

CASE REPORTS

The Charcot Neuroarthropathy as Onset of Type 2 Diabetes – a Diagnostic Challenge

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ABSTRACT

Introduction: The Charcot neuro-osteoarthropathy is a devastating complication of diabetes, with negative impact on both prognosis and quality of life. Moreover, the diagnostic is often missed or delayed.

Case report: A 50 years old male patient with dyslipidemia, overweight and hypertension was referred to our Diabetes Department in the context of newly diagnosed diabetes (HbA_{1c}=11.7%), four days after left hallux trans-metatarsal amputation and debridement of the dorsal collection, for wet gangrene of the left hallux, with dorsal extension. The diagnostic of diabetic neuro-osteoarthropathy of the left foot was delayed several months. A good glycemic control was achieved with insulin glargine and metformin. We look further to introducing modern antidiabetic drugs with not only proven cardiovascular benefit but also good impact on weight. The patient needs to be managed by a multidisciplinary team, which has to include a podiatrist and a vascular surgeon.

Conclusions: This case suggest the importance of rising diabetes and diabetic peripheral polyneuropathy awareness in all medical fields.

Keywords: Charcot, late diagnosis, amputation, obesity, podiatry.

INTRODUCTION

Charcot foot (CF) is a „potentially limb-threatening lower-extremity complication of diabetes”, “characterized by varying degrees of bone and joint disorganization”, according to Rogers et al. (1). The prevalence is vari-

able in the literature, ranging from 0.08% to 13% of diabetes patients, being one of the possible consequences of diabetic peripheral polyneuropathy (DPN) in this population (1, 2). Morbidity and mortality rates are very high, and the quality of life is also affected (2). Early intervention may lower the risk for severe foot deformities, ulcerations and amputations (3). □

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CASE REPORT

A 50 years old male with newly diagnosed diabetes was referred to our Diabetes Department from the General Surgery Department, four days after left hallux trans-metatarsal amputation and debridement of dorsal collection for wet gangrene of the left hallux with dorsal extension (Figure 1c). The patient was accusing weight loss (about 10 kg), polyuria, polydipsia and xerostomia in the last four months.

The patient’s medical history included arterial hypertension, obesity, dyslipidemia and cardiac ischemic disease – stable angina. His social history was also significant; he used to work in a slaughterhouse, using special shoes for food industry. Admission medication included enalapril, indapamide, metoprolol and simvastatin.

The current illness history is further described. Five months before admission, after a minor trauma, the left foot became swollen, erythematous, painful, with function laesa (Figures 1a and 1b). At that moment, medical evaluation indicated possible ankle sprain, but specific therapeutic measures (including orthopedic cast) failed to have the expected results. The patient resumed his professional activity in the slaughterhouse about three months after the initial trauma and he had shortly observed an ulceration of about 1 cm on the dorsal face of his left

hallux, along with left hallux color changes (Figure 1c). Two weeks later, he came at the emergency room, where surgical evaluation revealed wet gangrene of the left hallux with dorsal extension (Figure 1d). That was the moment when diabetes was diagnosed. The patient was admitted to the surgery department for amputation and four days later he was referred to our department.

On clinical examination, the patient was afebrile and had the following parameters: height 180 cm, weight 95 kg, maximum weight 105 kg, BMI=29.32 kg/m², BP=120/80 mm Hg, HR=72 bpm regular, and palpable peripheral pulses. Left foot inspection showed important deformity, the foot being swollen, with increased local temperature related to the contralateral foot. The post amputation wound site had a good evolution, with no signs of infection (Figure 2a). The right foot examination revealed intense skin dryness of the plantar foot and hammer toes.

Laboratory tests revealed: HbA1C 11.7%; glycemia 168 mg/dL; lipid profile including serum triglycerides 250 mg/dL, total cholesterol 154.45 mg/dL, HDL cholesterol 20.12 mg/dL, and calculated LDL cholesterol 84.3 mg/dL; eGFR 66.04 mL/min/1.73; and albumin/creatinine ratio 60.28 mg/g creatinine. Bacteriological examination of the wound revealed MRSA sensitive to quinolones, vancomycin, tigecycline, linezolid and resistant to beta-lactam antibiotics, macrolides, rifampicin, gentamicin, and doxycycline.

Other significant investigation were: plain radiographies for the left foot (Figures 2b and 2c) and the right foot (no signs of CF), fundoscopy revealing mild non-proliferative diabetic retinopathy (NPDR), ankle-brachial index 1.2 for the



FIGURE 1. Left foot clinical evolution: a) and b) aspects after initial trauma; c) two weeks before admission; d) in the morning of the presentation at the emergency room



FIGURE 2. Clinical (a) and radiological (b, c) aspects of left foot five days after surgery. Plain radiographies reveal Charcot-specific lesions involving tarsometatarsal region; arterial calcifications

right foot, and bilateral alteration of temperature sensation, vibration perception, and touch-pressure sensation more prominent on the left foot.

The main diagnostics established were as follows: type 2 diabetes mellitus, insulin-requiring and left hallux trans-metatarsal amputation for wet gangrene of the left hallux, associating Charcot neuroarthropathy (left foot) in the context of DPN. Diabetes appeared in the presence of metabolic syndrome, and at the time of diagnosis the patient had mild NPDR as microvascular complication and ischemic cardiomyopathy as macrovascular complication. Microalbuminuria may be explained by the acute glycemic imbalance and requires further assessment.

During hospitalization, the patient was given basal insulin therapy with glargine and metformin, with good glycemic control. He has also received daily surgical assessment and wound cleansing, antibiotic therapy according to antibiogram.

In this context, the recommended nutrition therapy at discharge included 1800 kcal/day distributed as 55% carbohydrates (247 g), 20% proteins (90 g), 25% fats (50 g), and Sodium <2,300 mg/day. The recommended antidiabetic therapy was long acting insulin analog glargine 30 units/day associated with metformin 2000 mg/day. The patient has also received levofloxacin 500 mg/day p.o. for seven days, high dose of atorvastatin, acetylsalicylic acid 75 mg/day, omeprazole, enalapril, metoprolol, a combination including benfotiamine, pyridoxine clorhydrate, cyanocobalamin, and tiotic acid. □

DISCUSSION

Given the patient's high HbA_{1c} level, the presence of symptoms suggesting insulin deficiency, and the recently occurred major surgical event, we considered that a basal insulin regimen associated with metformin was the most favorable option at the moment. However, according to the current guidelines, since the patient had ischemic cardiomyopathy, it would be a priority to introduce modern antidiabetic drugs with proven cardiovascular disease (CVD) benefit. On the other hand, an optimal weight management in a previous obese patient would be important, because it would reduce weight-bearing on the operated limb. The options would be either a sodium glucose cotransporter 2 inhibitor

with proven CVD benefit or a GLP1-receptor agonist with proven CVD benefit and good efficacy for weight loss. The choice will depend on the patient's metabolic and clinical evolution, avoiding medication that increase the risk of amputation. A HbA_{1c} target of 6.5-7% was recommended (4).

Nutrition therapy is important, since the offloading procedures may produce changes in lifestyle, including limitation of physical activity (5). Diet recommendations were in agreement to the current guidelines for diabetic patients, targeting weight loss (5-10% of his weight over the next six months); the other comorbidities have been also approached according to guidelines (4). Targeting oxidative stress may be an option in such patients, since it is linked to DPN (6).

The literature data show that in 25% of CF cases the diagnose is missed or delayed, due to the resemblance with more common clinical conditions, such as ankle sprain, osteomyelitis or cellulitis, deep venous thrombosis, gout (1, 3, 7). The diagnostic of acute CF must be suspected in any patient with diabetes and a red, swollen, painful and warm foot (8). However, in this case, diabetes was diagnosed only after the onset of major complication, although the patient presented many criteria for diabetes screening, and this late diagnosis was an important contributor to the defective management of the case prior to the current admission (9). Radiological findings confirmed the diagnosis.

Undiagnosed diabetes is a public health issue highlighted by this case. In Romania, the overall prevalence of diabetes mellitus in a population aged 20-79 years was 11.6%, of which 2.4% had unknown diabetes (10). The benefits of therapeutically antidiabetic interventions, such as reduction of complication rate, are lost for those with undiagnosed diabetes (11). One of the most important complications is DPN, which is estimated to affect about 30-50% of people with diabetes and which may lead to structural foot deformities, foot ulcers and amputations (1, 12). However, peripheral nerve dysfunction is not only specific to diabetes, the literature showing that sensory peripheral neuropathy is also linked to some conditions that present high risk for developing diabetes, such as prediabetes, obesity and metabolic syndrome (13).

It is noticeable that our case presented some typical features for patients with CF such as uni-

laterality, appearance in sixth decade of life, male gender (tending to prevail in some studies), involvement of midfoot and association with obesity (2, 7). A longer diabetes duration (>10 years) is correlated with CF. For our patient, it is difficult to estimate the real duration of diabetes (2). The absence of pain caused by DPN may expose the foot to external factors such as ill-fitting foot wear, and could lead to further complications, especially when the foot is already at risk for ulcers or amputation because of the deformity, as it happened the case described by us (4, 14).

Diabetic foot care must be performed by a multidisciplinary team, including a podiatrist and a vascular surgeon (15). Since patients associating peripheral artery disease and CF have a major risk for ulceration and amputation, it may be

useful for our patient to complete the vascular assessment (16). □

CONCLUSION

It is necessary to rise diabetes awareness and improve medical education regarding DPN and CF in all medical fields. An early detection may reduce the risk of deformities and fractures. Since the literature data show that prediabetes, obesity and metabolic syndrome are associated with sensory peripheral neuropathy, screening for this type of neuropathy might be necessary not only in patients with diabetes but also in those at risk for developing type 2 diabetes. □

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REFERENCES

1. **Rogers LC, Frykberg RG, Armstrong DG, et al.** The Charcot foot in diabetes. *Diabetes Care* 2011;34:2123-2129.
2. **Salini D, Harish K, Minnie P, et al.** Prevalence of Charcot Arthropathy in Type 2 Diabetes Patients Aged over 50 Years with Severe Peripheral Neuropathy: A Retrospective Study in a Tertiary Care South Indian Hospital. *Indian J Endocrinol Metab* 2018;22:107-111.
3. **Vopat ML, Nentwig MJ, Chong ACM, et al.** Initial Diagnosis and Management for Acute Charcot Neuroarthropathy. *Kansas J Med* 2018;11:114-119.
4. **American Diabetes Association.** Standards of medical care in diabetes- 2019. *Diabetes Care* 2019;42:S1-S193.
5. **Mrdjenovich DE.** Off-loading practices for the wounded foot: concepts and choices. *J Am Col Certif Wound Spec* 2010;2:73-78.
6. **Oyenih AB, Ayeleso AO, Mukwevho E, et al.** *Antioxidant Strategies in the Management of Diabetic Neuropathy.* BioMed Research International. Hindawi Publishing Corporation 2015, 15 pp.
7. **Kaynak G, Birsel O, Güven MF, et al.** An overview of the Charcot foot pathophysiology. *Diabet Foot Ankle* 2013;4.
8. **Yousaf S, Dawe EJC, Saleh A, et al.** The acute Charcot foot in diabetics: Diagnosis and management. *EFORT open Rev* 2018;3:568-573.
9. **Handelsman Y, Bloomgarden ZT, Grunberger G, et al.** American Association of Clinical Endocrinologists and American College of Endocrinology – Clinical practice guidelines for developing a Diabetes Mellitus comprehensive care plan – 2015. *Endocr Pract* 2015;21:1-87.
10. **Mota M, Popa SG, Mota E, et al.** Prevalence of diabetes mellitus and prediabetes in the adult Romanian population: PREDATORR study. *J Diabetes* 2016;8:336-344.
11. **Beagley J, Guariguata L, Weil C, et al.** Global estimates of undiagnosed diabetes in adults. *Diabetes Res Clin Pract* 2014;103:150-160.
12. **Mahfouz H, Hashem A, Mostafa Yasser Hamed.** Risk factors for early development of polyneuropathy among type II diabetic patients. *Int J Adv Res* 2017;5:1001-1006.
13. **Stino AM, Smith AG.** Peripheral Neuropathy in Prediabetes and the Metabolic Syndrome. *Journal of Diabetes Investigation* 2017;5:646-655.
14. **Bowling FL, Rashid ST, Boulton AJM.** Preventing and treating foot complications associated with diabetes mellitus. *Nat Rev Endocrinol* 2015;11:606-616.
15. **Chandra V, Glebova NO, Salvo NL, et al.** Partnerships between podiatrists and vascular surgeons in building effective wound care centers. *J Vasc Surg* 2017;66:902-905.
16. **Çildağ MB, Köseoğlu ÖFK.** The Effect of Charcot Neuroarthropathy on Limb Preservation in Diabetic Patients with Foot Wound and Critical Limb Ischemia after Balloon Angioplasty. *J Diabetes Res* 2017;2017:1-4.