Case Report

Neuropathic Arthropathy of the Hip as a Sequela of Undiagnosed Tertiary Syphilis

Nicholas A. Viens MD, Tyler Steven Watters BA,
Emily N. Vinson MD, Brian E. Brigman MD, PhD

Received: 19 September 2009 / Accepted: 25 January 2010 / Published online: 12 February 2010
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Abstract

Background Neuropathic arthropathy is characterized by rapidly progressive bone destruction in the setting of impaired nociceptive and proprioceptive innervation to the involved joint. It is seen most commonly in the foot and ankle, secondary to peripheral neuropathy in patients with diabetes mellitus. Other less common sites of involvement may include the knee, hip, shoulder, and spine, depending on the underlying etiology. Neuropathic arthropathy can be associated with tabes dorsalis, a unique manifestation of late, tertiary neurosyphilis that may arise in individuals with untreated syphilis many years after initial infection, and usually involves the knee, or less commonly, the hip. **Case Report** We report the case of a 73-year-old man with neuropathic arthropathy of the hip and tabes dorsalis attributable to previously undiagnosed tertiary syphilis. There was considerable delay in the diagnosis and unnecessary diagnostic testing owing to failure to consider syphilis as the cause.

Literature Review With the advent of effective antimicrobial therapy and public health campaigns, the relationship between untreated syphilis and neuropathic arthropathy has been primarily a historic point of interest. However, current epidemiologic research suggests a resurgence of syphilis in the United States, with an increased incidence of patients presenting with manifestations of tertiary syphilis from unidentified and untreated primary infections. Treatment options for neuropathic arthropathy of the hip are limited. Arthrodesis has had poor success and treatment with THA has had high complication rates.

Conclusions Syphilis is not merely a historic cause of neuropathic arthropathy. Neurosyphilis and tabes dorsalis should be considered in the differential diagnosis for patients presenting with rapid joint destruction consistent with Charcot arthropathy and no other apparent cause.

Introduction

Neuropathic or Charcot arthropathy is a condition of uncertain etiology. Neuropathic arthropathy is characterized by rapidly progressive bony destruction in the setting of impaired nociceptive and proprioceptive innervation to the involved joint [2, 4]. Historically, Charcot joints most commonly were associated with syphilitic (*Treponema pallidum*) infections before introduction of effective antibiotics in the mid-20th century. Jean-Marie Charcot's description of neuropathic joints in 1868 described patients with tabes dorsalis—a form of tertiary neurosyphilis that may develop months to decades after the patient's initial infection [6]. Currently the most frequent manifestations of this degenerative process arise in the feet and ankles of patients with diabetes mellitus [2]. Cases involving the hip are quite rare [12].

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Each author certifies that his or her institution either has waived or does not require approval for the reporting of this case, that all investigations were conducted in conformity with ethical principles of research, and informed consent was obtained for participation.

N. A. Viens, T. S. Watters (✉), B. E. Brigman
Division of Orthopaedic Surgery, Department of Surgery, Duke
University Medical Center, Durham, NC 27710, USA
e-mail: tsw9@duke.edu

E. N. Vinson
Division of Musculoskeletal Imaging, Department of Radiology,
Duke University Medical Center, Durham, NC 27710, USA

The clinical presentation of syphilis occurs in several distinct stages. Primary syphilis manifests as a painless chancre in the anogenital region shortly after exposure. If untreated, the infection may progress to the secondary stage, classically associated with a rash on the palms and soles along with generalized lymphadenopathy and oromucosal lesions. The infection then may become latent, or develop into the tertiary form of the disease. Tertiary syphilis can manifest as gummatous disease with the development of granulomatous lesions in various organ systems, or alternatively present with cardiovascular or neurologic involvement (eg, tabes dorsalis).

As public health campaigns expanded and penicillin in particular became increasingly available, the rates of syphilis decreased dramatically in the United States, in terms of the overall incidence and the prevalence of early and late stages of the disease [7, 8]. As these rates declined, so did the modern medical community's familiarity with its innumerable clinical presentations and long-term sequelae [7–9]. Although syphilis is not the dominating public health issue it once was, it remains an important disease for healthcare providers to keep in their differential diagnoses, particularly in light of the increasing rates of syphilis in the US since the start of the 21st century [5].

We describe a patient with an unexplained neuropathic hip who presented for a presumed malignancy or chronic septic joint, but in whom neurosyphilis ultimately was diagnosed and found responsible for his destroyed, yet painless hip.

Case Report

A 73-year-old man was evaluated by his primary care physician for progressive weight loss, lethargy, and anorexia. Three months earlier he had a routine primary right TKA for presumed osteoarthritis. Preoperatively, the patient was noted to have mild pain, swelling, and a progressive valgus deformity in his right knee. Physical examination reportedly showed normal ROM with prominent crepitus, and radiographs showed tricompartmental degenerative joint disease. The patient had required occasional use of a cane and had been living independently. Postoperatively he initially did well and was walking with a cane. However, his rehabilitation subsequently progressed slowly unrelated to the TKA, but secondary to progressive limp and weakness in the contralateral extremity about the hip. Nearly 3 months after the TKA the patient required a wheelchair compared with walking with a cane shortly after the initial procedure. He denied pain in the left hip but had slightly decreased ROM on examination. He had no history of trauma, malignancy, or infection, and his medical history was significant only for

hypertension and coronary artery disease. His primary physician obtained radiographs of the pelvis owing to the patient's progressive difficulty walking. Radiographs showed complete destruction of the patient's contralateral proximal femur and acetabulum, thereby leading to additional workup with a bone scan, CT, and MRI. Mass-like fluid collections about the left hip were observed on imaging and later sampled via CT guided fine-needle aspiration. Histologic examinations revealed necrosis and chronic reactive changes, but otherwise were nondiagnostic, and cultures for bacteria, fungi, and acid-fast bacilli remained negative. Staging CT scans of his chest, abdomen, and pelvis showed no primary malignancies or other suspicious areas, and laboratory results remained nonspecific. Nevertheless, given his imaging results and generalized clinical picture including decreased energy, anorexia, dysphagia, and progressive weight loss, it was presumed the patient likely had an advanced malignant disease and was referred to hospice care.

After 3 months of supportive care, his generalized health had improved and hospice care was discontinued. The patient at that point was able to return home under the care of his wife, although there had been no improvement in his ability to bear weight making him essentially non-ambulatory. Nevertheless, he continued to remain pain free. Nine months after the TKA, the patient and his family sought a second opinion and presented for evaluation by our orthopaedic oncology service.

The subsequent physical examination of the patient by our team was largely unremarkable, with the exception of a generalized decrease in left hip motion and his inability to ambulate. There was no specific weakness and there were no palpable masses, fluid collections, or appreciable lymphadenopathy. The patient had no pain with active or passive hip motion. New radiographs of the hip and pelvis again showed destruction of the left hip with extensive bone resorption and periarticular ossification without evidence of soft tissue mass (Fig. 1). Given the patient's lack of pain or constitutional symptoms and the radiographic appearance of his hip, we considered a neuropathic joint of unclear etiology as the most likely diagnosis. Syphilis, along with other causes of neuropathic joint (spinal cord disorder, syringa) were considered. However, without an explanation for a neuropathic hip and given concerns of previous physicians and his family for malignancy or infection with a nondiagnostic workup, the decision was made to proceed with advanced imaging, laboratory tests, and possible repeat biopsy.

CT scans of the chest, abdomen, and pelvis showed no evidence of neoplasm but did reveal a large central pulmonary embolism (PE) and deep vein thrombosis (DVT) in the proximal left femoral vein. The patient was largely asymptomatic, noting only some mild shortness of breath

during the preceding week that he associated with a recent viral upper respiratory infection but was admitted directly to the general internal medicine service from the radiology suite for monitoring and anticoagulation. CT scans also showed destruction of the left hip, with associated fluid collections and periarticular debris (Fig. 2). While an inpatient receiving care for the PE and DVT, MR images of the lumbar spine and pelvis (Fig. 3) were obtained; they again showed nonspecific hip destruction but an overall decrease in fluid signal in the surrounding soft tissues compared with his previous MR images obtained at an outside institution. His lumbar spine MR images showed degenerative disease but no lesions or fluid collections. A neuropathic joint again led the differential diagnosis given the substantial joint destruction, the interval decrease in periarticular fluid making infection less likely, and the lack of neoplastic disease found with radiographic or laboratory studies.

Fig. 1 A radiograph of the left hip shows extensive bone resorption of the femoral head and neck, along with superolateral subluxation of the hip and periarticular osseous debris.

During the first 3 days of this admission, at the request of the consulting orthopaedic service, the patient was tested for syphilis and tuberculosis to rule out other possible infectious causes of joint destruction. Rapid plasma reagin (RPR) screening was reactive, and subsequent confirmatory testing for immunoglobulin G antibodies to *T pallidum* was positive by immunologic assay, indicating active infection. To rule out secondary infection or underlying malignancy, an open biopsy of the left hip was performed during the patient's hospitalization. On open biopsy, there was substantial heterotopic ossification immediately deep to the fascia with destruction of the underlying greater trochanter and femoral head. Fibrinous tissue surrounding the remnants of the proximal femur was removed, along with bony fragments and synovial tissue which were sent for culture and pathologic examination. No gross purulence was noted. Histopathologic examination of the biopsy samples showed synovial lining and associated soft tissue with minimal chronic inflammation and fragments of necrotic bone and cartilage consistent with reactive

Fig. 3 A coronal T1-weighted MR image of the pelvis shows extensive destruction of the left hip with bone resorption.

Fig. 2A–B Axial CT images with (A) soft tissue and (B) bone windows show destruction of the left hip with fluid and soft tissue densities in the joint space, extensive resorption of bone from the left acetabulum and left femoral head, and foci of osseous debris about the joint.

Fig. 4 A low-power photomicrograph shows fragments of necrotic bone embedded in fibrous tissue (Stain, hematoxylin and eosin; original magnification, $\times 40$).

synovitis (Fig. 4). No acute inflammation, gummatous lesions, or malignancy was identified. Immunohistochemical staining for spirochetes did not reveal organisms. One culture sample eventually grew broth-only contaminants, as determined by the infectious diseases team assisting with the care of the patient.

After the biopsy, a lumbar puncture was performed by the internal medicine team and cerebrospinal fluid (CSF) samples showed a reactive Venereal Disease Research Laboratory (VDRL) test, thereby confirming the suspected diagnosis of neurosyphilis. The patient was treated with 14 days of intravenous penicillin and provided close outpatient followup to monitor the decline of his RPR in response to antibiotic therapy. Additional discussion with the patient and his family members to uncover the full extent of his newly diagnosed neurosyphilis suggested a progressive cognitive decline and difficulty walking during the preceding 4 to 5 years. Detailed peripheral nerve examination subsequently revealed the distinct loss of vibratory sensibility and proprioception in the bilateral distal lower extremities with intact pain and light touch sensation, consistent with degeneration of the dorsal columns of the spinal cord. Laboratory workup for other neuropathies remained unremarkable. As such, the patient ultimately was diagnosed with tabes dorsalis, which had led to the development of neuropathic arthropathy of the hip.

Given his general state of health, lack of pain, and the extensive bone loss involving his hip, after discussion with the patient and his family, it was determined that arthroplasty was not a reasonable treatment option.

Extensive physical and occupational therapy instead were arranged with the goal of improving his ambulatory status through the use of a walker. He continues to see the orthopaedic and infectious diseases teams to follow his progress.

Discussion

This case report highlights a 73-year old patient with Charcot arthropathy of the hip attributable to previously undiagnosed tertiary syphilis and tabes dorsalis. Despite the radiographic appearance consistent with neuropathic joint destruction and an extensive nondiagnostic workup for malignant and chronic infectious etiologies, the patient was falsely assumed by outside practitioners to have an advanced malignancy and ultimately was referred for hospice care. The patient later presented to our institution for additional workup for malignancy. Although his clinical picture and imaging were suggestive of a neuropathic joint, given the painless and profound destruction of the hip in the overall setting of his slow decline and gait ataxia, neuropathic hip had not been considered high on the differential because he had no clear reason to have had a neuropathic hip develop, such as syringomyelia or other spinal cord disorder [2, 3]. Multidisciplinary discussions between orthopaedic oncology, musculoskeletal imaging, and pathology specialists considered neurosyphilis as a possible cause of an unconfirmed Charcot hip in this patient, although it had not been seen clinically in many years by our group of specialists despite considerable years of experience. Neurosyphilis eventually was diagnosed and confirmed by positive RPR, confirmatory T pallidum assay, and positive CSF VDRL, and further reinforced with the negative histopathologic examinations of open biopsy specimens.

Tabes dorsalis is a unique manifestation of late, tertiary neurosyphilis that arises in 2% to 9% of individuals with untreated syphilis and can present between 3 to 50 years postinfection [8]. The incidence of neuropathic arthropathy in these patients ranges from 6% to 10% [9]. The exact pathophysiology underlying the rapid destructive process of Charcot arthropathy is unclear but likely involves a combination of mechanical, neurologic, and metabolic factors [9, 15]. The loss of proprioception and nociception likely results in repetitive mechanical trauma and neurogenic vasomotor disruption that may lead to increased bone resorption [10].

The most common conditions associated with neuropathic arthropathy include diabetes, syringomyelia, and syphilis although other less common entities have been described, such as leprosy, demyelinating peripheral neuropathies, congenital insensitivity to pain, alcoholism, and even repeated corticosteroid injections [2]. The

location of joint destruction along with a detailed clinical history are important factors in distinguishing the most likely etiology of the neuropathic joint. Neuropathic arthropathy associated with diabetes mellitus is seen most commonly in the midfoot, although it can be associated with other joints in the lower and upper extremities, and the spine. Syringomyelia is the most common cause of neuropathic arthropathy in the upper extremity. It is usually monoarticular and most commonly seen in the shoulder or elbow [2]. Syphilis can result in neuropathic arthropathy in various joints, but historically is the most common cause in the hip. In the patient presenting with tabes dorsalis, clinical examination revealing a loss of vibratory and proprioception but with intact pain sensation may be the distinguishing finding when compared with patients with neuropathic joints associated with diabetic neuropathy, as tabes dorsalis involves the dorsal columns of the spinal cord alone.

The best surgical treatment, if any, for neuropathic arthropathy of the hip is controversial. Historically, arthrodesis was the preferred management strategy and THA was discouraged [4], although this is no longer the case given high failure rates of hip fusion [2]. Later, however, Sprenger and Foley [14] described a successful result of a THA in a preataxic patient with a Charcot hip. Robb et al. [13] subsequently reported the failure of a Charnley THA in a similar patient who also presented without ataxia. Most recently, Rapala and Obrebski [12] described successful THAs in two patients with neuropathic arthropathy although, interestingly, both patients reportedly had received treatment for syphilis before tabes dorsalis developed.

We believed our patient was not an appropriate candidate for surgical management, given his relatively poor general health, personal and family members' goals of care, and the substantial bone destruction present at the time of diagnosis. In retrospect, we question whether the degenerative joint disease for which the patient underwent contralateral TKA was actually Charcot arthropathy as well, as the patient recalled only recurrent swelling of his right knee with only mild pain before undergoing the knee reconstruction procedure. Preoperative imaging of his knee reviewed in retrospect, however, showed tricompartmental degenerative disease, but no substantial deformity or bony destruction worrisome for advanced neuropathic arthropathy of the knee. Nevertheless, arthroplasty to treat Charcot arthropathy of the knee reportedly is more successful than hip reconstruction for a neuropathic hip and may be a reasonable option to relieve pain and restore knee function [11]. TKA in these cases often involves the use of augmentation for bony defects and constrained or long-stem prostheses to address ligamentous instability [11].

Reports during the past several decades of Charcot arthropathy from tabes dorsalis have been confined mostly to nations with a less robust public health infrastructure for disease surveillance, screening, and therapeutic management relative to the United States (eg, Morocco [1]) and populations with an increased incidence of primary syphilis. However, an alarming trend is developing in this country: in 2000, the rates of primary and secondary syphilis reported in the United States were the lowest since the 1940s when reporting began [5], but since that time reported cases have increased substantially. Between 2006 and 2007, the number of reported cases of all stages of syphilis increased 10.7% and the number cases of primary and secondary syphilis increased by 17.5% [5].

Syphilis is not merely an historical cause of neuropathic arthropathy. Our case report illustrates that tertiary syphilis and tabes dorsalis should be considered in the differential diagnosis for patients presenting with rapid joint destruction consistent with neuropathic arthropathy and no other apparent cause, especially when accompanied by other unexplained systemic or cognitive symptoms. By early consideration and confirmation of this diagnosis, important interventions such as antibiotic and physical therapy may be prescribed in a timely manner to address the patient's underlying disease process and avoid unnecessary delay and diagnostic tests.

Acknowledgments We thank Leslie G. Dodd, MD, of the Division of Soft Tissue and Bone Pathology at Duke University Medical Center for contributions with the histologic analyses in this report. We also thank Salutaris Martinez, MD, of the Division of Musculoskeletal Imaging at Duke University Medical Center for input in the radiographic imaging studies presented in this report.

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