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Trigger events for Charcot neuroarthropathy: A retrospective review

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Charcot arthropathy is a rare, but devastating disease process that has significantly debilitating sequelae. While several theories have been discussed within the literature regarding the causative factors, there remains much debate to the exact pathogenesis. Nevertheless, recognition and timely treatment of this issue remains a paramount task for every healthcare provider. In order to accomplish this, we investigated specific trigger events that led to the onset of the Charcot, by subjectively interviewing patients. Ultimately, we were able to identify acute trauma, surgical events, infections, and also overuse injuries all as inciting events to this disease process. The overall goal of this paper is to improve recognition of the possible triggers that leads to the Charcot disease process in order to better care for patients.

Keywords: charcot, diabetic foot, trigger event, neuropathy, neuroarthropathy

Charcot neuroarthropathy is a progressive and destructive process that can lead to debilitating sequelae such as ulcerations, foot deformity, fracture, dislocations, and even amputation [1]. Charcot has been associated with a number of different conditions; however, today diabetes mellitus is found to be the primary cause [2]. The epidemiological data shows that the prevalence of Charcot arthropathy in diabetic patients ranges from 0.08% to 13% while the incidence varies between 0.10% and 29% [1]. This wide difference in incidence within the literature is linked to higher index of suspicion from tertiary providers, such as wound care specialists.

The exact pathogenesis of Charcot remains ill defined. The neurotraumatic and neurovascular theories continue to be the fundamental teachings; however, it is likely that there are a combination of several mechanisms involved [3]. It is thought that autonomic neuropathy, creates a hyperemic response by means of arterio-venous shunting leading to bone resorption and osteopenia. Furthermore, it is suggested that motor neuropathy causes muscle imbalances within the foot, which leads to repetitive microtrauma. This alone, or in combination with a traumatic event begins the process of osseous destruction. Sensory neuropathy prevents the patient from recognizing this microtrauma, thus propagating the Charcot process [4].

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Newer studies relate the pathogenesis to the disruption in the Charcot patient's ability to regulate inflammation. This results in increased levels of proinflammatory cytokines, such as tumor necrosis factor alpha (TNF α) and interleukin-1 β (IL-1 β) and a decrease of anti-inflammatory factors interleukin-4 and interleukin-10. Increased TNF α leads to a cytokine cascade that eventually results in the activation of NF-κB, which causes osteoclast precursor cells to become mature osteoclasts. This process causes excessive bone turnover due to increased osteoclast activity, thus resulting in the Charcot process [5].

To our knowledge, there have been no published reports aimed specifically at the initial inciting event that triggers the acute Charcot cascade. The purpose of this study was to analyze the trigger events leading to the development of Charcot neuroarthropathy with the hope that this information will give rise to preventative measures for these at risk patients.

Methods

Data were obtained from the medical records of patients being treated by the primary author (BHB) with a diagnosis of Charcot neuroarthropathy between 2003 and 2010. The diagnosis of Charcot was based on clinical presentation and radiographic evidence, including advanced imaging studies. Swelling, erythema, warmth, pain, and a temperature gradient of four degrees Fahrenheit or more between the affected and contralateral limb were pertinent to the clinical diagnosis. The clinical diagnosis was then confirmed with MRI or triple phase bone scan.

A total of 211 feet from the records were identified with Charcot; however, only 179 had complete data available. The triggering event was identified through patient interview and clinical examination. Questions regarding prior trauma, surgery, infection, or overuse were discussed in detail in order to help determine the inciting event. In 70 of the feet, a trigger could not be identified, and thus were excluded from the data analysis. The triggering event preceding the acute onset of Charcot was analyzed and classified into five major categories. The first category was acute injury, which included any single, identifiable event such as fractures or sprains that resulted in the onset of the Charcot process.

Diabetic ankle fractures were placed in their own separate category from the acute injury category due to their higher morbidity rate and more unique surgical protocol vs. a non-ankle fracture. The surgical category consisted of patients who developed Charcot following recent non-elective or elective foot surgery. The patients who had a recent of history of infection as an inciting event, but did not undergo any surgical procedures was placed into the infection category. Lastly, the overuse category was for individuals who had an identifiable continued repetitive trauma from a particular event over a period of time. Each foot was then classified based on Sander's anatomic classification system as follows: Type 1=forefoot, Type II = tarso-metatarsal joint, Type III = naviculocuneiform and midtarsal joints, Type IV = ankle joint, Type V = calcaneus [1].

The frequency of each trigger category as well as each anatomic location was analyzed. For exploratory purposes only, given the small subgroup sizes, a chi square test of general association was conducted to compare trigger types by anatomic site. A p-value $\leq .05$ denotes statistical significance.

Results

Complete data was available on 179 out of 211 feet. A specific trigger event could not be identified in 70 feet and these were excluded from the data analysis; therefore, the final cohort included 109 feet. Demographic information is summarized in Table 1. The mean age was 55.97 years old ranging from 28 to 84. There were 64 males and 45 females included in the study. 90% of our patient population was diabetic while the other 10% had neuropathy from other etiologies. Other etiologies did include, but were not limited to Alcoholic Neuropathy, Cauda Equina Syndrome, Agent Orange Syndrome, Idiopathic and Hypothyroidism. Of note, there were two cases of combined Diabetic and Syphilitic Neuropathy.

Overall, the two most common trigger types identified were acute injury and overuse at 44% (48/109) and 18.3% (20/109) respectively as seen in Table 2. These were followed by diabetic ankle fracture and foot surgery (17/109) for the third most common trigger at 15.6% (17/109). Infection was the trigger event in 6.4% of the total feet (7/109).

Age ***(mean ± standard deviation)***	**Gender**	**Diagnosis**
55.97 ± 11.72 (range 28 - 84)	64 male (58.7%) 45 female (41.3%)	Type II IDDM: 48 (44%) Type II NIDDM: 26 (23.9%) Type I DM: 13 (11.09%) DM Type unspecified: 11 (10%) Idiopathic neuropathy: 2 (1.8%) Syphilis/Type I DM: 2 (1.8%) Alcohol/ETOH: 2 (1.8%) Agent Orange poisoning: 1 (.9%) Cauda Equina Syndrome: 1 (.9%) Hypothyroid: 1 (.9%) Type II IDDM/Agent Orange: 1 (.9%) Non-diabetic: 1 (.9%)

Table 1 Demographic Characteristics (N=109)

Trigger Type	**Frequency (%)**
Acute injury	48 (44%)
Overuse	20 (18.3%)
DM Ankle Fx	17 (15.6%)
Sx	17 (15.6%)
Infection	7 (6.4%)
TOTAL	109

Table 2 Trigger Category Percentages

After categorizing the inciting event into a classification of a trigger type, the data was analyzed to compare each event to its associated anatomic location. Acute Trauma was distributed affecting the forefoot 4.2% (2/48), the tarsometatarsal joint 45.8% (22/48), the midtarsal 22.9% (11/48), the ankle 18.8% (9/48) and the Calcaneus 8.3% (4/48). Diabetic ankle fractures accounted for 17 cases and led to a midtarsal arthropathy 5.9% (1/17) and an ankle arthropathy 94.1% (16/17) of the time. Surgical intervention resulted in 17.6% (3/17) forefoot arthropathy, 41.2% (7/17) tarsometatarsal arthropathy, 23.5% (4/17) midtarsal arthropathy and 7.6% (3/17) ankle arthropathy.

Infection, which accounted for 7 cases of arthropathy, was observed 71.4% (5/7) at the tarsometatarsal level and 28.6% (2/7) at the level of the ankle joint. Overuse injury was observed to lead to arthropathy in 20 patients with 50% of those observed at the tarsometatarsal level (10/20), 45% (9/20) at the midtarsal level and 5% (1/20) at the level of the ankle joint.

Based on a chi square test of general association, there is a statistically significant association between trigger category and anatomic classification ($p < .0001$) in terms of the difference in frequencies (Table 3).

			Anatomic Classification				
			I	***II***	***III***	***IV***	***V***
Trigger Category	Acute Trauma	Count	2	22	11	9	4
		% within Trigger Category	4.2%	45.8%	22.9%	18.8%	8.3%
	DM Ankle Fx	Count	0	0	1	16	0
		% within Trigger Category	.0%	.0%	5.9%	94.1%	.0%
	Sx	Count	3	7	4	3	0
		% within Trigger Category	17.6%	41.2%	23.5%	17.6%	.0%
	Infection	Count	0	5	0	2	0
		% within Trigger Category	.0%	71.4%	.0%	28.6%	.0%
	Overuse	Count	0	10	9	1	0
		% within Trigger Category	.0%	50.0%	45.0%	5.0%	.0%
Total		Count	5	44	25	31	4
		% within Trigger Category	4.6%	40.4%	22.9%	28.4%	3.7%

Table 3 Association Between Anatomic Site and Trigger Categories

Discussion

This study examines patients with Charcot neuroarthropathy and investigates the individual trigger events leading to the development of the disease process to further our insight as healthcare providers. The different trigger categories, as well as the anatomic classifications for each event were evaluated. Our results indicate that the two most common triggers for developing acute Charcot were acute trauma and overuse. Also, 40% of the total cases involved, developed Sanders type II Charcot. Anatomic site II arthropathy was the most common form of Charcot that developed in all of the trigger categories, with the exception of a diabetic ankle fracture, which was the second most common and generated mainly type IV arthropathy. This supports the general teaching that tarso-metatarsal joint Charcot arthropathy is traditionally the most common anatomic type that is observed [6]. In the process of investigating individual trigger events, the authors encountered patterns of inciting events, while no statistical significance could be drawn from these anecdotal incidences.

One mechanism that was most closely associated with a Sanders type II arthropathy was the action of stepping on a ladder. This becomes important as a significant number of our patients work in a more industrial environment and are likely prone to an overuse or acute type injury of the tarsometatarsal complex. A similar mechanism that was demonstrated in a handful of patients was the actions of stepping down to a lower level or onto a curb. Through these mechanisms was both Sanders II and Sanders IV type injuries were associated. Ultimately, while the collection of these events was not statistically significant, they have provided enlightenment to the providers and have affected the questions asked during intake today.

The results of this study were compared to current literature available where other researchers have attempted to understand the causes of Charcot neuroarthropathy. When looking further into the data it is interesting to note that 39% of the original 179 feet could not recall any precipitating event to their acute Charcot.

These patients were ultimately eliminated from data analysis for the purpose of this study. This is in contrast to Armstrong et al where 73% of the subjects could not identify a single trigger event; however, it is possible that there is overlap between the overuse category and these patients.[7] Furthermore, Papanas et al reported patients recalling a traumatic event in 36% of their patient population with a 12% association with surgical intervention [6]. Regardless, it is important to remember a singular trigger event may not always be identifiable and Charcot arthropathy should not be ruled out of the differential diagnosis subsequently.

In order to perform a comprehensive assessment of the diabetic foot, it is important to incorporate other considerations. Foltz et al evaluated both vascular and neurological findings in patients with Charcot foot deformity in order to identify high risk factors for development of a protocol for early detection in the non-hospital setting [8]. Additionally, Armstrong and Lavery analyzed peak plantar pressures of Charcot and non-Charcot feet to examine if this was a risk factor for or associated with the development of Charcot [7]. In conclusion, the authors felt that measuring these plantar pressures may be an effective addition to the screening protocol for these types of patients [9]. Rajbhandari et al proposed that pathognomonic factors for Charcot neuroarthropathy, likely involve a synthesis of competing classic theories [10]. It was believed that a substantial number of cases were likely triggered by a traumatic event, which also instigated an abnormal vascular reflex resulting in hyperemia to osseous components [11].

The limitations of this study includes the fact that it was a retrospective analysis. Additionally, the report of each trigger event was subjective and dependent upon the insight from each patient.

We believe that the information from this study could be used in order to better educate our diabetic neuropathic patients on the topic of Charcot neuroarthropathy to aid in preventing its onset or to expedite treatment modalities with earlier recognition. Another important point for both clinicians to remember and for patient teaching purposes, is that the repetitive and overuse activities should not be overlooked as these can lead to a significant amount of neuroarthropathy.

It is extremely important that all diabetic patients with peripheral neuropathy are properly educated on Charcot. The repercussions of a missed diagnosis given the expansive list of complications secondary to Charcot neuroarthropathy must be impressed upon high-risk patients. The intention of this paper was to display the different trigger categories and their frequencies so that this information could be used for prevention and educational purposes.

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