the left leg which masked the wasting, weakness of the left foot and leg, and wasting and weakness of the intrinsic muscles of both hands. Muscle tone and tendon reflexes were diminished, all modalities of sensation were impaired, and the left ankle was deformed with limitation of movement and crepitus. There was resorption of the

toes. The wrists, metacarpophalangeal and proximal interphalangeal joints were swollen. All affected joints were pain-free.

Case 3, a woman aged 60, had had weakness of the legs since the age of 7 years. The right ankle had been unstable since she was 51, had been arthrodesed 5 years later. Eight other members of her family had Charcot-Marie-Tooth disease.

Examination.—There was muscle wasting and weakness up to the knees. The upper limbs were not affected. Muscle tone and reflexes were depressed. All modalities of sensation were moderately impaired, except for deep pain sensation which was unaffected. There was varus deformity of the left ankle, with reduced but pain-free movement and crepitus. Motor nerve conduction velocity in the right ulnar nerve was normal (57.2 m/sec.). No motor units were detected in the right and left extensor digitorum brevis muscles on stimulating the lateral popliteal nerves. No sensory action potential was recorded from the right lateral popliteal nerve. Median and ulnar nerve sensory action potentials were diminished (7 μ V and 3 μ V respectively).

Case 4, a woman aged 51, had had weakness of the hands and feet since early childhood and some numbness

of the left foot since the age of 11. The left ankle was arthrodesed when she was 49 for inversion deformity and painless instability. Six of her relatives had Charcot-Marie-Tooth disease.

Examination.—Muscle wasting and weakness extended to mid-thigh and affected the hands. Muscle tone and reflexes were depressed, and all modalities of sensation (including deep pain) were markedly impaired, though this was less prominent in the right lower limb. The left ankle was arthrodesed and stable, and the other joints were unaffected. There was minor pes cavus deformity. The left ulnar nerve motor conduction velocity was normal (57 m/sec.). No motor units were detected in the extensor digitorum brevis muscle on stimulating the lateral popliteal nerve. No sensory action potential was recorded from the lateral popliteal nerve.

Case 5, a woman aged 68, had had weakness of the legs and hands since the age of 9 years, and numbness of the feet had come on a few years later. Her ankles had been giving way for the last 12 years. Two relatives had Charcot-Marie-Tooth disease.

Examination.—There was wasting to above the knees and wasting and weakness of the intrinsic muscles of the

Fig. 1.—Case 2. Absorption of bone from phalanges and distal halves of metatarsals, most marked around joints, causing "pencil-sharpened" effect. Many of the joints are subluxed or dislocated and subsequent over-riding of the bones, together with absorption, has caused shortening of the feet. These appearances are typical of chronic low-grade soft-tissue inflammation of neurotrophic origin. Soft tissue swelling is also evident.

hands. Muscle tone and tendon reflexes were depressed. Deep pain and position sense were moderately impaired, and vibration sense absent, but other modalities of sensation were normal. There was varus deformity, and increased mobility and crepitus of both ankles, but no pain.

Radiological Changes

The two patients with neurotrophic lesions and secondary infection showed the usually associated radiographic changes. In Case 2, with chronic infection of the soft tissues of the feet, there was marked resorption of the phalanges and adjacent parts of the metatarsals (Fig. 1), whereas in Case 1, with more acute ulceration under the fifth metatarsal head, there was periosteal reaction on the neck and shaft of the metatarsal. Later, the articular surfaces of the metatarsophalangeal joint were destroyed and subluxation occurred (Fig. 2).

Of the three patients with marked or total sensory loss, Cases 1 and 4 had typical Charcot ankles (Fig. 3, overleaf) and Case 2 is discussed above. The joints were subluxed, with small marginal osteophytes, and varying amounts of adjacent periosteal

bone reaction. This was partially fused causing external thickening of the cortex. Loose bodies were present in two joints and subarticular sclerosis in one.

Case 3, with moderate pain and temperature loss, and Case 5, with moderate loss of deep pain sensation, suffered more from weakness than from sensory deficit, and both had marked osteoporosis of the ankles and feet. There was some opening of the anterior margins of the ankle joints, and ossification near ligamentous insertions due to abnormal strains. The right ankle in Case 3 (Fig. 4, overleaf) was subluxed with subarticular sclerosis and minor marginal osteophyte formation.

Other Investigations

Blood and cerebrospinal fluid tests for syphilis were negative.

Oral glucose tolerance tests, serum vitamin B₁₂, and blood urea levels were normal, and there was no albuminuria in any patient.

Fig. 2.—Case 1. The head of the 5th metatarsal and the lateral border of adjacent articular surface of the proximal phalanx have been destroyed, leaving a few small loose fragments. The 5th metatarsal is sclerotic and there is periosteal bone on its medial surface. These appearances are typical of arthritis secondary to trophic ulceration.

Fig. 3.—Case 1. Typical Charcot ankle. There is lateral subluxation and tilting of the talus with sclerosis of adjacent bone. Loose fragments fractured from the joint margins and periosteal bone formed on the tibia and fibula account for the swelling at ankle level.

Fig. 4.—Case 3. Right Charcot ankle. There is anterior and lateral subluxation of the talus, periosteal bone formation on the tibia near the insertion of the medial ligament, and minor anterior osteophyte formation.

Discussion

The only serious differential diagnosis of the neurological syndrome is the familial interstitial hypertrophic polyneuropathy of Dejerine and Sottas (1893), and we acknowledge that this condition can be completely excluded only by nerve biopsy. This was not considered justifiable in our cases. However, there was no clinical evidence of cranial nerve involvement or thickened peripheral nerves in either these patients or their affected relatives, making the diagnosis of hypertrophic polyneuropathy very unlikely. Neuropathic joints have been described in this condition (Russell and Garland, 1930).

A detailed physical examination excluded most other causes of neuropathic joints (Bruckner, 1968a). Negative serological and cerebrospinal fluid tests for syphilis in the absence of previous treatment ruled out tabes: oral glucose tolerance tests excluded diabetes mellitus; and normal serum vitamin B₁₂ levels ruled out pernicious anaemia myelopathy (Halonen and Jarvinen, 1948).

The diagnosis of neuropathic changes is usually simple on clinical and radiological grounds. Pain and discomfort, which are usually disproportionately mild in relation to the degree of joint involvement, or tissue necrosis or superficial inflammatory changes suggest this aetiology, especially if the patient has appropriate neurological changes.

Nonspecific features which occur early are synovial effusion, joint subluxation or instability, and small marginal osteophytes (Storey, 1964). Additional lesions which occur later have greater diagnostic weight even when found alone. These include small periarticular fractures, intra- and pericapsular debris (Horwitz, 1948), loose bodies, and periosteal new bone formation, often of the chronic type partially fused with the cortex. Florid cases show total joint destruction and dislocation, usually with sclerosis, occasionally atrophy, of the bone ends, often with residual loose fragments. Chronic soft tissue inflammation may cause progressive absorption of metatarsals and phalanges leading eventually to "pencil sharpening" of the residual bone ends and shrinkage of the soft tissues as in the neuroarthropathy of leprosy (Paterson, 1955).

Difficulty in diagnosis occurs only if no sensory abnormality can be found in the presence of a suspected neuropathic lesion. Sensory action potentials should then be recorded; if these are reduced, they add confirmatory evidence. It is important to establish the diagnosis, because rapid destruction of the injured joint may occur unless measures are taken to protect it.

In the Table our five cases were added to the two previously described, and these seven are compared with fifteen cases of Charcot-Marie-Tooth disease

TABLE
COMPARISON OF 7 CASES OF CHARCOT-MARIE-TOOTH DISEASE WITH ARTHROPATHY
WITH 15 CASES WITHOUT ARTHROPATHY

Clinical Particulars		Cases of Charcot-Marie-Tooth Disease	
		With Joint Involvement	Without Joint Involvement
No. of Cases		7	15
Male: Female Ratio		2: 5	2: 3
Family History		3 (43 per cent.)	6 (40 per cent.)
Mean Age (yrs)	At Onset Now	11 (range 2 to 31) 61.4 (range 51 to 70)	20 (range 2 to 4) 40.7 (range 4 to 65)
Mean Duration of Symptoms (yrs)		51.4 (range 34 to 49)	20.7 (range 1 to 60)
Muscle Wasting	Severe Mild	7 0	10 5
Loss of Sensation	Deep pain Position Touch, pain, temperature Vibration	4/5 5/7 4/7 6/7	0 3 5 7
Pes cavus		4	7
Trophic Ulcers		3	0
Soft Tissue Infection		1	0
History of Joint Trauma		7	15
Lax Ligaments		7	14
Duration from Onset to Arthropathy (yrs)		23 (range 10-31)	
Joints Affected	Ankles Toes Mid-tarsal Wrists Fingers Elbows	5 Hypertrophic 3 (1H, 1D + H, 1D) 2 Destructive 1 Hypertrophic 1 Hypertrophic 1 Hypertrophic	

in which the joints were clinically and radiologically normal (Bruckner, 1968 b). Neuropathic changes were most frequent in women whose peroneal muscular atrophy had been present for a long time and was severe. Deep pain and position sense were impaired and trophic ulceration was frequently present in those with neuroarthropathy and absent in the other group. The arthropathy affects the ankle and foot; occasionally, the peripheral joints of the upper limb are afflicted.

Eloesser (1917), working with cats, demonstrated that neuropathic changes could be induced in joints deprived of their sensory innervation and subjected to trauma. Soto-Hall and Haldeman (1940) suggested that, in addition to these two factors, instability caused by loss of tone in the muscles and stretching of the ligaments supporting the joints were important.

Loss of pain and position sense was shown to be a prime factor in the development of the neuroarthropathy in our cases. Muscle weakness, ligamentous laxity, pes cavus deformity, and multiple joint traumata occurred just as frequently in the group without joint involvement confirming again the primary significance of diminution of pain sensation.

Soft tissue infection was certainly a major factor in Case 2 and to a lesser extent in Case 1.

It is unfortunate that more detailed reports on the examination of sensation were not included in the two French cases, and that sensory action potentials were not recorded, especially in the patient with apparently normal sensation. There is no

doubt that our present clinical tests of sensation in deep structures are very crude and that any abnormality must be considerable before it is recognizable. It is probable that lesser degrees of sensory loss may still allow the development of a Charcot joint, and it would be most interesting to know whether electrical tests are always abnormal at this stage.

Summary

- (1) Five cases of neuropathic joints in Charcot-Marie-Tooth disease are described.
- (2) Impairment of pain and position sense was a prime factor in the evolution of the neuropathic joints in our cases, although this was not recorded in two French cases described previously.
- (3) Local infection was important in two cases.
- (4) Muscle weakness, ligamentous laxity, and minor trauma play a subsidiary role to sensory impairment in the development of the neuroarthropathy.

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La névropathie dans la maladie de Charcot-Marie-Tooth

RÉSUMÉ

(1) Cinq cas d'articulations névropathiques dans la maladie de Charcot-Marie-Tooth sont décrits.

(2) La diminution de la douleur et du sens de la position était un facteur principal dans l'évolution des articulations névropathiques de nos cas, malgré que ces deux signes n'aient pas été décrits dans deux cas français rapportés précédemment.

(3) L'infection locale était importante dans deux cas.

(4) La faiblesse musculaire, la laxité ligamenteuse et le traumatisme léger jouent un rôle subsidiaire dans l'atteinte sensorielle pendant le développement de la névropathie.

Neuropatía en la enfermedad de Charcot-Marie-Tooth

SUMARIO

(1) Se describen cinco casos de articulaciones neuropáticas en la enfermedad de Charcot-Marie-Tooth.

(2) El empeoramiento del sentido de dolor y de posición fue un factor principal en la evolución de las articulaciones neuropáticas en *nuestros* casos, si bien esto no se registró en dos casos franceses descritos previamente.

(3) La infección localizada fue importante en dos casos.

(4) La debilidad muscular, la laxitud ligamentosa y el trauma leve desempeñan un papel secundario en el empeoramiento sensorio del desarrollo de la neuroartropatía.