Neuropathic Arthropathy: Review of Current Knowledge

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Abstract

Neuropathic arthropathy is a chronic, progressive degenerative disorder affecting one or more peripheral or vertebral articulations, which develops as the result of a disturbance in the normal sensory (pain or proprioceptive) innervation of joints. Diabetes, syphilis, and syringomelia are the most commonly associated clinical entities. When neuropathic arthropathy is suspected, careful clinical evaluation should be performed to identify an underlying neurologic disorder. Patient education, joint protection, and early recognition of fractures are the most important general management principles. Surgery can be considered in cases of advanced joint destruction when there is significant disability.

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Neuropathic arthropathy remains one of the more interesting and unusual degenerative joint disorders encountered by orthopaedic surgeons. It is defined as a chronic progressive degenerative arthropathy affecting one or more peripheral or vertebral articulations, which develops as the result of a disturbance in the normal sensory (pain and proprioceptive) innervation of joints. Therefore, a diagnosis of neuropathic arthropathy can be made only in the presence of an underlying neurologic disorder.

The first description of neuropathic arthropathy was by Musgrave in 1703, in his book *De Arthritide Symptomatica*. He described the swollen, inflamed joints of a patient who was left "flaccid by paralysis." In 1831, Mitchell reported "bizarre" joint changes in a patient with spinal cord paralysis secondary to tuberculosis. In 1868, Jean-Marie Charcot provided the first detailed description of the rapid development of joint deterioration and instability in several patients with tabes dorsalis. In 1892, Sokoloff described the association of neuropathic joints of the upper extremity with syringomyelia. In 1936, Jordan[1] described the association of diabetes mellitus with neuropathic changes in the foot and ankle. Neuropathic changes associated with intra-articular corticosteroid injections were described by Chandler and Wright[2] in 1958.

Diabetes, syphilis, and syringomyelia are the clinical entities most commonly associated with neuropathic arthropathy. Leprosy, spinal dysraphism, congenital insensitivity to pain, and many other disorders are also associated with the condition, although much less commonly.

Pathogenesis

The etiology of neuropathic arthropathy has been a topic of debate since Charcot's description in 1868. The most widely accepted theory is the "neurotraumatic" theory, which postulates that a joint with abnormal sensory innervation, if unprotected, will undergo rapid destruction as a result of minor traumatic events.[3] In 1917, Eloesser[4] designed an experimental model to test this theory. He resected the posterior nerve roots in cats, thereby leaving them active yet ataxic. He then induced a consistent injury by cauterizing the medial femoral condyles. The combination of neurologic injury and local injury resulted in rapid joint deterioration. Clinical evidence to support this theory was presented by Johnson,[5] who reported a large series of neuropathic joints in which fracture appeared to be the inciting event that led to rapid joint destruction.

A second frequently discussed theory is the "neurovascular" theory, which postulates that neurologic changes produced by an underlying medical disorder create a hypervascular region in the subchondral bone that is characterized by increased osteoclastic resorption and osteoporosis.[6] This state leads to

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pathologic microfractures and eventual subchondral collapse, followed by joint destruction. Although this is an attractive theory, histologic support is lacking; the presence of vascular connective-tissue reticulum with large dilated channels and resorption of subchondral trabeculae by osteoclasts has been an inconsistent finding.

The neuropathic joint generally progresses through three distinct phases.[7] The first is the destructive phase, which is characterized by hyperemia, swelling, and osteoclastic bone resorption. Recurrent joint trauma is another component of the vicious circle that ultimately results in total joint destruction. The second, or reparative, phase begins once the joint is placed at rest and is protected from further trauma. This stage results in the formation of dense fibrous tissue within the joint, as well as dense sclerotic bone at the joint line and in the surrounding tissue. Osteophyte production, myositis ossificans, and the coalescence of osseous and cartilaginous debris can also occur, which may improve joint stability. The third, or quiescent, phase is characterized by decreased vascularity, stabilization of the periarticular reaction, and significant osseous sclerosis.

Diagnosis

Histology

The most consistent histologic finding in neuropathic arthropathy is the presence of osseous and cartilaginous debris deep within the synovium. This allows differentiation from osteoarthritic joints, in which fragments of bone and cartilage are often present just below the synovial lining. Special staining techniques have shown this tissue to be metaplastic in nature. Because of frequent intra-articular hemorrhage, abundant hemosiderin is usually present.

Radiography

Radiographically, two patterns have been described: atrophic and hypertrophic.[8] The atrophic form is characterized by massive bone resorption with virtual disintegration of the joint. This pattern is encountered most commonly in the hip, shoulder, and foot. The hypertrophic form is characterized by severe joint destruction, periarticular new-bone formation, osteophytes, fractures, and osseous debris. Migration of bone fragments along tissue planes has also been described. This pattern is most commonly seen in the knee, elbow, and ankle.

Clinical Presentation

Patients most often present with a diffusely swollen, warm, erythematous joint. A vague or nonspecific history of trauma may be obtained. It has been stated that neuropathic joints are "painless," but this is certainly not the case. Some pain or discomfort is almost always present, although generally much less than might be expected on the basis of the clinical and radiographic findings. The white blood cell count and erythrocyte sedimentation rate are generally normal, and aspiration of the joint usually produces a large quantity of clear yellow fluid.

Clinical findings vary depending on the duration of the disease. Early in the course, a large joint effusion is usually present. In the later stages, swelling may subside, and the joint may have a boggy character. Joint instability becomes more evident as the disease progresses. If significant fragmentation has occurred, osseous debris may be palpable in the soft tissues surrounding the more superficial joints. Swelling is often associated with mild erythema, which raises the suspicion of septic arthritis. Gram stain and culture of the aspirate may be necessary to rule out septic arthritis.

When neuropathic arthropathy is suspected, careful clinical evaluation should be performed to identify an underlying neurologic disorder. A neurologic consultation is frequently helpful in elucidating subtle findings.

Diabetes mellitus is currently the most common cause of neuropathic arthropathy.[9] Neuropathic joint destruction develops in approximately 0.1% of patients with diabetes and 5% of those with peripheral neuropathy. The tarsal, midtarsal, tarsometatarsal, metatarsophalangeal, and interphalangeal joints are most commonly affected. Involvement of the ankle, wrist, hand, and knee has also been reported, although less frequently.

Neuropathic arthropathy secondary to syphilis usually presents in patients over age 60. It occurs in 5% to 10% of patients with tabes dorsalis[10] and most commonly involves the hip, knee, or spine. Involvement of the upper extremities is much less common but may be encountered with polyarticular disease. In the past, syphilis was the most common cause of joint neuropathy; with the advent of treatment, however, it has become a distinctly uncommon cause.

Syringomyelia is the most common cause of upper extremity neuroarthropathy. Joint involvement occurs in 20% to 40% of patients with syringomyelia.[10,11] It generally is characterized by a monarticular presentation, most commonly involving the shoulder and less commonly the elbow. Approximately 20% of cases are characterized by involvement of multiple upper extremity joints.

Other disorders reported to be associated with neuropathic arthropathy include the peripheral neuropathies of leprosy, amyloidosis, Charcot-Marie-Tooth disease, multiple sclerosis, chronic demyelinating polyradiculopathy, gigan-

tism, and alcoholism. The arthropathy associated with multiple intra-articular corticosteroid injections has been described as a type of neuropathic arthropathy, although the pathogenesis appears to be chemical in nature.[2] Several authors have described a condition termed "subclinical inherited neuropathy" to explain idiopathic cases of neuropathic arthropathy.

Neuropathic arthropathy is very uncommon in the pediatric population. When it does occur, it is most commonly associated with congenital insensitivity to pain, spinal dysraphism, and Riley-Day syndrome.

Management

The management of neuropathic joints has ranged from protection and bracing to arthrodesis and prosthetic replacement. Identification and treatment of the underlying neurologic disorder, especially in treatable systemic disorders, such as diabetes mellitus, is the essential first step in management. Patient education, joint protection, and early recognition of fractures are the most important general management principles. Measures taken for joint protection may include limb immobilization, restricted weight-bearing, and functional bracing. Surgery can be considered in cases of advanced joint destruction when there is significant disability. If surgery is performed during the active stage of the disease, however, there is a high risk of failure.

With these general treatment principles in mind, we will now discuss management of neuropathic arthropathy in specific joints and anatomic areas.

Spine

Historically, spine neuropathy has been associated with syphilis.[12] More recently, however, syringomyelia, diabetes, congenital insensitivity to pain, spinal cord injury, and old age have been identified as underlying causes. The thoracolumbar junction and the lumbar spine are most frequently involved. However, involvement of the cervical spine has been noted in syringomyelia.

The patient most often presents with a painless, progressive spinal deformity, which may range from significant hypermobility to ankylosis.[13] Occasionally, in long-standing cases, nerve-root compression or bladder dysfunction may be part of the clinical presentation.

Radiographically, massive new-bone formation is characteristic of the neuropathic spine. Destruction of the articular facets occurs initially. Subsequently, large marginal osteophytes develop secondary to instability; this has been described as a "parrot-beak" appearance (Fig. 1).

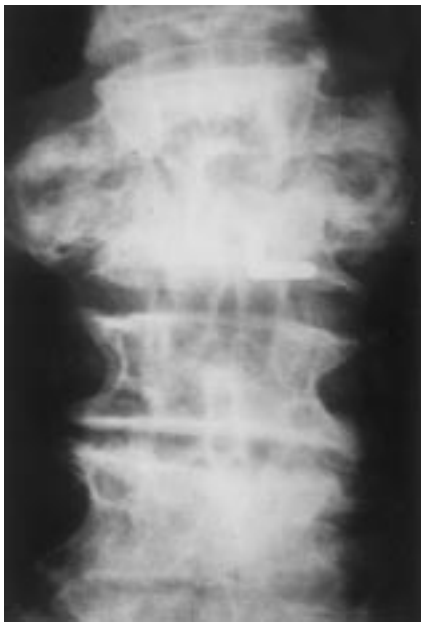


Fig. 1 Anteroposterior radiograph of the thoracolumbar spine of a patient with tabes dorsalis demonstrates large marginal osteophytes, or "parrot-beak" appearance.

The intervertebral disk spaces narrow, and retrolisthesis can occur. Frank dislocation may occur in severe cases. The differential diagnosis includes severe osteoarthritis, osteomyelitis, Paget's disease, and skeletal metastasis. Magnetic resonance imaging may be useful in distinguishing between neuroarthropathy and infection.[14]

Treatment of the neuropathic spine generally involves immobilization of the hypermobile segment.[15] The older literature recommended long periods of cast or brace immobilization. More recently, however, anterior and posterior fusion with instrumentation and bone grafting has been advocated to prevent the disastrous neurologic sequelae that may accompany instability and marked deformity.[16] Brown et al[17] reported successful fusion in eight patients with neuropathic arthropathy of the spine using this combined anterior and posterior technique; successful fusion required either extensive debridement or vertebrectomy with bridging of the defect with bone graft. Although a second level of Charcot arthropathy developed below the level of the previous fusion in three patients, the authors did not recommend routine fusion to the sacrum in patients with involvement in the lumbar area. One should, however, restore the normal sagittal contour and avoid leaving unfused segments between new and old fusions in the area of the neurologic deficit. A high complication rate and the possibility of developing arthropathy below the fused segments make this a demanding procedure.[18]

Upper Extremity

Involvement of the relatively non-weight-bearing joints of the upper extremity, especially the elbow, wrist, and hand, probably occurs more frequently than has been reported. This is due, in part, to the general observa-

tion that upper extremity joint problems are usually less symptomatic than those of the weight-bearing joints of the lower extremity. In addition, marked joint destruction and instability are not as commonly encountered with neuropathic arthropathy of the upper extremity.

Shoulder

Neuropathy in the shoulder is most commonly associated with syringomyelia,[11,19] but has been reported in association with syphilis, diabetes, Arnold-Chiari malformation, cervical spondylosis, adhesive arachnoiditis, tuberculous arachnoiditis, and posttraumatic syringomyelia. Patients usually present with painless swelling of the shoulder. Active motion may be limited, but passive motion is usually maintained. Joint aspiration produces large amounts of straw-colored fluid with particulate debris. Specimens should be sent for culture to rule out infection. The radiographic appearance usually suggests osteolysis, with evidence of osseous fragmentation and destruction, which can result in subluxation or frank dislocation (Fig. 2).

Initial treatment should include protective immobilization with a sling and restriction of activity. If marked instability is present, arthrodesis may be considered. Glenohumeral arthrodesis is particularly difficult to achieve, however, because of the significant bone resorption that often occurs. Arthrodesis should not be attempted in the acute inflammatory stage because of continued bone erosion. Inadequate glenoid bone stock, prosthetic loosening, and instability secondary to soft-tissue compromise make prosthetic arthroplasty a poor choice.

Sternoclavicular Joint

Sternoclavicular joint involvement has been reported in the presence of syringomyelia and results in massive, progressive swelling at the medial end of the clavicle. Because the condition is so uncommon, the differential diagnosis should include osteomyelitis and tumor. When a diagnosis of joint neuropathy is confirmed, supportive and symptomatic treatment is warranted, unless there is compromise of the vital structures posterior to the sternoclavicular joint.

Elbow

Elbow involvement is usually associated with syringomyelia,[20] syphilis,[11] or congenital insensitivity to pain.[21] However, diabetes, Charcot-Marie-Tooth disease, and a rare idiopathic form are other potential causes. Isolated involvement of the elbow is most common with syringomyelia. Syphilis accounts for most cases of polyarticular involvement. Clinically, significant swelling is usually present; deformity and instability may be minimal but can become marked as joint destruction progresses. In later stages, radiographs show marked joint destruction with subluxation of the radiohumeral and ulnohumeral articulations (Fig. 3). Sclerosis, extensive osteophyte formation, periarticular swelling, and calcification are often present.

Initial management of the neuropathic elbow involves functional bracing that allows flexion and extension but neutralizes varus and valgus stresses. For cases resistant to bracing, arthrodesis can be considered. However, long periods of immobilization are required to obtain a successful fusion; the nonunion rate for arthrodesis of a neuropathic elbow is very high.

Wrist and Hand

Neuropathic arthropathy of the wrist and hand has been reported in patients with diabetes, leprosy, congenital indifference to pain, syringomyelia, and syphilis. Often, the patient presents with swelling and deformity of the wrist without significant pain. There is usually no history of a preceding traumatic event. Radiographic changes include narrowing of the intercarpal joint spaces, disorganization of carpal alignment, and disintegration of the carpal bones. Cyst formation and subchondral sclerosis of the radiocarpal, intercarpal, and carpometacarpal joints are often noted, along with diffuse periostitis and joint debris.

Management of the neuropathic wrist and hand is directed at protection from further mechanical trauma by using prolonged immobilization and functional bracing. Joint de-

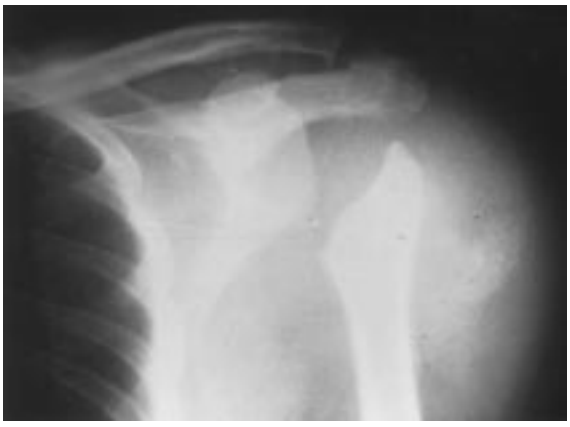
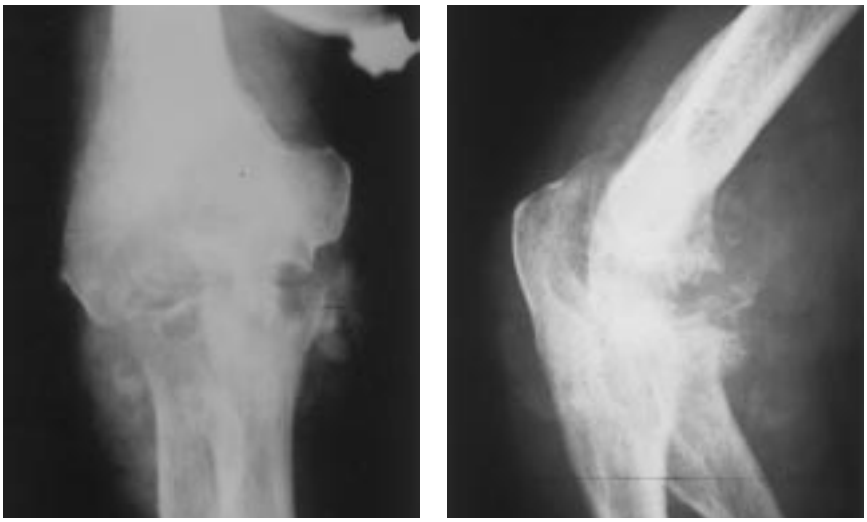


Fig. 2 Anteroposterior radiograph of a neuropathic shoulder demonstrates dissolution and subluxation of the proximal humerus.



A B

Fig. 3 Anteroposterior **(A)** and lateral **(B)** radiographs of the elbow of a patient with syringomyelia depict destruction of the ulnohumeral and radiohumeral joints. Note the periarticular calcification and osteophyte formation.

bridement and/or arthrodesis should be considered when gross instability is present. Total wrist arthroplasty and arthroplasty of the small joints of the hand are contraindicated.

The Lower Extremity

Hip

Neuropathic arthropathy of the hip is most commonly associated with syphilis.[11] Two patterns of involvement have been described.[22] The first generally involves fracture of the femoral head or neck due to minimal trauma. The second is an "arthritic" type, in which progressive wear and fragmentation of the femoral head and acetabulum result in extensive joint destruction. Patients usually present with a painless but progressively worsening limp. Range of motion is maintained, but crepitus may be present. Radiographic examination characteristically shows resorption of a significant portion of the femoral head and neck (Fig. 4). Fragmentation and periarticular new-bone formation may also be visualized.

Patient management is directed at symptomatic relief. Some patients may require only use of a cane despite extensive radiographic changes. Joint debridement and synovectomy with loose-body removal may provide some pain relief in carefully selected patients. However, it is important to leave the periarticular bone and scar tissue undisturbed to maintain joint stability.

Treatment of femoral-neck fractures in the neuropathic hip may involve either closed reduction and internal fixation or primary-resection arthroplasty. Unfortunately, there is little in the literature to help predict which treatment will be more successful. The nonunion rate after internal fixation is excessively high in this setting; when this method is chosen, one should consider prolonged postoperative protection in traction or a spica cast.[5] Prosthetic replacement has been used to a limited extent but also has a very high complication rate.[5]

Treatment of the arthritic type of neuropathic hip is problematic. Arthrodesis is almost always unsuccessful.[22] Dissolution of the femoral head and neck limits the available

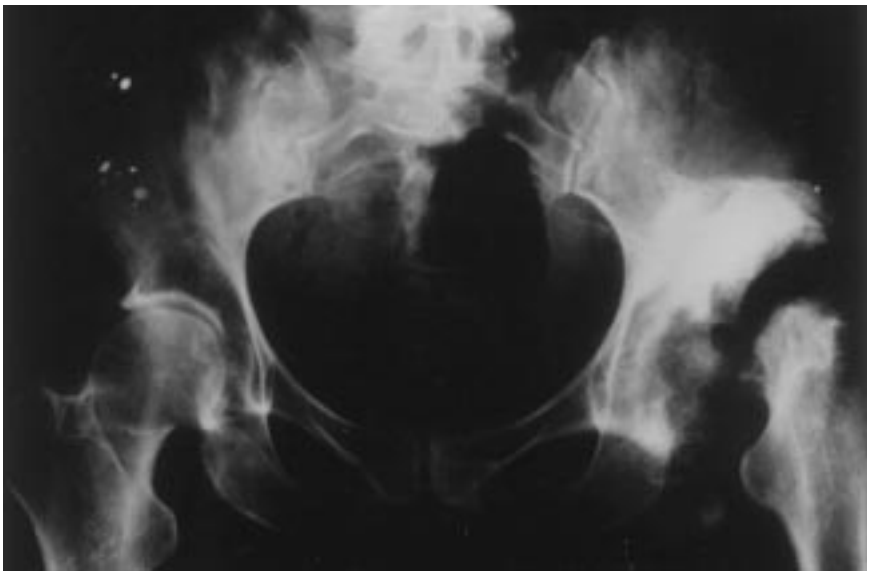


Fig. 4 "Arthritic" type of neuropathic hip joint in a patient with tabes dorsalis. Note the absence of the femoral head and the marked destruction of the acetabulum.

bone stock, and autogenous and banked graft is quickly resorbed, leading to early failure. Total hip arthroplasty has a high rate of complications, which include early dislocation, component loosening, and periprosthetic fracture despite postoperative immobilization, trochanteric advancement, and protected weight-bearing.[23]

Knee

Neuropathic arthropathy of the knee is usually associated with syphilis[11] and diabetes. The significant joint forces on the knee during weight-bearing and the absence of surrounding soft tissue for stabilization make the knee particularly susceptible to progressive destruction and instability. Patients present with varying degrees of joint instability, crepitus, and pain. Spontaneous dislocation of the knee has been reported. Radiographs demonstrate progressive bone destruction, fragmentation, hypertrophic new-bone formation, and subluxation (Fig. 5).

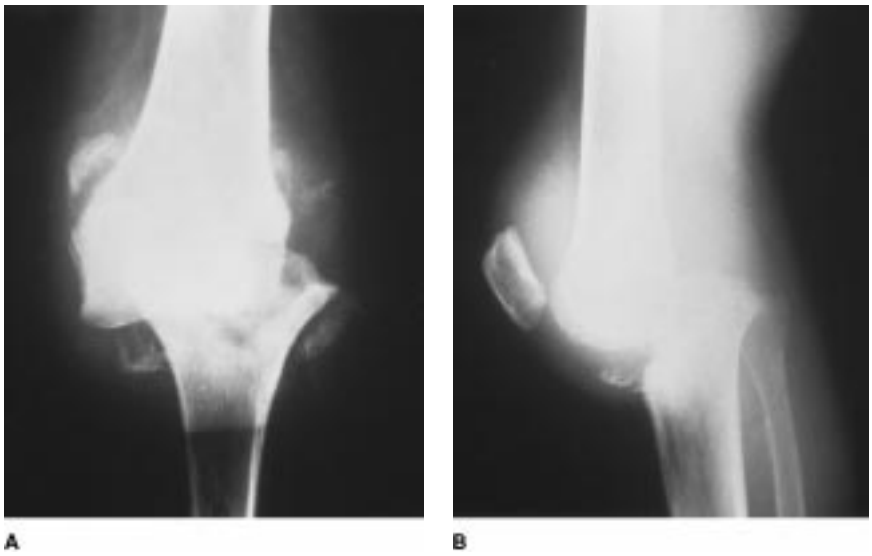


Fig. 5 Anteroposterior **(A)** and lateral **(B)** radiographs of the knee of a patient with tabes dorsalis demonstrate gross subluxation of the tibiofemoral joint as well as joint-space obliteration and periarticular calcification.

Initial management of the neuropathic knee should include protective bracing to provide stability and reduce shear stresses across the joint. If bracing fails to provide adequate stability, arthrodesis should be considered. Arthrodesis of the neuropathic knee has had reasonable success.[24] Before knee fusion is performed, local warmth and swelling should be controlled with casting or bracing; the disease must be in the quiescent phase for successful union to occur. External fixation, intramedullary fixation, or both must be combined with adequate resection of sclerotic bone, apposition of bleeding bone surfaces, and prolonged immobilization. Synovectomy in conjunction with arthrodesis has been reported to improve the arthrodesis rate.[25]

Total joint arthroplasty in the neuropathic knee is controversial.[26-28] Soudry et al[26] reported on nine posteriorly stabilized knees in seven patients with neuropathic arthropathy; eight had excellent results at the 3-year follow-up examination. The long-term results of total joint replacement in the neuropathic knee, however, are still unknown.

Foot and Ankle

Neuropathic arthropathy of the foot and ankle will be considered together because weight-bearing force transmission biomechanically links the ankle, subtalar, midtarsal, tarsometatarsal, metatarsophalangeal, and interphalangeal joints. Disturbances in any of these joints will induce changes in the others due to increased weight-bearing stresses. In the neuropathic foot and ankle, this linkage often results in severe destructive arthropathy.

Long-standing diabetic peripheral neuropathy is the most common cause of neuropathic changes in the foot and ankle.[9,11,29] Leprosy, congenital indifference to pain, myelomeningocele, and peripheral neuropathies are other potential causes. Diabetic patients typically present with decreased vibratory sense, anhidrosis, and loss of ankle reflexes in their fifth and sixth decades. Joint manifestations are often unilateral. Bilateral involvement occurs in as many as 25% of adult patients; it does not appear to be related to the severity of other disease manifestations (retinopathy and nephropathy). In contrast, the few reports of neuropathic joint changes in patients with juvenile-onset diabetes note bilateral involvement in up to 75% of cases.[30]

Patients usually present with warmth, swelling, and erythema of insidious onset in a painless foot or ankle. Examination of the ankle may reveal instability, crepitus, or a fixed varus or valgus deformity. The foot is often shortened or thickened, and collapse of the longitudinal arch can produce a rocker-bottom deformity. Patients often complain of inability to fit into their shoes. Hammer toes and thinning of the fat pad beneath the metatarsal heads can result in ulcers and painful callosities.

Radiographs typically demonstrate fractures or peritalar dislocations, periarticular calcification, loose bodies, subchondral sclerosis, tibiofibular dissociation, and osteophyte formation (Fig. 6). Valgus or varus deformity is often present. The talus may show signs of osteonecrosis and collapse, and talar disintegration has been reported. Vascular calcification is also a common finding.

The patterns of destruction of the tarsus have been described by Harris and Brand.[31] The changes are usually hypertrophic, with various stages of fragmentation, resorption, sclerosis, periarticular calcification, and new-bone formation (Fig. 7). Collapse of the longitudinal and transverse arches results in bony prominences, which can lead to plantar ulcerations. Navicular dislocations, Lisfranc fracture-dislocations, calcaneal tuberosity avulsions, and cuneiform destruction have all been reported.

Involvement of the metatarsophalangeal joint can result in dorsal dislocation of the proximal phalanx. The fat pad becomes thinned and displaced distally, away from the weight-bearing surface. Plantar callosities and ulcerations are common. Dissolution of the metatarsal neck and shaft, whether due to infection or a hypervascular state, produces the "pencil-in-cup" deformity. Similar changes in the proximal phalanges may result in an hourglass appearance.

The differential diagnosis in patients with these changes about the foot and ankle includes psoriatic arthritis, rheumatoid arthritis, gout, neoplasm, tuberculosis, and osteomyelitis. The possibility of osteomyelitis is particularly troublesome because it can coexist with neuropathic joints. Accurate differentiation between the two conditions can mean the difference between amputation and protective casting. Three-phase bone scans show uptake in all three phases in both osteomyelitis and neuropathic arthropathy. Gallium scans are nonspecific due to uptake in the overlying tissues. The value of indium labeling of white blood cells is still controversial.[32] Some reports indicate effective differentiation between the two, while others have shown problems with false-positive studies. In one small series, dynamic bone scanning, the combination of a three-phase bone scan and a computerized blood-flow study, was successful. Magnetic resonance imaging has proved to be nonspecific. The best diagnostic study is histologic examination of synovial and bone biopsy specimens.

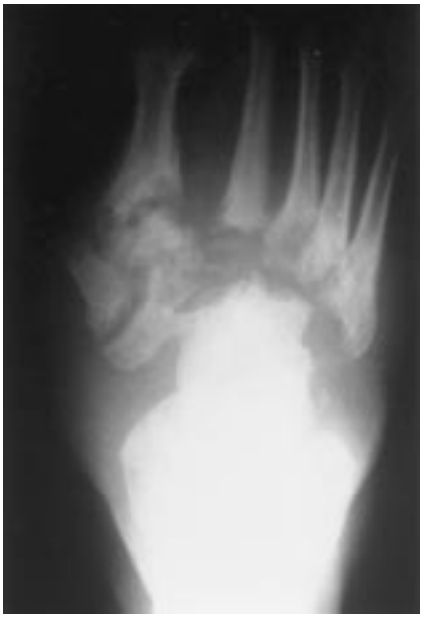


Fig. 7 Anteroposterior radiograph of the foot of a patient with diabetes illustrates massive destruction of the tarsometatarsal articulation (Lisfranc's joint).

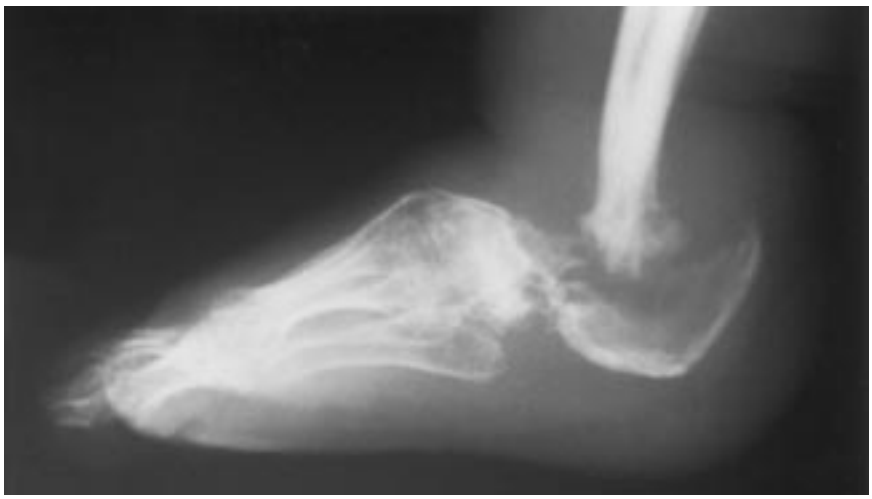


Fig. 6 Lateral radiograph of the foot of a patient with insulin-dependent diabetes mellitus shows complete dissolution of the talus and most of the distal tibia and calcaneus.

The treatment of the neuropathic foot and ankle begins with patient education and control of the underlying disease.[33] Foot care and daily inspection are important components of management, particularly before the development of arthropathy. Vitamin B_{12}, thiamine, and pyridoxine supplements have been shown to be efficacious in patients with leprosy.

Acutely, the foot and ankle should be protected in a well-padded cast or a polypropylene

splint. Although swelling usually resolves in 6 to 12 weeks, the patient should be kept non-weight-bearing until there is radiographic evidence of healing. Casting may be necessary for as long as 6 months. Once weight-bearing is allowed, custom-molded extra-depth shoes should be worn for further protection. Some have recommended double upright patellar-tendon-bearing orthoses to decrease weight-bearing across the foot and ankle.[34] The orthosis is worn for up to 1 year or until osteopenia has resolved.

Occasionally, plantar ulceration and instability are resistant to conservative measures, and surgical management is required. Aggressive removal of plantar ulcers and exostectomy of the bony prominences should be considered. Arthrodesis has been performed successfully[35-37]; the goals of arthrodesis of the neuropathic foot and ankle are to establish normal weight-bearing axes, create a plantigrade foot, and eliminate the need for prolonged bracing. Surgery should be performed only during the quiescent phase of the disease. Internal and external fixation have both been used. Prolonged immobilization is necessary to increase the chance of a successful arthrodesis. Early weight-bearing, even in the presence of abundant callus formation, can result in resorption at the fusion and subsequent nonunion.

A failed arthrodesis in good alignment can be treated successfully with a brace. Joint replacement has not been reported in the neuropathic foot or ankle. Amputation may ultimately be necessary in the face of uncontrollable infection or severe, disabling instability.

Summary

Neuropathic arthropathy is an uncommon but potentially devastating joint disorder. The exact pathogenesis of the disease remains in question. Management principles include both identification and treatment of the underlying disorder and early recognition and management of the neuropathic joint. These measures provide the best possibility for preventing the progressive joint destruction that is inevitable in the neglected case.

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