Clinics in Surgery

Research Article
Published: 21 Sep, 2017

Charcot Cysts: A Rarely Reported Finding

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Abstract

Aims/Goals: Charcot arthropathy is a debilitating condition affecting the lower extremity of persons with long established peripheral neuropathy. Deformities of the midfoot can place the foot at risk of ulceration and subsequent amputation if infection ensues. Although surgical management has become much more common for this disorder, there has been little, if any, mention of a peculiar cystic proliferation noted in the deep soft tissues upon surgical dissection. We herein report our observations on several patients who were found to have what we have termed "Charcot Cysts."

Methods: Three type 2 diabetic patients are presented who reported to our High Risk Foot Clinic with Charcot arthropathy of the midfoot represented by a collapse of the midfoot and loss of calcaneal inclination. These patients were treated per our customary treatment of wound care, offloading boots, and instructions for non weight bearing as indicated. Although all patients were given instructions and supplies for wound care and provided with therapeutic footwear appropriate for their condition, two patients persisted with midfoot ulceration. The other went on to develop a plantar soft tissue mass. Despite further casting, the ulcers and mass remained recalcitrant to conservative care. All patients were taken to surgery for a simple plantar exostectomy to reduce the plantar bony prominence underlying the chronic ulceration or mass.

Results: Upon deep exploration a translucent, fluctuant, multi-loculated cystic mass was encountered that extended throughout a considerable portion of the dissection. Upon resection, the masses were found to be spongy and contained what appeared to be synovial fluid. Pathology confirmed that these were simple benign cysts. Importantly, however, we found a delay in wound healing caused by persistent synovial fluid leakage.

Conclusions: This rarely reported complication of the diabetic Charcot foot has been noted by the senior author (RGF) in many such operative patients over the last several decades. Since most patients with Charcot foot are treated conservatively, these cysts are not usually recognized surgically. Once the foot becomes ulcerated or is treated surgically, however, the Charcot cysts can be shown to have impeded normal wound healing. While the pathogenesis of Charcot neuroarthropathy has been previously described, the formation of such related cysts has yet to be explained. We, therefore, encourage clinicians and surgeons to corroborate our findings with further study of this interesting pathology.

Keywords: Charcot; Charcot foot; Charcot arthropathy; Charcot neuroarthropathy; Cyst; Synovial cyst

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Received Date: *29 Jun 2016*
Accepted Date: *10 Sep 2017*
Published Date: *21 Sep 2017*

Citation:
Banks J, Jong A, Frykberg R. Charcot Cysts: A Rarely Reported Finding. Clin Surg. 2017; 2: 1630.

Introduction

Charcot Neuropathic osteoarthropathy (CN), commonly referred to as the Charcot foot is a serious and potentially limb-threatening lower-extremity complication of diabetes. First described in 1883, by a French neurologist, Jean-Martin Charcot (1825–1893), this condition continues to remain a challenge even for the most experienced practitioners [1,2]. Now considered an inflammatory syndrome, the diabetic Charcot foot is characterized by varying degrees of destruction of osseous and articular structures of the foot and ankle joint secondary to underlying neuropathy, trauma, and perturbations of bone metabolism [3,4]. It has been suggested that the onset of the condition is triggered by a preceding event such as minor trauma, previous ulcer, infection or foot surgery with the common factor to all of these events is local inflammation [5].

Charcot arthropathy is a debilitating condition affecting the lower extremity of persons with long established peripheral neuropathy caused by many complicated yet interconnected etiologies; however, diabetic neuropathy has become the most common etiology [3,6-8]. The interaction of certain key factors (diabetes, sensory-motor neuropathy, autonomic neuropathy, trauma, and metabolic abnormalities of bone) results in an acute localized inflammatory condition that may

lead to varying degrees and patterns of bone destruction, subluxation, dislocation, and deformity. The hallmark deformity associated with this condition is midfoot collapse, described as a "rocker-bottom" foot [3,9]. Deformities of the midfoot can place the foot at risk of ulceration and subsequent amputation if infection ensues. Annually, $25 billion are expended for the treatment of chronic wounds, with the number growing due to the aging population and increased incidence of diabetes and obesity [10]. Therefore a timely, orderly and effective wound management and treatment are crucial.

In poorly controlled diabetics, peripheral sensory neuropathy allows for repetitive micro or macro trauma to the foot and ankle [11]. This causes an increased release of inflammatory cytokines IL-6, IL-1, and TNF-a, which, in turn, promotes osteoclast recruitment, differentiation, and proliferation [12]. Receptor activator of nuclear factor-kappaB (RANK) ligand (RANKL) has been identified as an essential mediator of osteoclast formation and activation. RANKL mediates the process of osteoclastogenesis by binding to its RANK, which is expressed on mononuclear osteoclast precursors [13,14]. The effects of RANKL–RANK interaction are physiologically counterbalanced by osteoprotegerin (OPG), which acts as a soluble receptor decoy for RANKL and blocks the interaction of RANKL with RANK [15-17]. The ratio of RANKL to OPG has been suggested to regulate the extent of osteoclast formation and resorption. Therefore, any alteration in the RANKL/OPG ratio could be critical in the pathogenesis of osteolytic bone disorders [14-18]. The likelihood that this pathway is involved is increased by the fact that the same signaling system, RANKL/OPG, is also intimately involved in the process of calcification of the media of arterial cell walls and such calcification is a feature of diabetic neuropathy and especially of CN [19]. The association between neuropathy and increased osteoclastic activity can also be attributed to Calcitonin Gene Related Peptide (CGRP), a neuropeptide that functions within the circulatory and digestive systems and aids in the maintenance and growth of stem cells [16-20]. Decreased levels of CGRP have been demonstrated in study specimens with Charcot neuroarthropathy and diabetic neuroarthropathy [21]. Because CGRP also acts as a RANKL inhibitor, antagonizing its functions in osteocalstogenesis and bone resorption, a decrease in CGRP allows for increased RANKL and receptor binding, leading to unrestrained bony resorption [16-21]. Furthermore, decreases in nitric oxide synthase (eNOS) have also been liked to diabetic sensory neuropathy [22]. Nitric Oxide (NO), a free radical mediated by eNOS, functions at low levels to promote osteoclastic bone resorption [23]. A decrease in NO levels, thus, potentiates unrestricted osteoclast proliferation and bony resorption. Poor glycemic control also produces an increase in advanced glycation end products (AGE) [24], glycated compounds that form due to glucose exposure [25]. These products within the intra and extra cellular environment contribute too many of the vascular and nephrologic complications of diabetes [25]. Along with RANKL, however, AGE has also been demonstrated to play a role in inhibiting osteoblastic proliferation and differentiation [26] and enhancing induced osteoclastogenesis [27]. This is yet another inflammatory pathway associated with Charcot arthropathy that leads to increased bony resorption. The diagnosis of Charcot neuroarthropathy is based upon the clinical examination of the patient. During the acute phase, a patient will present with gross warmth (calor), redness (erythema), and edema to their foot and/or ankle, which is often clinically indistinguishable from infection [2,28,29]. These patients will present with insensitivity to a Semmes-Weinstein 5.07 monofilament, which is indicative of peripheral neuropathy; however, they will have a palpable, often bounding, pulse. The patient will often complain of instability in the foot and a feeling of "crunching" with ambulation [2,3,30]. Plain X-ray may or may not document evidence of fracture and/or dislocation at presentation. In those in whom the X-ray is normal, an isotope bone scan or magnetic resonance imaging (MRI) will provide evidence of inflammation involving the bone, as well as adjacent soft tissues, although differentiation from osteomyelitis may be difficult in those who have an overlying ulcer. Loss of protective sensation will increase the likelihood of trauma to the foot, while motor neuropathy could result in altered structure of the foot (with exaggeration of the plantar arch and clawing) and changed gait with resultant abnormal loading.[3] With the full collapse and destruction of the normal foot architecture, the patient's residual deformity will assume a characteristic rocker-bottom appearance caused by plantar flexion and lateral deviation of the talus in conjunction with collapse of the midfoot joints. This plantar prominence leads to increased plantar pressures and shear stress during ambulation causing a breakdown of the skin and ulceration to form. It is imperative to treat and prevent ulcerations from increasing in depth and severity to prevent erosion of soft tissue down to the level of bone. A wound that probes to bone leaves the boney structures susceptible to osteomyelitis complicating the wound healing process and making healing more challenging. Patients with such presentation or those patients who have had wounds overlying bony deformity for some arbitrary period of time are likely to have osteomyelitis. It is unlikely that these patients will achieve resolution of the osteomyelitis without resection of the infected bone.

The medical treatment of CN is aimed at offloading the foot to alleviate pressures, treating bone disease with antibiotic therapy (based on wound pathogen cultures), and preventing further foot fractures [4,31]. In addition, employing a thorough patient and wound assessment, optimizing glycemic control, and weekly sharp debridement until healthy, granular, bleeding tissue is obtained is of importance [2,4,32-35]. Treatment of chronic wounds should be essentially directed against the main etiologic factors responsible for the wound [36-41]. Because of the various etiologies of increased local bone resorption and/or secondary osteoporosis in patients with CN and limited randomized placebo-controlled trials in this area, treatment guidelines are largely based on professional opinion rather than the highest level of clinical evidence. The main stay of acute phase nonsurgical treatment is immobilization. This is often done using a total contact cast, which is changed every 1 to 2 weeks. During the course of this active phase of the disease, the bones remain fragile and there is evidence of increased bone turnover and associated osteolysis. If the inflamed foot is splinted in a non-removable cast, the inflammation usually settles rapidly – even though the underlying process remains active. Splinting often needs to be maintained for up to 3-6 months or until the physician can accurately discern that the patient has now transitioned into stage III of the Charcot cascade by comparing both radiographic and clinical exam evidence. At this time the patient is evaluated for long-term management of their condition.

The surgical treatment of Charcot foot arthropathy has historically been limited to debridement of infected wounds, correction of deformity where accommodative bracing has been unsuccessful and amputation when the foot was deemed non-reconstructable. A recent review that aimed to provide an update on the current surgical procedures routinely performed included amputation, arthrodesis, debridement of ulcers, drainage of infections, and exostectomy. The

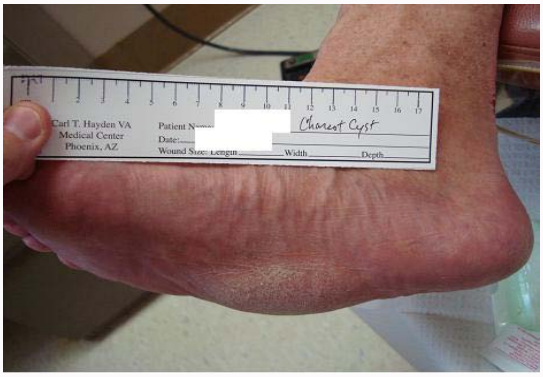

Figure 1: Physical exam reveals a solid, spongy/boggy, mobile, compressible mass located near the plantar lateral fourth and fifth metatarsal bases.

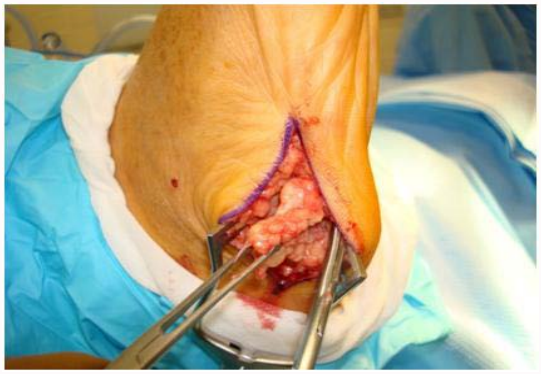

Figure 2: Surgical dissection Charcot cyst.

use of internal or external fixation and the need for posterior muscle group lengthening was also recorded. Though there remains to be a lack of randomized, prospective, multicenter trials, Schneekloth et al. [42] also found that published data now exist comparing fixation techniques, reconstruction and amputation, and cost evaluations of limb salvage. The group reported that arthrodesis, especially tibiotalocalcaneal (TTC) arthrodesis seems to be gaining popularity as a surgical treatment option for CN [42]. The goal of treatment, whether nonoperative or operative, remains the same: to achieve a plantigrade, stable foot that remains ulcer free. Although surgical management has become relatively more common for this disorder, there has been little, if any, mention of a peculiar cystic proliferation noted in the deep soft tissues upon surgical dissection. We herein report our observations on three patients who reported to our High Risk Foot Clinic with Charcot arthropathy of the midfoot. All three patients were type two diabetic patients that presented with a collapse of the midfoot and loss of calcaneal inclination that were found to have what we have termed "Charcot Cysts."

Methods and Results

Case 1

A sixty-one year old male with past medical history of type 2 diabetes, peripheral neuropathy, chronic inflammatory demyelinating polyneuropathy for which he takes methadone and tiagabin, post-traumatic stress disorder, hypertension, hypercholesterolemia, history of abdominal aortic aneurysm, benign prostatic hyperplasia, and a twenty-two-and-a-half pack year tobacco history. His chief complaint was a one month history of right midfoot collapse with associated swelling, change in shape, and a clicking noise with weight bearing. Patient denied pain. Pertinent physical exam revealed palpable pedal pulses, with right mid foot erythema, edema, calor – 94 degrees Fahrenheit compared to 85 degrees Fahrenheit contralaterally, absent sensation to Semmes Weinstein monofilament, a rocker bottom appearance, with no open lesions. Bone scan revealed hyperemia with increased midfoot uptake. Radiographs of the right foot revealed a washed out appearance, flattening of the arch, talonvicular fault, and periosteal reactive changes in the third, fourth, and fifth metatarsals with subluxation of fourth and fifth metatarsal tarsal joints. These findings were consistent with active stage Charcot foot neuroarthropathy. Patient was treated with CAM boot immobilization and a discussion of the stages of Charcot foot neuroarthropathy and the importance of decreased weight bearing. Throughout the course of patient's preoperative care, he was followed every three to four weeks with new radiographs and continued CAM boot immobilization. Seven weeks after initial presentation, patient reported a "lump is moving from the side of my foot to the bottom of my foot," and "it is occasionally painful." Pertinent physical exam revealed an increase in superficial temperature compared to left foot, particularly over the solid, spongy/boggy, mobile, compressible mass located at the plantar lateral sub fourth and fifth metatarsal bases (Figure 1). Ultrasound of the area revealed a cyst in the soft tissue. Patient was treated with continued CAM boot immobilization. Ten months after initial presentation, with continued CAM boot immobilization, radiographic examination revealed some resorption with consolidation of dislocated midfoot. Patient had begun the chronic stage of Charcot foot neuroarthropathy. Eleven-and-a-half months after initial presentation, patient received excisional surgery of this Charcot cyst (Figure 2). A six centimeter linear incision was made at the lateral aspect of the right foot over the palpable mass. After careful dissection, the mass was delineated, including the source and stalk of the mass. This was then removed from the operative field in one large section (Figure 3). The incision site was flushed, and closed with nylon sutures. Patient was placed in post-operative shoe. Anatomic pathology revealed tan to pink portions of benign simple cyst and cystic wall (Figure 4). Postoperatively, patient was followed on a one to two week basis. At patient's first postoperative visit, there was absence of fluctuant or boggy masses. Incision site was macerated but without dehiscence. The incision site was dressed with betadine and dry sterile dressings to be changed daily. Sutures were taken out at

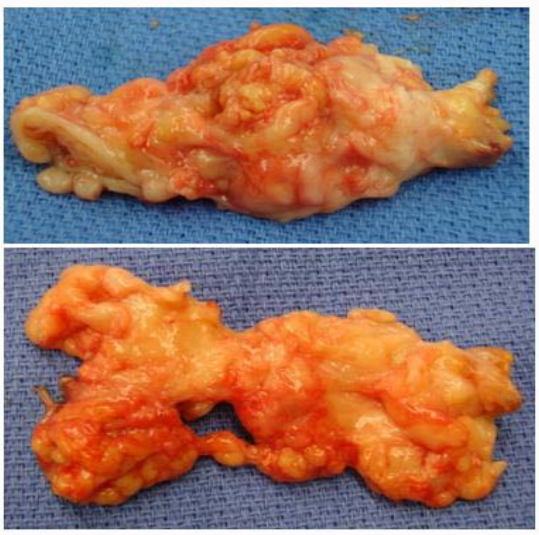

Figure 3: Excised Charcot cyst.

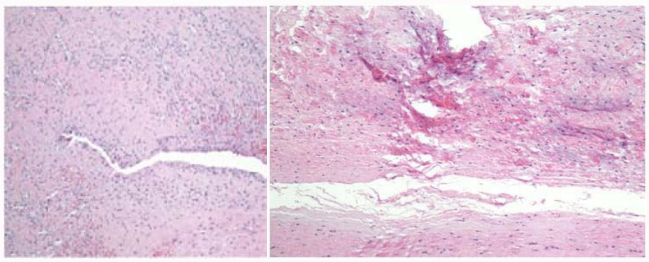

Figure 4: Pathology analysis revealing tan to pink portions of benign simple cyst and cystic wall.

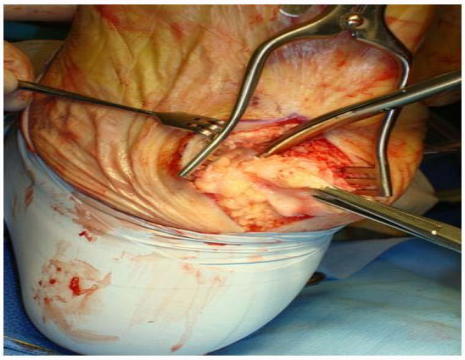

Figure 5: Surgical excision of Charcot cyst.

fourth postoperative appointment, where an incision site dehiscence was noted centrally. Patient was started on a seven day course of Augmentin. Appligraft was applied at the patient's fifth postoperative visit. On patient's thirteenth postoperative visit, physical exam revealed mild, localized bogginess on plantar lateral right foot with calor. Serous sanguinous fluid was drained without need of incision or anesthesia. Patient was instructed to finish another seven day course of Augmentin. By patient's nineteenth postoperative visit, the incision site closed, and there were no open lesions noted. Patient now continues to ambulate without issues in extra depth shoes.

Case 2

A fifty-five year old male with past medical history of type 2 diabetes, peripheral neuropathy, hyperlipidemia, and hypertension presented to clinic with a chief complaint of a left foot plantar ulcer. Patient reports about sixteen months ago he fell, sustained a midfoot fracture, and subsequently developed the plantar ulcer. Patient relates he was weight bearing on the left foot for about six weeks before he was diagnosed with the Charcot foot collapse. At the time of patient's initial presentation, his blood glucose was measured at 422 mg/dL and rechecked at 429 mg/dL. Focused physical exam of left foot revealed palpable pedal pulses, diminished sensation to Semmes Weinstein monofilament, a sub cuboid ulcer measuring two-and-a-half centimeters by three centimeters without acute signs of infection, decreased ankle joint dorsiflexory range of motion, collapse of midfoot consistent with Charcot, and plantar bony prominence corresponding to ulcer location. Radiographs, negative for osteomyelitis, revealed advanced deformity and stable appearing disorganization with lateral subluxation of the midfoot tarsometatarsal joint complex relative to tarsal navicular bones. Patient was treated with wound debridement, betadine wet to dry dressings with supplies for daily changes, and was instructed to remain in walking boot offloaded with padding. Preoperatively, this patient was seen every three weeks and treated

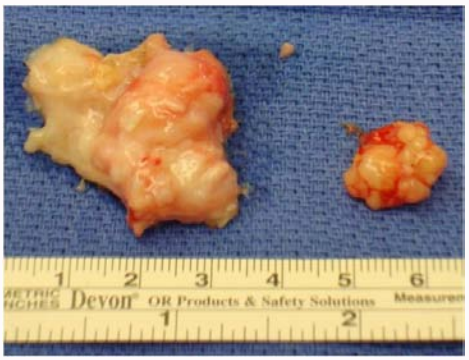

Figure 6: Charcot cyst.

with wound debridements and dressings to include Promogran, betadine ointment, and covaderm, each time instructed to remain in offloaded walking boot. Fourteen weeks after initial presentation, patient underwent surgical intervention on the left foot. A four centimeter incision was made directly over the ulceration site, and the ulcer was excised (Figure 5), as was an underlying soft tissue mass to be sent for pathological examination. Midfoot plantar planing was performed to resect bony prominences via osteotome. A Tendo Achilles lengthening was also performed via three stab incisions. Patient was initially placed in a posterior splint. Per Pathology, the "cyst left foot" consisted of two fragments of tan-pink soft tissue with the larger mass measuring three-and-a-half centimeters by one-and-a-half centimeters by one centimeter. This larger fragment on cut section showed a one centimeter ill-defined, gelatinous and tan-white central portion. Diagnosis was fibrotendinous tissue with edema, myxoid and hyaline degeneration (Figure 6 and 7). Postoperatively, patient was treated about every one to three weeks based on postoperative healing and wound severity for about two-and-a-half years. Wound care treatments included negative pressure therapy, Dermagraft, Prisma, Oasis, Betadine, and Iodosorb. Patient was also treated with offloading modalities, including posterior splint, offloaded walking boots, total contact casts, and, ultimately, modified custom shoes. Radiographs throughout this treatment period did not demonstrate significant bony changes in patient's Charcot foot deformity. Upon final wound closure, the patient was graduated to regularly scheduled preventative appointments.

Case 3

A fifty-eight year old male with a past medical history of type 2 diabetes, peripheral neuropathy, congestive heart failure, and chronic obstructive pulmonary disease, history of cerebral vascular accident, peripheral vascular disease, and hypertension presented to clinic with a chief complaint of a one year history of right midfoot collapse with new associated plantar midfoot wound. Patient denied pain. Pertinent physical exam revealed nonpalpable pedal pulses, absent sensation to Semmes Weinstein monofilament, and a rocker bottom appearance with equinus deformity. The wound was also noted to have serous drainage. Patient was treated with silvadene, dry sterile dressings and custom diabetic shoes. Throughout the course of patient's preoperative care, he was followed every one to three weeks with continued wound care and offloading shoe gear. Four months after initial presentation, patient's wound remained open with persistent serous drainage and patient received an excisional biopsy of wound tissue. Surgical pathology revealed soft tissue with necrosis, acute and chronic inflammation and granulation tissue. Five months

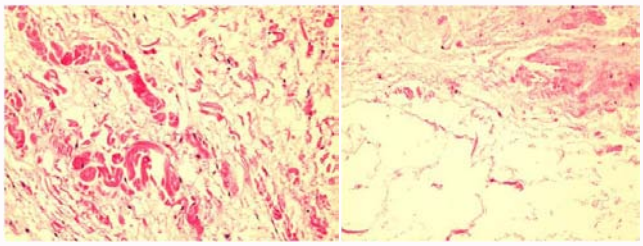

Figure 7: Pathology analysis revealing ill-defined, gelatinous and tan-white central portion of mass. Diagnosis consistent with fibrotendinous tissue with edema, myxoid and hyaline degeneration.

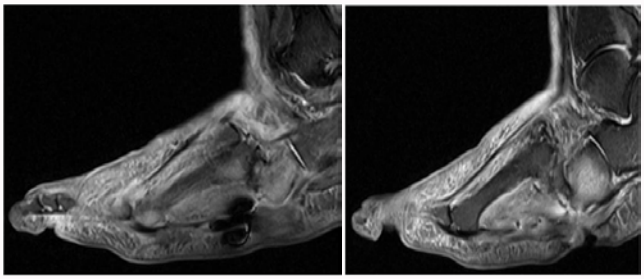

Figure 8: MRI revealing findings consistent with known neuropathic joint, surrounding cellulitis, and myositis with osteomyelitis of cuboid.

after initial presentation, patient's wound still remained unhealed. A wound culture was taken, revealing the presence of Methicillin Sensitive Staph Aureus (MSSA). Radiographs revealed pes planus with Charcot joint changes, negative for osteomyelitis. Patient was started on Dicloxacillin 250 milligrams four times a day and received continued wound care and offloading shoe gear. Six months after initial presentation, patient presented with complaints of new onset right lower leg redness and swelling, foot pain and purulent drainage from wound. Patient was admitted to hospital for clinical diagnosis of right leg cellulitis with associated Charcot foot wound and possible osteomyelitis. Pertinent physical exam revealed erythema noted on foot and leg, extending to knee level and a positive probe to bone test in the foot wound. Patient was started on Vancomycin and Zosyn and admission labs and imaging were ordered. MRI revealed findings consistent with known neuropathic joint, surrounding cellulitis and myositis with osteomyelitis of cuboid (Figure 8). Based on culture and sensitivities (MSSA), patient's antibiotics were also narrowed to Nafcillin. On hospital day seven, patient received plantar exostectomy/planning and a Tendo Achilles lengthening. Intraoperatively, cystic material was noted upon deep wound debridement. The wound site was primarily closed, and patient was placed in a posterior splint, instructed to be non-weight bearing. Surgical pathology of wound specimen revealed soft tissue with granulation, mild acute and chronic inflammation and benign bone with attached soft tissue showing fibrosis and mild chronic inflammation. On hospital day ten, patient was discharged on Keflex with total contact cast placement. Post operatively, patient was followed every week, and sutures were removed at post op week five. Patient then transitioned into CAM boot. Radiographs at this time were negative of osteomyelitis. By post op week seven, the plantar ulcer was closed.

Discussion

Although surgical management has become relatively more common for this disorder, there has been little, if any, mention of a peculiar cystic proliferation noted in the deep soft tissues upon surgical dissection. In our experience such cysts drain synovial fluid, impeding healing of ulcerations. Most times these patients have adequate blood flow to heal what appears to be the usual ulcers but remain resistant to traditional wound care and even advanced modalities. Brenner et al. [43] the only related study that we have found, reports a case of a sixty-two year old diabetic neuropathic male with a Charcot foot type with an obvious palpable mass five centimeters in diameter located superior to the left calcaneocuboid joint with consistency suggestive of cystic neoplasia. Fluid aspirations, vascular studies, and laboratory tests were negative and/or within normal limits. Intraoperatively, a large spherical, fluid-filled sac was revealed that extended deeply within the calcaneocuboid joint, confirmed to be a synovial cyst. Consistent with his findings, our patients also exhibited a translucent, fluctuant, multi-loculated cystic mass present throughout a considerable portion of our dissection. Upon resection, the masses were found to be spongy and contained what appeared to be synovial fluid. Pathology confirmed that these were simple benign cysts. Importantly, however, we found all patients exhibited a delay in wound healing caused by persistent synovial fluid leakage. Some differential diagnoses include dermoid cyst, teratoma, and epidermal inclusion cyst, and steatocystoma. Contents of these cysts may be keratin as in posttraumatic cysts, skin and its appendages as in dermoid cysts, and germ cell derivatives as in teratomas [44]. During wound healing, trapped squamous epithelium, undergoing keratinisation leads to cyst formation. Very few authors have reported such condition making it difficult to retrieve proper articles in the medical literature and derive a relevant message regarding incidence and guidelines for diagnosis and management. A long term follow-up after surgical removal is highly recommended.

Conclusions

Three (3) example cases illustrated what seems to be simple benign cysts all had similar characteristics of translucent, fluctuant, multi-loculated appearance that extended throughout a considerable portion of the dissection. Though observed in many of our diabetic Charcot patients, we have also observed such pathology in our non-diabetic population. Interestingly, we have found a delay in wound healing in these patients due to the persistent synovial fluid leakage. Since most patients with Charcot foot are treated conservatively, these cysts are not usually recognized surgically. While the pathogenesis of Charcot neuroarthropathy has been described, the formation of such related cysts has yet to be explained. We, therefore, encourage clinicians and surgeons to corroborate our findings with further study of this interesting pathology.

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