Baillière's Clinical Rheumatology
Vol. 14, No. 2, pp. 325–343, 2000
doi:10.1053/berh.1999.0068, available online at http://www.idealibrary.com on IDEAL®

8

Musculoskeletal problems of neurogenic origin

Caroline Collange
Assistant of Rheumatology

Marie-Anne Burde
Resident of Rheumatology

Fédération de Rhumatologie, Hôpital Lariboisière, 2 rue Ambroise Paré, 75010 Paris, France

A number of neurological disorders can manifest as isolated pain or as joint, muscle or bone alterations. These manifestations can raise significant diagnostic challenges when they occur early, before the development of neurological and/or radiological abnormalities. This chapter discusses neuropathic osteoarthropathies, neurofibromatosis, Parkinson's disease, multiple sclerosis and the complications of central nervous system lesions.

Key words: neuropathic osteoarthropathies; Parkinson's disease; von Recklinghausen's disease; neurofibromatosis; multiple sclerosis; stroke; arthropathies; osteoporosis; reflex.

A number of neurological disorders can masquerade as rheumatic conditions, leading the patient to seek advice from a rheumatologist, sometimes before seeing another physician. Rheumatologists should have sufficient knowledge of the rheumatic manifestations of neurological disorders to select the most appropriate diagnostic and therapeutic strategy. This chapter describes the distinctive features of these manifestations, their outcomes and their treatment.

NEUROPATHIC OSTEOARTHROPATHY

Neuropathic osteoarthropathy can complicate many diseases in adults and children (Table 1), although it has become infrequent in industrialized countries.[1] The distribution of the joint disease reflects that of the underlying neuropathy. Nevertheless, the pathophysiology of the lesions remains debated, and several theories have been put forward over the years.[2]

Charcot's joint

In 1868, Charcot reported that some patients with central nervous system lesions developed joint destruction.[3] Charcot's joint is now defined as a progressive, destructive arthropathy in an area of sensory loss. The spectrum of causes is vast, including diabetic neuropathy, syringomyelia, developmental defects of the spine and the now uncommonly encountered manifestation of syphilis called tabes dorsalis (Table 2).

1521–6942/00/020325 + 19 $35.00/00

Table 1. Neuropathic osteoarthropathies.

Acquired causes	Congenital causes
Tabes dorsalis (syphilis)	Congenital insensitivity to pain
Diabetes mellitus	Spina bifida, myelomeningocele
Syringomyelia	Thévenard's disease
Head and spinal cord injuries (hemiplegia, paraplegia)	Familial dysautonomia of Riley–Day
Peripheral nerve injuries	
Infections (leprosy, yaws)	
Amyloid neuropathy	
Ulcerative-mutilating acropathy (Thévenard, Bureau–Barrière)	
Spinal cord tumours and compression	
Combined degeneration of the spinal cord, multiple sclerosis	
Alcohol-related neuropathy	

Table 2. Main characteristics of neuropathic osteoarthropathies (Charcot's joint).

	Diabetes mellitus	Tabes dorsalis	Syringomyelia	Developmental spinal defects
Features	Age: 50–65 years Long-standing poorly controlled IDDM	60-year-old males Rare in industrialized countries Advanced disease TPHA and VDRL tests ++	Primary or secondary to an injury	
Painless arthropathies	Foot ++ Ankle +	Lower limb ++ (increased range of flexion and extension) Thoracolumbar spine	Common Upper limb Asymmetrical distribution Severe deformity with cracking sounds	Chronic unilateral arthropathy Pes cavus or pes equinus Scoliosis common
Skin	Perforating plantar ulcers Pseudoinflammatory changes	Smooth thick skin Gummas	Swollen, red and indurated Scars and burn marks	Perforating plantar ulcers Trophic disorders Hair growth along the mid-line of the back
Neurological findings	Ankle reflexes absent Loss of pain and temperature sensation in a stocking distribution	Posterior cord pain Insensitivity to pain Loss of deep sensation Ataxia	Decreased sensation of pain and temperature Suspended asymmetrical distribution Pyramidal signs under the lesion	Nerve root pain Cauda equina syndrome
Radiological findings	Talar bone collapse Bony sclerosis Calcific deposits about the joint	Predominance of productive forms (except at the hip and shoulder)	Hypertrophy with osteosclerosis, loose bodies and calcific deposits about the joints Demineralization MRI: syrinx	Bony spur along the mid-line between T12 and L4 Spina bifida Vertebral lamina thickening CT or MRI to confirm the diagnosis

IDDM = insulin-dependent diabetes mellitus; MRI = magnetic resonance imaging; CT = computed tomography.

The pathogenesis of Charcot's joint remains controversial. The first theory, put forward by French physicians, ascribed the joint destruction to sympathetic system dysfunction. In contrast, the neurotraumatic theory developed by German, British and American physicians suggested that a loss of sensation in the joint results in repeated subclinical trauma, leading to accelerated degenerative disease that ultimately causes complete destruction of the joint. The subchondral bone is, however, affected earlier than the cartilage. The joint capsule and synovial membrane are hypertrophic.[3]

Decreased muscle tone and ligament hyperlaxity may lead to subluxation, and loss of deep sensation may cause joint instability. The excessive joint mobility may promote osteophyte development, cartilage loss and ossification of the ligaments. Mono-, oligo- and polyarticular forms have been reported. The onset is usually insidious. In most cases, there is a striking contrast between the absence of pain and the presence of severe joint destruction, with subluxation, malalignment and instability. However, 15% of patients report pain. An effusion of clear yellow or blood-tinged fluid is found in some cases. Crepitus caused by intra-articular loose bodies can be a feature. There is no local evidence of inflammation, but joint swelling with bruising of the overlying skin is common. Trophic abnormalities are occasionally present (increased sweating, cyanosis, oedema, atrophy of the skin, loss of pigmentation and loss of hair). There is little functional disability until late in the disease. Neurological evaluation shows abnormalities in deep sensation and an absence of the deep tendon reflexes, with preservation of motor function. Nerve root pain resulting from arachnoiditis or spinal stenosis is a feature in some patients.

Diabetes mellitus

Diabetes mellitus has replaced tabes dorsalis as the leading cause of Charcot's joint. The duration of diabetes at development of the joint lesions is usually longer than 15 years. The typical patient is 50–65 years of age and has poorly controlled insulin-dependent diabetes. The foot is the most common site of involvement (the tarsal and metatarsal joints in 60% of cases), followed by the ankle (fewer than 10% of cases). The prevalence of Charcot's joint is about 5%.

Although the onset is usually gradual, it can be acute, particularly after an injury. In insidious forms, the earliest manifestation is often an ulcer on the sole of the foot, sometimes at a distance from the affected joint. Major deformities develop. Oedema and red or purple discolouration of the skin can suggest inflammation. Because there is little pain, patients are often seen late. The ankle reflexes and sometimes the knee reflexes are absent, and there is a loss of sensation to pain and temperature, as well as in some cases to touch and proprioceptive stimuli, in a stocking distribution. X-rays disclose severe bone and joint destruction, with tarsal bone collapse, bony sclerosis and calcific deposits about the joint (Figure 1). This pattern can suggest an infection, a possibility ruled out by the absence of a high signal on magnetic resonance imaging (MRI) T2-weighted sequences.

Atrophic forms are as common as hypertrophic forms. The navicular bone is often selectively involved early in the destructive process. Fractures, fragmentation of bone and tendon ruptures occur in some cases.[4] Ultimately, fusion of the tarsal bones with adjacent sclerosis and calcific deposits produces the cubic foot described by Charcot. The metatarsal and phalangeal lesions result in shortening and broadening of the forefoot. Radiological changes predominate in the heads of the metatarsals and proximal segments of the phalanges. Involvement of the knee or spine has been reported in a handful of cases.

Figure 1. Diabetic neuropathic osteoarthropathy of the foot. Note the sclerotic and lytic involvement mainly affecting the tarsal bones, soft tissue swelling and calcification.

Tabes dorsalis

Tabes dorsalis is a manifestation of neurosyphilis. Ten per cent of patients with tabes dorsalis develop destructive joint lesions associated with the loss of pain and proprioceptive sensation characteristic of the disease. This neuropathic arthropathy occurs late in the course of tabes dorsalis and has become exceedingly rare since the introduction of early penicillin therapy for syphilis.

The typical patient is a middle-aged man presenting with destructive lesions in a knee and/or other lower limb joint (60–75% of cases) (Figure 2), or in the thoracolumbar spine (20% of cases) (Figure 3). Some patients develop incapacitating

Figure 2. Destructive arthropathy of the right hip in a tabetic patient.

Figure 3. L4–L5 spondyloarthropathy in a tabetic patient, featuring a combination of vertebral lysis and sclerosis with osteophytosis and dislocation.

disarticulation of the knee requiring bracing or surgery.[3] A massive, shortened foot with lateral deviation, collapse of the arch of the foot, and joint dislocation are other possible consequences of the disease. Lesions of the great toe are usually hypertrophic. Axial involvement is less common and frequently painful. The X-ray changes are suggestive; the lesions are generally productive, except at the hip and shoulder, where osteolysis is more common. A few cases of severe cortical and trabecular osteoporosis complicated by fracturing have been reported.[5]

The diagnosis is confirmed by the identification of anti-treponemal antibodies in the blood, cerebrospinal fluid and joint fluid.

Syringomyelia

The upper limb is the main target of neuroarthropathy in syringomyelia, with involvement in decreasing order of frequency of the shoulder, elbow, wrist and

fingers. Nearly 30% of syringomyelia patients develop neuroarthropathy. A minority of cases of syringomyelia are secondary to post-traumatic paraplegia.[6] The joint lesions usually occur in the later stages of the disease, although they are occasionally inaugural. Severe deformities can develop, with swelling, redness and induration about the joint. There is little pain initially. Radiographic changes include hypertrophy, osteosclerosis, loose bodies, peri-articular calcifications, and demineralization or lysis of the epiphyses or metaphyses (Figure 4).

At the elbow, hypertrophy with limitation of the range of motion is the most common pattern. Hypertrophy is also the rule at the wrist. In the hand, the lesions are often mild but can result in hypertrophy of the hands and fingers. Spinal involvement may lead to kyphoscoliosis and degenerative facet joint lesions. The lower limit of the syrinx is often level with the concavity of the scoliotic curvature.[7] In the fingers, trophic disorders can occur, producing painless finger pad ulcers and lysis of the distal phalanges. Overall, fractures are less common than in tabes dorsalis.

The presence of neuropathic arthropathy in the upper limb joints should prompt a search for clinical features of syringomyelia and abnormalities of the occipitocervical junction (basilar impression, widening of the upper cervical funnel, and the malformation of nervous structures with herniation of the cerebellar tonsils). MRI should be performed if there is the slightest doubt; this investigation demonstrates not only the syrinx, frequently in a central location, but also any associated bony or neurological malformations.

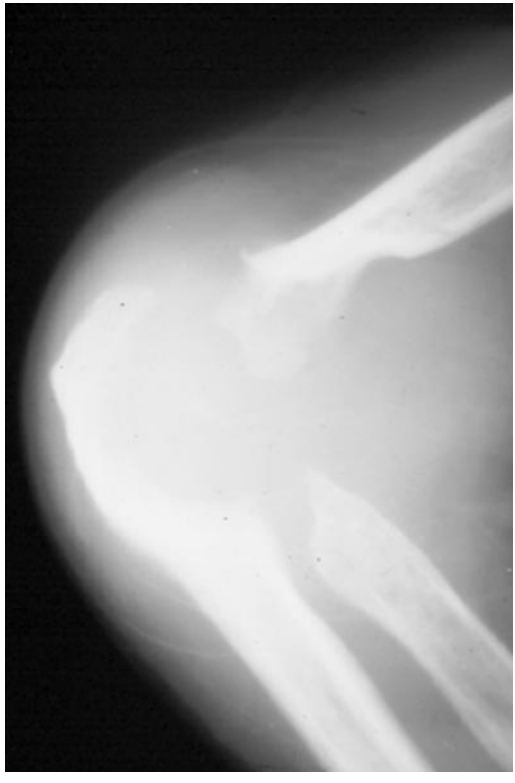

Figure 4. Destructive arthropathy of the elbow in a syringomyelia patient.

Developmental spinal defects

Patients with a unilateral, chronic painless arthropathy in a lower limb should be investigated for a lumbosacral abnormality, which is usually a mid-line closure defect or a diastematomyelia (a spinal cord cleft under the fifth thoracic vertebra associated with a developmental vertebral abnormality). Plantar ulcers, vasomotor and trophic disorders, pes cavus or pes equinus, and distal hypo-aesthesia with an absence of the Achilles or knee reflexes are features in some patients. The affected limb is usually shortened. Congenital hip dysplasia, pes planus and hammer toe deformity are found occasionally. Hair growth along the mid-line in the lumbar area is the rule. A lipoma, nevus, haemangioma or atresic meningocele can suggest the diagnosis. Scoliosis is common and frequently accompanied by nerve root pain or urinary sphincter disorders.

X-rays usually show a bony septum along the mid-line between T12 and L4, spina bifida and abnormally thick vertebral lamina. Computed tomography and MRI findings confirm the diagnosis.[8] Spina bifida occulta at the S1 level may promote the development of disc protrusion.[9]

Ulcerative-mutilating acropathies

Ulcerative-mutilating acropathies (Table 3) were first described by Thévenard in 1942, and then by Bureau and Barrière. Similar clinical pictures were subsequently reported in association with various anatomical and biological abnormalities. Severe osteolysis, sometimes so extensive as to result in amputation, is the hallmark of the disease. Thévenard's disease is the main inherited form of ulcerative-mutilating acropathy. Among the classification schemes for inherited forms, the most recent was developed by Dyck and co-workers in 1975, being based on mode of inheritance, natural history and affected neurone type.[10] Non-inherited forms can be caused by a broad range of conditions; the disorders discussed in the previous section can also result in ulcerative-mutilating acropathy.

Thévenard's disease

Thévenard's disease, or type I hereditary sensory radicular neuropathy, is inherited as a dominant trait. Most patients develop their first symptoms around puberty, although a few later-onset forms have been reported. The earliest manifestations consist of paraesthesia and blistering of the skin resulting from vasomotor disorders. Perforating plantar ulcers and trophic disorders develop at a later stage. Oedema and a purplish discolouration of the skin are seen at the forefoot, where excessive sweating occurs during flares. Early in the disease process, some patients experience shooting pain, particularly during episodes of lymphangitis; otherwise, pain is absent or minimal. The bone lesions often develop as an extension of the skin lesions. The disease progresses by a succession of flare-ups, sometimes separated by prolonged remissions. Shortening of the foot to a cube-like shape is the ultimate outcome. Involvement of the hands is considerably less common and usually manifests only as thickening of the fingers. Neurological findings include loss of pain and temperature sensation in a stocking distribution, followed after a considerable time by a loss of deep sensation. Sphincter function is normal. The ankle and knee reflexes are absent. Wasting of the peroneal muscles is a feature in some cases. X-rays generally show distal demineralization, and then at a later stage microgeodes and osteolysis with tapering of the metatarsals producing the licked candy-stick appearance.

Table 3. Main characteristics of ulcerative-mutilating osteoarthropathies.

	Familial forms	Sporadic forms	Leprosy	Amyloidosis
Features	Thévenard's disease Autosomal dominant Onset in childhood	Negative family history 50-year-old males Local trauma ++ Poor nutrition	Developing countries	Haemopathies Familial amyloid polyneuropathy (individuals of Portuguese descent) Monoclonal gammopathies Rectal or nerve biopsy +
Mutilating arthropathies	Major foot deformities Thickening of the fingers	As in the familial form	Involvement of the hands + + Loss of phalanges	Major foot deformities Knees ++ Ankles ++
Neurological findings	Paraesthesia Loss of pain and temperature sensation in a stocking distribution Absent ankle reflexes	As in the familial form	Nerve trunk enlargement Muscle wasting Loss of pain and temperature sensation	Impotence Urinary retention Postural hypotension (familial form) Motor loss Absent ankle reflexes
Skin	Blisters Perforating plantar ulcers Oedema Purplish discolouration Sweating	As in the familial form	Hypopigmented macules	Perforating plantar ulcers
Radiological findings	Demineralization Microgeodes Osteolysis Licked candy-stick appearance	As in the familial form Reconstitution possible by periosteal reaction	Osteoporosis with fractures Diaphyseal atrophy Distal resorption	As in the familial form or in diabetes (see Table 2)

Sporadic forms

Sporadic forms are far more common than inherited forms. They were first described by Bureau and colleagues in 1957. The clinical and radiological findings are the same as in the inherited forms. Recurrent fractures have been reported.[11] The negative family history, the onset in middle age and the marked male bias provide diagnostic orientation. Important causative factors include local injuries such as frostbite or direct trauma, the infection of minor wounds, poor nutrition (in 60% of cases), alcohol abuse and diabetes mellitus (usually without abnormalities in deep sensation).

In contrast to the inherited forms, the sporadic forms sometimes respond to adequate immobilization by a process of reconstitution involving callus formation and the development of a periosteal reaction along diaphyseal shafts.[10]

Osteoarthropathy resulting from leprosy

Tuberculoid leprosy can be responsible for bone and joint lesions similar to those seen in ulcerative-mutilating acropathy. In the past, these lesions occurred in as many as 30% of leprosy patients, but they are now considerably less common, particularly in industrialized countries.

The long bones and large limb joints are usually spared, the most common targets being the metacarpophalangeal and proximal interphalangeal joints. Loss of the phalanges may ensue. Early in the disease, osteoporosis can result in spontaneous fractures. Nerve trunk enlargement, muscle wasting and loss of pain and temperature sensation are highly suggestive. Touch and deep sensation are affected later. The skin should be painstakingly inspected for hypopigmented insensible macules. X-rays show concentric diaphyseal atrophy and resorption starting distally.[10]

Amyloidosis

Neuropathic osteoarthropathy of the feet and plantar ulcers similar to those seen in diabetes mellitus can occur in association with all forms of amyloidosis, particularly familial amyloid polyneuropathy and AL amyloidosis.[3] The knees and ankles are predominantly affected. The diagnosis is dependent on the identification of amyloid in biopsies of nervous, rectal and/or subcutaneous tissue.

Other mutilating osteoarthropathies[10]

Mutilating osteoarthropathies can be observed in a number of rare neurological disorders, including hereditary sensory neuropathies, developmental defects and intramedullary haemangiomas.

Congenital indifference to pain is characterized by a striking contrast between normal results from the evaluation of superficial and deep sensation (with the exception of corneal hypo-aesthesia) and the complete absence of pain from the bones, muscles, ligaments and viscera. Multiple mutilations and neglected fractures are typical. Osteoarticular lesions include circumscribed foci of osteomyelitis, epiphyseal thickening, fractures followed by malunion or non-union, and foci of osteonecrosis.

Other causes

Alcoholism rarely causes neuropathic osteoarthropathy, although neuropathy is present in one-third of chronic alcoholics, the foot being the main site of involvement. Local or systemic glucocorticoid therapy and long-term non-steroidal anti-inflammatory drug therapy have been implicated in the genesis of rapidly progressive neuropathic osteoarthropathy at the hip and knee. Other possible causes include arteriovenous malformations, radiation-induced lesions, transverse myelitis and arachnoiditis.

Several cases of neuropathic osteoarthropathy have been reported in patients without identifiable neurological disorders. Dyck et al[10] have suggested that these patients may have an inherited subclinical disorder in periosteal proprioception.[12] An alternative theory involves the induction by a neurological signal of vascular disturbances responsible for heightened osteoclastic resorption and increased blood flow in adjacent soft tissues. The osteoarthropathy sometimes antedates the development of objective neurological disorders, indicating that patients should be closely followed.

Management of neuropathic osteoarthropathy

Specific therapy of the cause is required in some cases, for example those due to diabetes, syphilis, leprosy and syringomyelia. Unfortunately, in most patients either the neurological damage is irreversible or aetiological therapy is unavailable. Local care and appropriate nutrition are of the utmost importance and can halt progression or prevent relapses.[13] Reconstitution of the normal joint architecture occurs in some cases after early treatment. Immobilization of the joint and cessation of weight-bearing have been recommended to prevent further progression. Rehabilitation therapy has also been advocated. A brace is often used to immobilize the spine, and joint effusions should be aspirated. Local glucocorticoid injections are often of limited efficacy and carry a risk of infection. Diabetic patients should use appropriate footwear. There is general agreement that disinfection and antibiotic treatment of any infection are important.

Surgery is rarely required and should be performed with the utmost caution because of the high risk of infection. Arthrodesis of the joint is the most commonly used procedure. Joint replacement surgery is often considered inadvisable because of the risks associated with tendon hyperlaxity and loss of deep sensation. Vascular surgery is highly controversial; dearterialization of the tibial artery is now preferred to sympathectomy and plantar vessel ligation. Amputation is required in some patients but can be followed by a recurrence of the trophic disorders in the stump.

Practice points

- the contrast between the lack of pain and the presence of severe joint destruction is highly suggestive of neuropathic osteoarthropathy
- the leading cause in industrialized countries is diabetes mellitus
- septic arthritis is the main differential diagnosis
- early local care by immobilization of the joint and cessation of weight-bearing, together with specific therapy for the cause and the prevention of superinfection, is of the utmost importance

NEUROFIBROMATOSIS

The neurofibromatoses are inherited on an autosomal dominant basis and exist as two variants: types I and II.[14]

Type I neurofibromatosis, also known as von Recklinghausen's disease, is the most common, with an incidence between 1 in 2500 and 1 in 3000 births. The diagnosis is usually made in childhood based on the presence of light brown skin lesions called café-au-lait spots, subcutaneous and deep neurofibromas, and ocular abnormalities (iris nodules and optical glioma). Osteoarticular involvement has been reported in 51–74% of cases (Table 4). In type II neurofibromatosis, the neurofibromas develop mainly in the acoustic nerves, bilaterally in most cases, and there are usually no rheumatic manifestations.

Spinal alignment abnormalities

Spinal misalignment is the most common skeletal abnormality in neurofibromatosis, scoliosis having been reported in 10–69% of cases. Two patterns have been described:

Table 4. Main rheumatic manifestations of von Recklinghausen's disease.

Spinal alignment abnormalities	Bony abnormalities	Destructive arthropathies	Nerve sheath tumours
Scoliosis: dysplastic 80–90% non dysplastic 10–20%	Congenital bowing of the long bones	Neuropathic osteoarthropathies	Neurilemmomas
Kyphosis	Fractures 19%	Hip dysplasia	Neurofibromas
Thoracic lordosis	Non-union	Bony alterations by neurofibromas	Peripheral nerve tumours
	Craniofacial abnormalities		Intraspinal nerve root tumours

with and without dystrophic changes such as anterior or posterior vertebral scalloping, major wedging of the spinal column, rotation of the apical vertebrae (rib pencilling), hypoplasia of the pedicles, neural arches and transverse processes, tumours in the paraspinal soft tissues, and widening of the neural foramina and spinal canal.

The dysplastic variant is more common and more severe. Its onset is in childhood or early adulthood.[15] An older age of onset should prompt the search for a benign or malignant spinal tumour. Thoracic kyphosis or lordosis[15–18] has been noted in 35–40% of cases of dysplastic scoliosis. The severity of the scoliosis increases with the severity of the dysplastic abnormalities. Typically, dysplastic scoliosis occurs as a single acute angulation of the thoracic spine; thoracolumbar and lumbar angulation is less common. Pain is usually moderate. Adverse consequences include disfigurement, neurological compromise, respiratory failure and spinal dislocation.[19] Dural ectasia is common in the vicinity of major deformities or dislocations. Non-dysplastic scoliosis appears at an earlier age, contributes only 10–20% of cases but has a better prognosis.[15] However, the curvature tends to worsen spontaneously, and dystrophic changes can develop; close follow-up is therefore mandatory.

In both the dysplastic and the non-dysplastic variants, involvement of the cervical spine is frequently accompanied by thoracic kyphoscoliosis. Cervical spine involvement carries a risk of spinal cord compression and should be looked for routinely, particularly if anaesthesia or spinal traction is planned.[15] The onset can be in childhood. Many patients remain free of symptoms, although some develop cervical pain, neurological compromise and a loss of the normal cervical lordosis or cervical kyphosis. A cervical mass corresponding to a plexiform or malignant neurofibroma is present in a few cases.[20] X-rays may demonstrate a loss of the lordotic cervical curvature, anterior vertebral slippage and/or atlantoaxial or occipitoaxial dislocation.

Bony abnormalities

Neurofibromatosis is associated with dysplastic periosteal abnormalities. Trivial trauma is often responsible for subperiosteal bleeding, probably as a result of periosteal detachment. This explains the frequently irregular appearance of the cortices and the twisted, ribbon-like configuration of the ribs.[16] Congenital anterolateral bowing of the shafts of the long bones has been found in 19% of cases. The bowing usually becomes apparent before the age of 2 years. There is a well-recognized risk of fracture, and about 20% of fractures fail to heal because of defective callus formation by the

periosteum. The most common site of non-union is the tibia, followed by the radius, ulna and fibula.[16]

Bony hypertrophy or neurofibromatous infiltration of the bone occurs in some patients. Unilateral hypertrophy of all or part of a limb has been noted in 16% of cases and can result in length inequality (elephantiasis neuromatosa). Hypertrophy is the result of abnormalities in the growth of the bone and/or soft tissue. The hypertrophic bony segment is longer than normal and has thick, irregular cortices. The adjacent soft tissues show hypervascularization and in some cases contain plexiform neurofibromas.[16]

Lesions of the skull base and calvarium can result in pulsating exophthalmos or, less often, in enophthalmos. Macrocephaly is the rule, usually developing during the first few years of life; microcephaly is uncommon.[21] X-rays may show hypoplasia of the greater wing of the sphenoidal bone with widening of one or both orbits ('empty orbit') due to the absence of the posterior or lateral orbital wall. Other abnormalities of the skull include hypoplasia of the zygomatic processes, thinning and erosion of the temporal bones, enlargement of the sella turcica, hypoplasia of the ethmoidal cells, enlargement of the optic canal and auditory canal by neurofibromas, bony defects in the calvarium and/or maxillary bones, separation of the sutures, most notably the lambdoid suture, and thinning of the calvarium.

Arthropathies

Arthropathies resulting from nerve entrapment or neurofibromatous infiltration of the synovium have been reported.[22]

Nerve sheath tumours

Nerve sheath tumours are common and, if multiple, strongly suggestive of neurofibromatosis. The most common forms are the neurilemmoma, usually solitary, and the neurofibroma or plexiform neurofibroma, usually multiple. These tumours develop on the peripheral nerves. Nerve root tumours arise within the spine but can extend outside it. Plexiform neurofibromas are large tumours that sometimes incorporate a plexus. Intramedullary tumours (astrocytomas) are less common; they cause pain and non-dysplastic scoliosis.[16,23] Meningoceles occur in 60–85% of patients with type I neurofibromatosis. They are frequently multiple and usually arise in the thoracic or lumbar spine, more rarely in the cervical spine.[24] Presenting symptoms of large meningoceles include back pain, nerve root pain, spinal cord or nerve root compression, and symptoms caused by intrathoracic extension, such as dysphagia, dyspnoea and coughing. The pain is worse during the night.

Malignant tumours have been reported in 3–5% of cases, young males being at highest risk; the tumour can be either primarily malignant or the result of the transformation of a benign tumour. Signs that should alert the clinician to the possibility of malignancy include the appearance or alteration of pain, the development of a neurological deficit, the onset of scoliosis after early adulthood, and an increase in the size of a superficial tumour. The diagnosis is often made late, and as a result the prognosis is bleak. X-rays may show bone changes in contact with the tumour, such as scalloping, thinning of a pedicle or rib, or focal or diffuse osteopenia. Imaging studies usually fail to differentiate benign from malignant tumours. MRI shows the tumour and allows the evaluation of its effects on adjacent bony and nervous structures. The tumour generates a low signal on T1-weighted images, with no post-gadolinium enhancement, and a high signal on T2-weighted images.[23]

Disorders in the metabolism of phosphate and calcium

Osteomalacia or hypophosphataemic vitamin D-refractory rickets has been reported in about 40 cases.[25] The pathophysiology of these conditions remains unclear but may be similar to that of oncogenic osteomalacia. The clinical manifestations arise in young adulthood or childhood. There are no noticeable clinical differences between this condition and osteomalacia caused by vitamin D deficiency. Radiographic findings are also non-specific; the fractures and pseudofractures are often multiple and symmetrical. Evidence of hyperparathyroidism has been found in three cases.[26] Laboratory test findings are the same as in osteomalacia caused by renal phosphate wasting.

Other variants of osteomalacia reported in association with neurofibromatosis include oncogenic osteomalacia caused by a neurofibroma, osteomalacia due to malabsorption after resection of gastrointestinal tumours, and osteomalacia secondary to the use of barbiturates or other enzyme inducers. Phosphate and calcium levels should be assayed in all patients with von Recklinghausen's disease, particularly if bone pain is present.

Management of von Recklinghausen's disease

In patients with congenital bowing of the long bones, plaster cast immobilization to prevent fractures or worsening of the deformity has still to be evaluated.[17]

Dysplastic scoliosis with risk factors for progression should be treated surgically before the curvature causes complications or becomes resistant to reduction, regardless of the age of the patient.[16] Posterior or anterior fusion with or without grafting or instrumentation is recommended, although the optimal technique remains debatable. Routine post-surgical immobilization in a brace has been advocated.[15,16] A MRI or computed myelotomography study should be undertaken to look for potential causes of post-surgical neurological compromise (neurofibroma, dural ectasia, artificially widening the spinal canal, threatening rib). If the first procedure is unsuccessful, further attempts should be made. Patients with spinal cord compression may benefit from halo traction until surgery can be performed. Fusion of the cervical spine is indicated in patients with compression of nervous structures, refractory pain or vertebral dislocation; all neurofibromas found during the procedure should be removed.

Non-dysplastic thoracolumbar scoliosis is managed in the same way as idiopathic scoliosis. Non-union is universally difficult to manage, the goal being to obtain healing within a few months with no deformity or loss of limb length. Limb lengthening using the Ilizarov technique may be required. In some patients, multiple procedures fail, leaving amputation as the only option. The management of limb hypertrophy involves resection of the excess tissue and early epiphysiodesis; amputation may be necessary in severe cases.

The management of neurofibromas and meningoceles relies primarily on symptomatic measures such as analgesic therapy and transcutaneous or epidural electrical nerve stimulation. Surgery is warranted in patients with refractory pain, neurological deficits, impending compression or a malignant lesion. Neurofibromas should be removed and meningoceles excluded, although the exclusion of multiple meningoceles or meningoceles with large communication orifices may not be feasible. Osteomalacia caused by renal phosphate wasting should be treated conservatively since the large number of tumours defies their surgical removal. Phosphate supplements and cholecalciferol should be given. If this treatment is effective, the phosphate level

increases and the clinical evidence of osteomalacia resolves, although the renal excretion of phosphate remains high. Oncogenic osteomalacia resolves after removal of the causative tumour.[16]

Practice points

- von Recklinghausen's disease patients should be monitored for rheumatic complications, especially the progressive dysplastic form, which may require surgery
- osteomalacia caused by renal phosphate wasting is a rare feature that can be corrected by giving phosphate and vitamin D derivates

PARKINSON'S DISEASE

As many as 38–65% of all Parkinson's disease patients experience pain and/or a wide variety of unpleasant and incapacitating sensations[27–30], which can antedate the neurological symptoms by several years. In a retrospective study of 60 Parkinson's disease patients, Gonera found that fibromyalgia and shoulder pain were significantly more common during the 10 years before disease onset than in same-age controls.[31] In patients with established Parkinson's disease, the pain is often asymmetrical, predominating on the most severely affected side. Two categories are generally distinguished, namely primary pain syndrome caused by neurological dysfunction of unclear pathophysiology, and pain syndrome secondary to well-defined physical problems.

Primary pain syndrome

Primary pain syndrome manifests as intermittent, diffuse, hard-to-define painful sensations such as proximal muscle tension or cramp-like pain, arthralgia, joint stiffness or pain in the distribution of a nerve root or trunk. Patients also report a wide range of subjective symptoms suggestive of neurological involvement, including tingling, burning or prickling sensations, numbness and electrical shock-like sensations. These symptoms are not elicited by palpation or motion. Sensory function is usually normal, although in some cases subtle disturbances in superficial or deep sensation are found. Restless legs syndrome is more prevalent in Parkinson's disease patients than in the general population.

The symptoms of primary pain syndrome vary closely in step with motor fluctuations and dopamine agonist doses, a feature that provides valuable diagnostic and therapeutic orientation. The symptoms usually occur during the beginning-of-dose or end-of-dose off periods, particularly in the morning upon awakening, and during on–off switching. Some of the symptoms are, however, precipitated or exacerbated by dopamine agonists.[27,30]

Secondary pain syndrome

Dystonia can cause pain predominating in the lower limbs, particularly the feet. Dystonia usually occurs during off periods; peak-dose dystonia is uncommon. Choreic

dystonia is sometimes painful and, in conjunction with the tremor, can cause neuralgia due to nerve trunk compression. Spinal alignment abnormalities, most notably scoliosis, are responsible for back pain in some patients.[27,29] Reflex sympathetic dystrophy manifesting as shoulder pain or shoulder and hand syndrome is more common than in the population at large and can antedate the development of parkinsonian symptoms.

Other rheumatic manifestations

The pseudorheumatoid parkinsonian hand described by Charcot is characterized by adduction and opposition of the thumb, flexion of the metacarpophalangeal joints, and ulnar drift. There is no radiographic evidence of bone destruction. The parkinsonian foot, a combination of varus equinus, claw toe deformity and in some cases fibular drift, is probably caused by dystonia.[30]

Management of the rheumatic manifestations of Parkinson's disease

Primary pain syndrome fails to respond to analgesics and non-steroidal anti-inflammatory drugs. Both primary pain syndrome and dystonia are best treated by giving smaller levodopa doses at more closely spaced intervals, increasing the daily levodopa dosage, switching from a standard to a sustained-release form of levodopa, or using other anti-parkinsonian medications in combination with or instead of levodopa. Pain precipitated by dopamine agonists responds well to dosage reduction or interruption of the treatment. Tricyclic antidepressants are often effective on the symptoms of primary pain syndrome, although they worsen restless legs syndrome, for which benzodiazepines, codeine and other opiates have been recommended. Botulinum toxin therapy has been found to be effective in refractory painful dystonia.[27–30]

Practice point

- Parkinson's disease patients may present with various pain syndromes. This should be kept in mind by rheumatologists in order to recognize the disease and treat the pain syndrome according to its mechanism

MULTIPLE SCLEROSIS

Some multiple sclerosis patients develop atypical manifestations, including rheumatic symptoms, usually early in the disease. Rheumatic manifestations may be more common in later-onset forms and in men.

Sciatica is occasionally the presenting symptom, especially in late-onset forms. The pain is often less well systematized than in common sciatica and frequently has a burning or lightening-like quality. The time pattern is not mechanical, and there is no back pain. These features should suggest the diagnosis.

Spasmodic torticollis can occur during flare-ups of central nervous system demyelination. This symptom abates during remissions of the disease.[32]

Symptoms resembling those seen in cervical spondylosis occur in some patients. These include motor and sensory loss under the level of the lesion, sphincter dysfunction and vertigo-like sensations. These forms often start relatively late in life and

tend to progress continuously without remission. Somatosensory evoked responses fail to distinguish between compression caused by spondylosis and that due to multiple sclerosis. Cervical MRI and computed myelotomography, in contrast, provide accurate information on the relationships between degenerative spinal lesions and the spinal cord. Examination of the cerebrospinal fluid removed during myelography is helpful. If there is any doubt, MRI of the brain should be performed to look for disseminated plaques.

Fractures with a decrease in bone mass are a well-established complication of multiple sclerosis. Studies of women with multiple sclerosis have found bone mass decreases of about 1 SD at the lumbar spine and 1.7 SD at the femoral neck, predicting a 2–6-fold fracture rate increase compared with healthy, age-matched controls. Causative factors may include vitamin D deficiency, an increased risk of injury resulting from falls, and glucocorticoid therapy.[33]

Rheumatoid arthritis, psoriatic arthritis[34] and focal myositis[35] have also been reported in multiple sclerosis patients.

Management

Pharmacotherapy and rehabilitation therapy should be used in combination. Flare-ups are treated with intravenous bolus glucocorticoid therapy followed by oral glucocorticoid therapy, immunosuppressive agents (cyclophosphamide and azathioprine) and alpha-interferon. Attention should be directed towards preventing the potential complications of glucocorticoid therapy, particularly by giving vitamin D and calcium supplements, and, if appropriate, bisphosphonate therapy or menopausal hormone replacement therapy. Rehabilitation therapy focuses on maintaining joint motion range and muscle strength, and on preventing contractures.

Practice points

- rheumatic syndrome, including sciatica and symptoms mimicking cervical spondylosis, can occur in multiple sclerosis
- a history of previous flare-ups and evidence of pyramidal, cerebellar and cranial nerve involvement should suggest the diagnosis
- examination of the cerebrospinal fluid and MRI of the brain should be performed in doubtful cases

OSTEOARTICULAR COMPLICATIONS OF CENTRAL NERVOUS SYSTEM DISORDERS RESULTING FROM INJURY, VASCULAR DISEASE AND ENCEPHALITIS

Hemiplegia can result in rheumatic or orthopaedic complications that add to the patient's disability.[36,37] The range of joint motion can be limited by a number of factors, including weakness, inadequate nursing and contractures of muscles, tendons, ligaments and joint capsules. Pes varus equinus resistant to reduction develops in some patients. Spasticity or dystonia can result in claw toe deformities with pain upon weight-bearing. Flexion contracture of the hip or knee can also occur. Anteroinferior

subluxation of the shoulder occurs in 30–60% of patients with hemiplegia but can be prevented by appropriate positioning of the shoulder in bed and by the use of supporting orthoses and slings. An abduction pad is helpful in preserving internal rotation and adduction.

Reflex sympathetic dystrophy is a frequent and dreaded complication of hemiplegia that develops after 1–12 weeks. The pain is permanent during the day and often continues into the night. Barbiturate therapy, a coma immediately after the injury or neurosurgical treatment may exacerbate the symptoms. Osteoporosis can develop as a complication of the reduced mobility associated with many neurological disorders.

Heterotopic ossification was first described in 1918 by Dejerine and Ceillier[38] in patients with paraplegia and is now known also to occur in association with hemiplegia, coma caused by a head injury or vascular event, encephalitis, encephalopathy and spinal cord lesions. Its rate of occurrence is usually 20–25% but has reached 45% in some studies. The ossification develops in the vicinity of one or more large joints, causing painful limitation of the range of movement.[39] In some cases, the neurological deficit results in an absence of pain and local inflammation. Recognized risk factors include autonomic system dysfunction and a coma that is deep and/or lasts longer than 1 month. An increased frequency of the HLA B18 gene has been reported.[40] The knee is the most typical site of involvement, followed by the shoulders and elbows; involvement of the hands are less common. The onset of symptoms usually occurs during the second month after the neurological insult, although longer intervals have been reported. Joint inflammation and effusion are common. Ossifications appear about the joint after 3–6 months. The X-ray appearance ranges from punctate ossifications to peri-articular osseous bridging. The ossifications do not consistently predominate on the side most severely affected by the neurological disorder. The uptake of bone-seeking radiopharmaceuticals is increased in the early stages of the process. Laboratory tests show evidence of inflammation and an elevation in the alkaline phosphatase level. Immobility may be a major risk factor for heterotopic ossification.[41]

The prevention of the osteoarticular complications of central nervous system disorders rests on adequate orthopaedic nursing care and intensive physical therapy involving alternated postures, specific devices and orthopaedic footwear. Some patients require surgical procedures such as Achilles tendon lengthening, arthrodesis or tendon transplantation. Reflex sympathetic dystrophy syndrome is treated with gentle physical therapy below the pain threshold and local glucocorticoid injections. Heterotopic ossification at the inflammatory stage is best managed by analgesics and non-steroidal anti-inflammatory agents. After resolution of the inflammation, rehabilitation therapy is indicated. Surgical removal of the ossification is sometimes warranted in patients with limitation of the range of movement and no evidence of activity of the ossification (a normal alkaline phosphatase level and normal radionuclide uptake). Anti-inflammatory radiation therapy has also been used.[41]

Practice points

- reflex sympathetic dystrophy and heterotopic ossification are dreaded complications of various central nervous system disorders that add to the patient's disability
- their prevention by adequate orthopaedic care is of the utmost importance

SUMMARY

A number of neurological diseases can masquerade as rheumatic manifestations. Diagnosis may be easy if neurological features are present but sometimes much more difficult if the rheumatic manifestations precede the neurological symptoms. A search for a family history, neurological features, even if minor, and radiological anomalies is important in making an appropriate diagnosis. Neuropathic osteoarthropathy can arise from numerous aetiologies (diabetes mellitus, tabes dorsalis, syringomyelia, alcoholism, hereditary sensory neuropathies, leprosy and amyloidosis) and is frequently indolent albeit mutilating. X-rays usually show a juxtaposition of bony construction and osteolysis. Parkinson's disease patients may seek medical advice for various pain syndromes. von Recklinghausen's disease may be responsible for numerous rheumatic conditions (spinal alignment abnormalities, arthropathies and bony abnormalities). The rheumatic complications of central nervous system disorders, mainly heterotopic ossifications, may further increase the handicap related to these conditions. Multiple sclerosis is a common demyelinating disease of the central nervous system, which can simulate sciatica or cervical spondylosis.

REFERENCES

* 1. Joubert JM & Laredo JD. Ostéoarthropathies nerveuses. In Laredo JD, Morvan G & Wybier M (eds) *Imagerie ostéo-articulaire*, pp 485–497. Paris: Flammarion Médecine-Sciences, 1998.

2. Gupta R. A short history of neuropathic arthropathy. *Clinical Orthopaedics and Related Research* 1993; **296:** 43–49.

* 3. Hubault A. Ostéoarthropathies nerveuses. In Editions scientifiques et médicales *Encyclopédie médico-chirurgicale*, 14285 A10, *Appareil locomoteur*. Paris: Elsevier, 1991.

4. Truon DT, Dussault RG & Kaplan PA. Fracture of the os peroneum and rupture of the peroneus longus tendon as a complication of the diabetic neuropathy. *Skeletal Radiology* 1995; **24:** 626–628.

5. Marc V, Dromer C, Sixou L & Fournié B. A new case of insufficiency fracture in a patient with tabes dorsalis. *Revue du Rhumatisme (English Edition)* 1997; **64:** 271–273.

6. Serratrice G, Acquaviva PC, Olivares JP & Guerra L. Arthropathie de l'épaule révélatrice d'une syringomyélie post-traumatique. *Rhumatologie* 1985; **37:** 63–68.

7. Lesoin F, Devos P, Leys D et al. Syringomyélie, cyphoscoliose et arthrose interapophysaire. *Semaine des Hôpitaux de Paris* 1986; **62:** 3039–3042.

8. Serratrice G. Les arthropathies indolentes des membres inférieurs. *Revue du Rhumatisme* 1991; **58:** 16S–21S.

9. Avrahami E, Frishman E, Fridman Z & Azor M. Spina bifida occulta of S1 is not an innocent finding. *Spine* 1994; **19:** 12–15.

10. Dyck PT, Melinger JF & Reagan TJ. Not 'indifference to pain' but varieties of hereditary sensory and autonomic neuropathy. *Brain* 1983; **106:** 373–390.

11. Dyck PJ, Stevens JC, O'Brien PC et al. Neurogenic arthropathy and recurring fractures with subclinical inherited neuropathy. *Neurology* 1983; **33:** 357.

12. Brower AC & Allman RM. The neuropathic joint: a neurovacular bone disorder. *Radiologic Clinics of North America* 1981; **19:** 571–580.

13. Hoppenfeld S, Gross M & Giangarra C. Nonoperative treatment of neuropathic spinal arthropathy. *Spine* 1990; **15:** 54–56.

*14. National Institutes of Health. Neurofibromatosis. Conference statement. National Institutes of Health Consensus Development Conference. *Archives of Neurology* 1988; **45:** 575–578.

15. Kim HW & Weinstein SL. Spine update. The management of scoliosis in neurofibromatosis. *Spine* 1997; **22:** 2770–2776.

*16. Feldman D. Tuberous sclerosis, neurofibromatosis and fibrous dysplasia. In Resnick D (ed.) *Diagnosis of Bone and Joint Disorders*, 3rd edn, pp 4353–4396. Philadelphia: WB Saunders, 1995.

*17. Disimone RE, Bermann AT & Schwentker EP. The orthopaedic manifestation of neurofibromatosis. *Clinical Orthopedics and Related Research* 1988; **230:** 277–284.

18. Funasaki H, Winter RB, Lonstein JB & Denis F. Pathophysiology of spinal deformity in neurofibromatosis. *Journal of Bone and Joint Surgery* 1994; **76A:** 692–700.
19. Wilde PH, Upadhay SS, Orth D & Leong JC. Deterioration of operative correction in dystrophic spinal neurofibromatosis. *Spine* 1994; **19:** 1264–1270.
20. Craig JB & Govender S. Neurofibromatosis of the cervical spine. Report of eight cases. *Journal of Bone and Joint Surgery* 1992; **74B:** 575–578.
21. Jackson IT. Neurofibromatosis of the skull base. *Surgery of the Cranial Base* 1995; **22:** 513–530.
22. Lokiec F, Arbel R, Isakov J & Wientroub S. Neuropathic arthropathy of the knee associated with an intra-articular neurofibroma in a child. *Journal of Bone and Joint Surgery* 1998; **80B:** 468–470.
23. Varma D. MR in extracranial nerve sheath tumors. *Journal of Computer Assisted Tomography* 1992; **16:** 445–454.
24. Rainov NG, Heidecke V & Burkert W. Thoracic and lumbar meningocele in neurofibromatosis type 1. Report of two cases and review of the literature. *Neurosurgery Review* 1995; **18:** 127–134.
25. Konishi K, Nakamura M, Yamakawa H et al. Case report: hypophosphatemic osteomalacia in von Recklinghausen neurofibromatosis. *American Journal of Medical Sciences* 1991; **301:** 322–328.
26. Wattiaux MJ, De Vernejoul MC, Bletry O et al. Maladie de Recklinghausen avec hypophosphorémie et ostéomalacie. *Revue de Médecine Interne* 1985; **6:** 495–501.
27. Goetz CG, Tanner CM, Levy M et al. Pain in Parkinson's disease. *Movement Disorders* 1986; **1:** 45–49.
*28. Quinn NP, Koller WC, Lang AE & Mardsen CD. Pain in Parkinson's disease. *Lancet* 1986; **i:** 1366–1369.
29. Snider SR & Sandyk R. Sensory dysfunction. In Koller W (ed.) *Handbook of Parkinson's Disease*, pp 171–180. New York: Marcel Dekker, 1987.
*30. Serratrice G & Michel B. Pain in Parkinson's disease. *Revue du Rhumatisme (English Edition)* 1999; **66:** 331–338.
31. Gonera EG, van't Hof M, Berger HJC et al. Symptoms and duration of prodromal phase in Parkinson's disease. *Movement Disorders* 1997; **12:** 871–876.
32. Svetel M, Sternic N, Filipovic S & Kostic V. Spasmodic torticollis associated with multiple sclerosis: report of two cases. *Movement Disorders* 1997; **12:** 1092–1094.
33. Cosman F, Nieves J, Komar L et al. Fracture history of bone loss in patients with MS. *Neurology* 1998; **51:** 1161–1165.
34. Midgard R, Gronning M, Riise T et al. Multiple sclerosis and chronic inflammatory diseases: a case–control study. *Acta Neurologica Scandinavica* 1996; **93:** 322–328.
35. Taussig D, Fenelon G, Baudrimont M et al. Myosite focale de la jambe chez une femme atteinte de SEP. *Presse Médicale* 1993; **22:** 1881.
36. Vautravers P & Isch F. Les complications osteoarticulaires de l'hémiplégie. *Journal de Médecine de Strasbourg* 1986; **17:** 77–80.
37. Flipo RM, Castelain V, Sutter B et al. Heterotopic ossification of the hands in patients with neurologic disorders. *Revue du Rhumatisme (English Edition)* 1993; **60:** 378–380.
*38. Dejerine M & Ceillier A. Paraosteoarthropathies of paraplegic patients by spinal cord lesion. *Clinical Orthopaedics and Related Research* 1991; **263:** 3–12.
39. Garland DE, Blum CE & Waters RL. Periarticular heterotopic ossification in head-injured adults. *Journal .of Bone and Joint Surgery* 1980; **62A:** 1143.
40. Minaire P. Les paraostéoarthropathies neurogènes. *Annales de Médecine Physique* 1982; **25:** 51–55.
41. An HS, Ebraheim N, Kim K et al. Heterotopic ossification and pseudoarthrosis in the shoulder following encephalitis. *Clinical Orthopaedics and Related Research* 1987; **219:** 291–298.