CHAPTER **42**

NEUROPATHIC ARTHROPATHY SECONDARY TO CONGENITAL INSENSITIVITY TO PAIN WITH ANHYDROSIS

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Neuropathic arthropathy of the foot and ankle has been linked to several different disease processes such as diabetes mellitus, tabes dorsalis, syringomyelia, etc. A very rare cause of neuropathic arthropathy is a group of diseases classified as congenital indifference to pain.[1] This group includes congenital insensitivity to pain and hereditary sensory neuropathies Type I - IV. Congenital insensitivity to pain with anhydrosis (CIPA) makes up an even smaller percentage of patients classified with hereditary sensory neuropathy. Episodes of fever, lack of perspiration, absence of pain, self-injury, painless fractures and mental retardation characterize CIPA. Usually it is recognized early in infancy, because of high fevers secondary to the lack of perspiration. The primary clinical feature of CIPA is congenital analgesia, with no response to painful stimuli, which can lead to self-mutilation, multiple orthopedic fractures and sometimes Charcot joints.[1-11]

CASE STUDY

An 8-year-old female patient was seen after referral with chronic ulcerations over her right medial malleolus and a complex history of possible neuropathic arthropathy, chronic osteomyelitis and apparent recurrent right ankle infections with swelling, redness and fevers. The patient had increasing valgus deformity of the ankle with instability, exceeding the capacity of a patellar tendon brace especially over the dislocated medial malleolar region. The deformity led to the pressure ulcerations.

Musculoskeletal examination revealed a normal left foot and ankle for the patient's age. Her right foot and ankle on the other hand was grossly deformed with a significant amount of heterotopic bone formation. The ankle joint was extremely unstable with significant crepitation. Similarly the subtalar joint had excessive completely non-anatomic motion. In stance the patient's calcaneus was almost completely laterally dislocated from underneath the tibia.(Fig. 1) The neurological

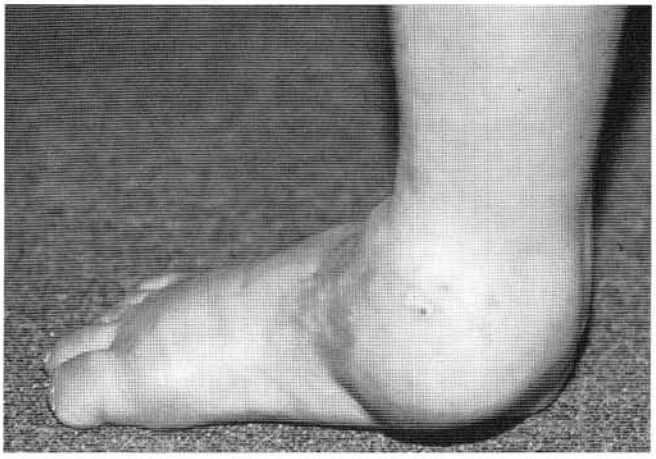

Figure 1A. The severe valgus deformity of the ankle with instability lead to pressure ulcers over the dislocated malleoli.

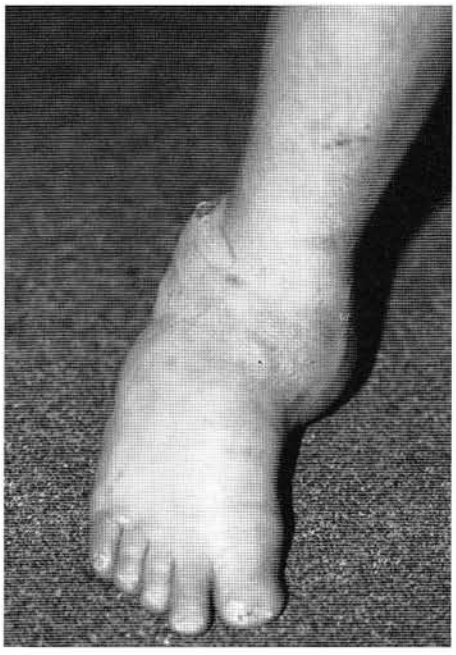

Figure 1B. Anterior view of the severe deformity.

examination revealed normal deep tendon reflexes bilaterally. The patient did not respond to painful stimuli and had no ability to differentiate sharp and dull sensations. However, the patient was hyperesthetic to light touch and vibration sensation was normal. Muscle strength was normal and rated at 5/5 for all lower extremity groups. Radiographic evaluation revealed complete destruction of the right ankle joint. There was complete avascular necrosis and disintegration of the talus with a significant amount of heterotopic bone formation. (Fig. 2) There was no evidence of a focal lytic area (Brodie's abscess) or periostitis. The destruction was so severe that the distal tibial and fibular physeal regions appeared involved in the destructive process as well.

A detailed history revealed problems with fevers of unknown origin as an infant which went undiagnosed until the patient was three-years-old. At that time, her pediatrician diagnosed her with anhydrosis. Over the next several months, an eventual diagnosis of congenital insensitivity to pain with anhydrosis was made. At that time she had experienced no orthopedic problems. However, at age 5 she had an infection from a sore on her right hallux that developed osteomyelitis and eventually required a partial hallux amputation. During her postoperative convalescence she developed a pressure sore from a bandage (cast). At the same time her ankle became red, hot and swollen. Aspirations of the ankle were all negative, however, cultures of the soft tissue pressure wound yielded Staph aureus and pseudomonas. A bone scan (Tc99mdp) was performed and a presumptive diagnosis of osteomyelitis was made. Intravenous antibiotics were then utilized for several months with no improvement noted. Serial radiographs taken during this time revealed progressive talar destruction, which was considered an avascular necrosis or a septic process. At this time the patient had an incision and drainage, however, all cultures were negative. The open wound eventually healed with decreased activity and bracing, and the acute inflammation also subsided. At this time neuropathic osteoarthropathy was considered as part of the cause of the ankle deterioration. However, chronic osteomyelitis at this stage was also possible due to multiple deep ulcerations and open wounds which could have caused a contiguous spread osteomyelitis. During the next two years increasing ankle deformity was noted, low-grade inflammation continued to be present, and neurotrophic ulcerations began to develop. Increasing deformity,

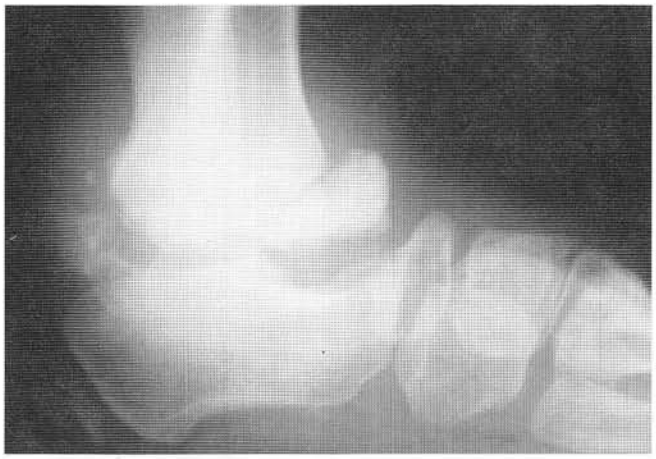

Figure 2A. Radiographic evaluation revealed complete destruction of the right ankle joint. There was complete avascular necrosis and disintegration of the talus with a significant amount of heterotopic bone formation.

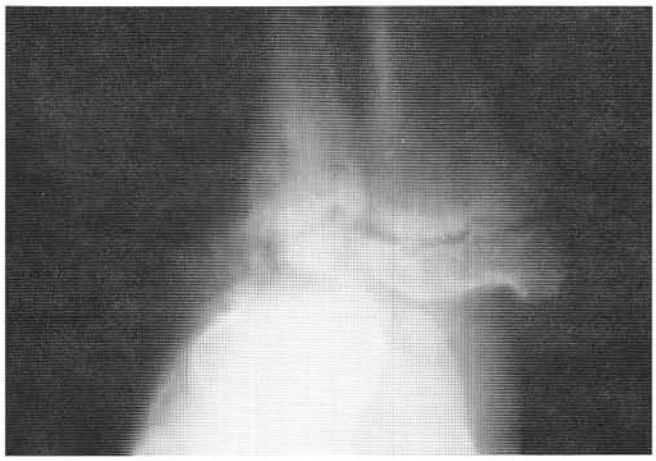

Figure 2B. AP view.

decreasing function and consideration of amputation lead to an eventual referral to the author's office for surgical consultation.

After the initial visit, a period of prolonged immobilization and external bone stimulation was recommended in an attempt to gain more stability, and avoid the need for surgery. After a period of approximately 3 months, no significant improvement in the right ankle was noted. During this time, the patient dislocated her contralateral hip on two different occasions without a severe traumatic history. In both situations, the hip was reduced without the need for surgery. During the recovery period of the second left hip dislocation it was decided to proceed with right ankle surgery. It was felt that the altered mechanics of the right ankle was probably affecting the other lower extremity joints. The ankle was so non-functional at the time,

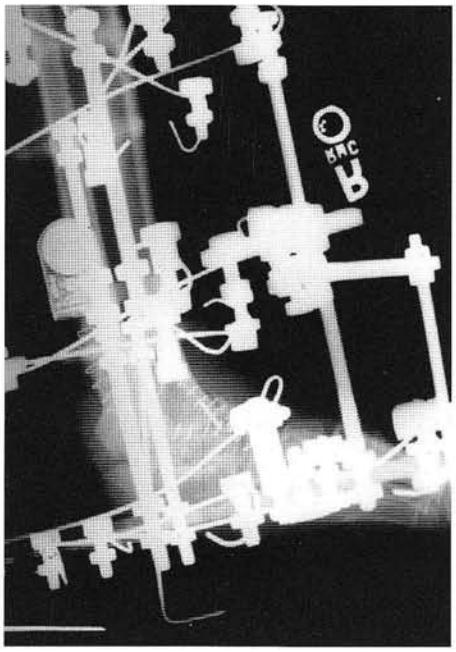

Figure 3A. Postoperative radiographic appearance of the tibiocalcaneal arthrodesis with Ilizarov frame.

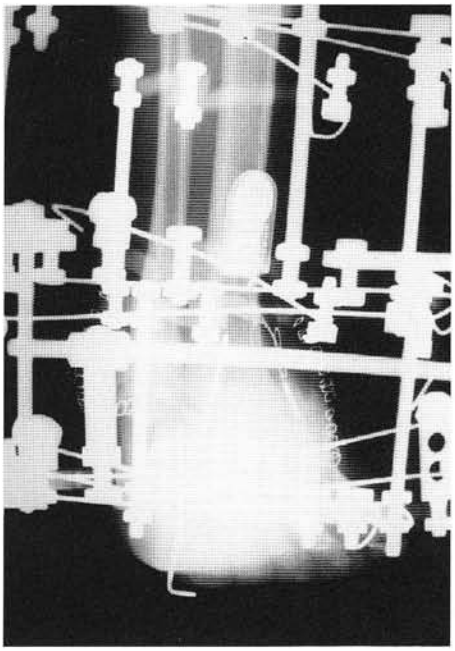

Figure 3B. AP view of the ankle/leg.

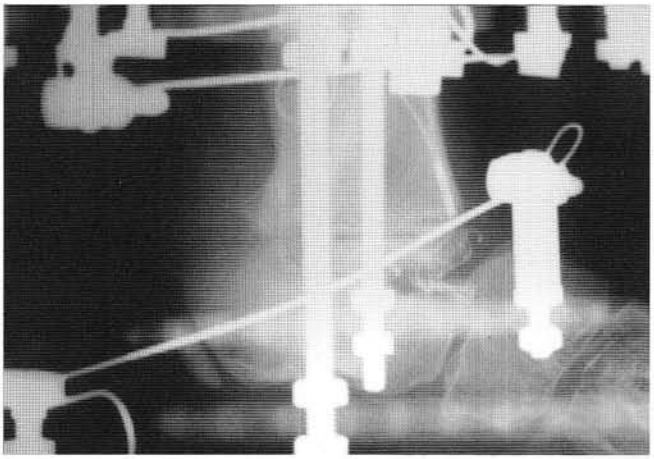

Figure 3C. Lateral view of the foot.

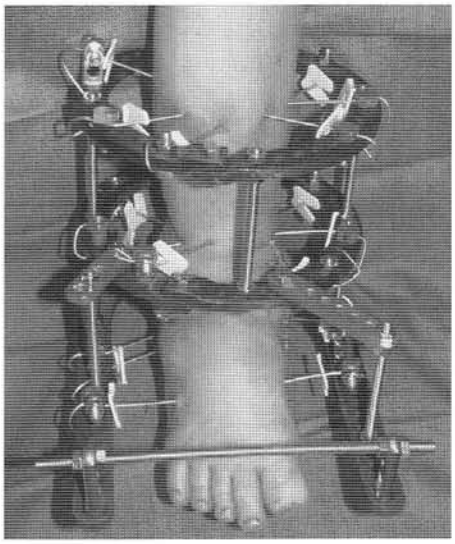

Figure 4. Postoperative clinical appearance of the tibiocalcaneal arthrodesis with Ilizarov frame.

amputation had already been recommended by other physicians.

A tibiocalcaneal arthrodesis with an Ilizarov frame was recommended. Other fixation modalities were considered but, since the patient had significant problems with pressure sores and compliance with non-weightbearing casts, external fixation was deemed the most appropriate. Use of an Ilizarov frame would also avoid crossing the growth plates with internal fixation. No further work-up regarding the patient's possible osteomyelitis was performed prior to surgery, however intra-operative cultures and bone biopsy were planned.

The patient successfully underwent tibiocalcaneal arthrodesis with implantation of an internal bone stimulator and application of an Ilizarov frame. (Figs. 3, 4) Intraoperative bone biopsy revealed marked degenerative joint disease consistent with neurotrophic arthropathy with no evidence of osteomyelitis. However, intra-operative bone culture was positive for Staph aureus. Since the culture and biopsy provided conflicting results a long-term course of chronic antibiotic suppression therapy was instituted. The patient was kept non-weightbearing during the initial postoperative period because the left hip was still healing from its

second dislocation. At six weeks postoperatively the patient fractured her tibia just above the superior ring of the Ilizarov frame likely from a stress riser that developed from the patient crawling on her hands and knees. Closed reduction with external fixation was performed, bridging this fracture with another ring superiorly. Shortly after this fracture, the patient began full weightbearing with the Ilizarov frame. During the postoperative convalescence, several postoperative pin tract infections were encountered and appropriately treated.

Approximately four months status post tibiocalcaneal arthrodesis, and just over two months after closed reduction and external fixation of the tibial fracture the Ilizarov frame was removed. The tibial fracture healed uneventfully without malunion. The tibiocalcaneal arthrodesis did not entirely consolidate, but was stable. (Figs. 5-7) The stability of the ankle was confirmed with live C-arm fluoroscopy. Ambulation with a custom-made shoe with a 3/4 inch lift correcting for the leg length discrepancy and a MPJ rocker was ordered. Approximately two weeks after ambulation with the custom-made shoe was begun, swelling and redness developed once again. Radiographic evaluation revealed fragmentation of the internal bone stimulator wire. This was clearly caused by motion. The midtarsal joint (navicular) was extremely hypermobile and had fragmented the wire in the region of the sinus tarsi and navicular, anterior to the tibiocalcaneal arthrodesis site.(Fig. 6) Another Charcot event was suspected, but with the history of the previous osteomyelitis and the previous positive bone culture, the internal bone stimulator was removed and an I&D was performed. Infectious disease started intravenous antibiotics. All cultures were negative except for one which grew a coagulase negative staph. The patient healed quickly and the swelling and redness improved.

During her immobilization on the right leg she suffered a midshaft tibia fracture from a simple hop on her left leg. Two months later while still nonweightbearing because of her left tibial fracture, localized redness, increased temperature and swelling over the lateral aspect of her right ankle reoccurred in the region of old pin sites. A local I&D was performed by another surgeon in the author's absence, which grew Staph aureus. Infectious disease and others recommended a below-the-knee-amputation with the patient becoming neutropenic from IV antibiotics. Their feeling was that it was a primary infectious process (chronic osteomyelitis and a septic joint).

Considering the very confusing history with conflicting bone culture and bone biopsy results and bouts of recurrent inflammatory processes, a T-99 coupled with an I-111 bone scan was ordered with a 24 hour delayed reading. The hospital substituted a T-99 HMAPO scan which showed no focal activity in the right ankle in the delayed images. In the T-99 bone scan only the left healing tibial fracture showed an increase in uptake compared to the contralateral extremity.

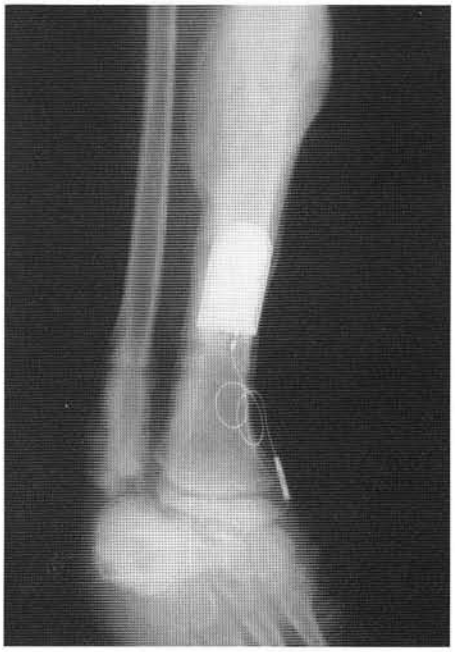

Figure 5. Postoperative radiographic appearance of the tibiocalcaneal arthrodesis and tibial fracture after Ilizarov frame removal (oblique ankle/leg view). The bone callous bridging the tibial fracture is clearly seen.

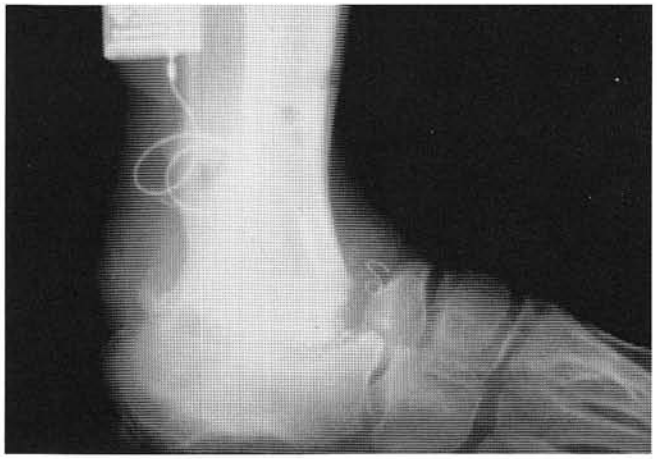

Figure 6. Postoperative radiographic appearance of tibiocalcaneal arthrodesis after Ilizarov frame removal (lateral view). Note the fragmentation of the internal stimulator wire in the region of the navicular.

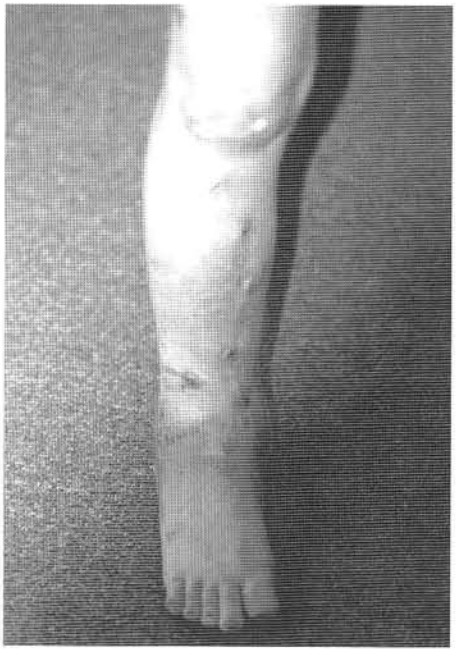

Figure 7. Postoperative clinical appearance of tibiocalcaneal arthrodesis 2 weeks after Ilizarov frame removal.

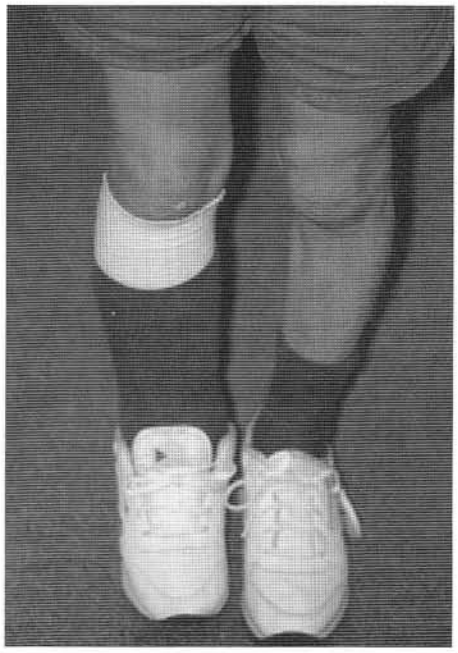

Figure 8. A custom made shoe with a 3/4 inch lift correcting for the leg length discrepancy and a MPJ rocker was ordered for ambulation as well as a patellar tendon brace.

The patient was taken off all IV antibiotics due to her neutropenia. Once again the inflammation eventually resolved and her wound healed conservatively without antibiotics. The patient was placed back into a patellar tendon brace for ambulation, which has worked well over the last four months. (Fig. 8) The tibiocalcaneal arthrodesis remains a stable pseudoarthrosis with no varus or valgus motion. Dorsiflexion is present, but this occurs in the midtarsal joint. There has been no further skin breakdown or ulceration in the right foot, ankle or leg. The patient is currently ambulating in her patellar tendon brace and adjusted shoe with no complaints or difficulty and has significantly increased her activity. However, the patient and her family know that further orthopedic problems are likely to occur in the future. The family has declined the recommendation for household ambulating only, with use of a wheelchair for other activity.

DISCUSSION

This case is a typical example of congenital insensitivity to pain with anhydrosis. Dearborn first described congenital insensitivity to pain in 1932.[2] The syndrome with anhydrosis was classified by Dyck and Ohta as type IV hereditary sensory neuropathy.[3] The cause of this disorder is unknown, however, the pathophysiology has been linked to abnormalities in the peripheral sensory nerves. Several authors have reviewed peripheral nerve biopsies under electron microscopy.[3-6] Goebel et al. examined sural nerve biopsies and observed an almost complete absence of unmyelinated fibers and a slight decrease in small myelinated fibers.[6] Rafel et al. also showed similar findings.[4] Itoh et al. noted extreme paucity of unmyelinated fibers and a reduction in myelinated fibers, especially small fibers. They also reported that the endoneurium consisted of abundant collagen fibers.[5] In summary, biopsies of peripheral nerves in patients with this condition have shown a severe decrease in the number of small (A-delta) myelinated fibers and a marked decrease in the number of unmyelinated (type C) fibers. These fibers are a very important component for the sensation of pain.[3-6] Swanson et al. showed that there was an absence of small neurons in the dorsal ganglia, a lack of small fibers in the dorsal roots and the absence of Lissauer's tract in a necropsy of a twelve-year-old who died secondary to a febrile illness. Therefore, he suggested that this condition could be secondary to a migration defect in the neuron precursors and an interruption in maturation.[7]

Goebel et al reported on two patients who died at an early age secondary to not being able to

control body temperature in the presence of severe infection.[6] Unfortunately, the patient in this case study lost an older sister to such a circumstance at just over a year old. Skin biopsy results in patients with this condition have shown normal sweat glands with no unmyelinated nerve fibers around the sweat glands leading to the anhydrosis and decreased ability to thermoregulate.[3]

The lack of sensation (indifference to pain) causes the inability to perceive or prevent trauma, or to avoid overuse injuries, which leads to the increased risk of multiple orthopedic complications and possibly Charcot joints. The pathogenesis of this type of arthropathy is the same as that in other causes of Charcot joints.[8] A loss in pain sensation and/or proprioception leads to abnormal relaxation of supporting periarticular structures. This laxity results in joint instability and continuous microtrauma. Eventually chronic inflammation causes joint degeneration, incongruity, fracture and neuropathic changes from continued weightbearing forces. Eventually, x-rays reveal marked osteopenia, sclerosis, fragmentation, large osteophytes and joint subluxation.

In retrospect, the case presented began as an acute tibiotalar Charcot joint that was not properly immobilized and eventually became infected from a contiguous spread osteomyelitis from deep neurotrophic ulcerations rather than from a hematologic osteomyelitis or a septic joint. It is clearly evident in the literature that these patients have an extremely high incidence of fracture/dislocations especially in the tibia and femur causing the vast majority of these patients to become wheelchair bound.[3,8] Theodorou et al. reported two cases of CIPA which resulted in neuropathic arthropathy, bilateral Charcot ankle joints and in the other case affected a foot.[9] Other reported orthopedic complications have included spinal instability and lumbar neuropathic arthropathy.[8] Amputations have been necessary for some patients with CIPA due to multiple fractures, instability, malunion, infections and gangrene.[10,11]

When considering surgery on patients who suffer from CIPA, one must consider the importance of the management of body temperature. Typically, only light anesthesia is necessary due to the lack of pain perception. Also positioning and maneuvering are extremely important to avoid joint extension and further injury.[10]

SUMMARY

Neuropathic arthropathy of the foot and ankle is a well-recognized condition in diabetes mellitus and other more common forms of neuropathy. This case study reviews another possible cause of neuropathic osteoarthropathy. Congenital insensitivity to pain with anhydrosis (CIPA) is characterized by episodes of fever, lack of perspiration, absence of pain, self-injury, painless fractures (multiple orthopedic complications including Charcot joints) and mental retardation. The case reported showed the importance of a proper initial diagnosis and management of neuropathic arthropathy in avoiding the potential morbidity associated with Charcot joints.

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