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Multifocal (tarsus and knee) activation of neuroarthropathy following rapid glycaemic correction

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ABSTRACT

Objective: To report a case of neuroarthropathy in the tarsus and knee following rapid glycaemic normalisation in a female patient with type I diabetes.
Methods: A retrospective review of case notes.
Results: We describe the case of a female patient with type I diabetes who had developed a multifocal neuroarthropathy in only six months, probably due to a rapid glycaemic normalisation. The onset of this neuroarthropathy was not only fast but mostly multifocal affecting two levels of joints.
Conclusion: The link between the onset of multifocal neuroarthropathy and the rapid correction of chronic hyperglycaemia is probably proven in our case. Patients with chronic hyperglycaemia with sensitive neuropathy should benefit from a gradual correction of their glycaemic imbalance in order to avoid the apparition of neuroarthropathy.

1. Introduction

Rapid normalisation of hyperglycaemia may, in some cases cause acute neuropathy affecting small peripheral nerve fibres.[1] Such neuropathy generally presents as a diffuse disorder of the sympathetic and parasympathetic fibres in the form of pain, characteristic of small neurological fibres (Electric discharges, burning sensation) or as cardiovascular signs, orthostatic hypotension, tachycardia, and diarrhoea associated with colonic activity. These signs could usually be reversed after several months.

Neuroarthropathy (NA) or "Charcot neuroarthropathy" (CN) consists of acute osteoarticular destruction occurring in the context of neuropathy, most commonly in the foot, and in some cases in the knee.[2] The physiopathology of this disorder is poorly understood. The onset of CN has been reported during weight loss following bariatric surgery[3] and after kidney-pancreas transplantation,[4] but its relationship with the rapid reduction of blood glucose levels is unclear.

Herein, we report a case, to our knowledge unprecedented, of CN in the tarsus and knee following rapid glycaemic normalisation in a female patient with type I diabetes.

2. Patients and methods

Our patient was 25 years old and was being treated for type I diabetes diagnosed at the age of nine years. She had no other medical history. She was initially hospitalised in 2017 for the management of major glycaemic imbalance with an HbA1c of 12%. She was 167 cm tall and weighed 62 kg. The clinical examination revealed peripheral neuropathy with paraesthesia in the lower limbs and pathological results in the monofilament test. The laboratory tests showed microalbuminuria (289 mg/l) with normal Glomerular filtration Rate (GFR 80 ml/min/1.73 m^2) evocative of incipient nephropathy. Her sole treatment consisted of insulin (via a subcutaneous insulin pump). Two months later, she consulted for unplanned pregnancy at six weeks' amenorrhoea. Her HbA1c at this point was 9%. Ophthalmology results were normal (no diabetic retinopathy). Intensive glycaemic management was initiated. At 24 weeks' amenorrhoea, the patient was hospitalised due to vomiting and suspected pregnancy-related thyroiditis. HbA1c was 7.4% (60% reduction over a six-month period). Her weight was 72.6 kg.

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Corticosteroids (Prednisone® 40 mg/day) were given intravenously for three days. The patient reported an injury to her right ankle three weeks earlier with the presence of untreated peri-malleolar swelling, and this oedema of the right ankle and foot were still present. Thrombophlebitis was ruled out by venous Doppler ultrasound. X-rays showed no fractures but complete Chopart luxation, highly evocative of acute CN of foot zone III.[5] An ultrasound of the ankle showed no signs suggestive of the ruptured ligament. Aircast® pneumatic boot was prescribed with reduced weight-bearing.

Ten weeks later, the patient underwent an emergency caesarean delivery due to an impaired foetal cardiac rhythm at 34 weeks' amenorrhea (HbA1c was 7.1%).

An magnetic resonance imaging (MRI) was performed two months after childbirth for persistent foot oedema, which yielded a specific and typical image of active CN in the mid-tarsal zone with the appearance of a displaced joint fracture of the navicular bone, talonavicular luxation, and fracture of the cuboid joint (Fig. 1).

The patient was referred to the orthopaedics department. Weight relief with a plaster cast was prescribed, and surgery was carried out to stretch the knee ligaments (gastrocnemius) in order to correct the support on the foot. The HbA1c was 7.2%, and the patient weighed 68.7 kg.

Two weeks later, the patient was seen for an urgent consultation for three-day-old oedema in the right knee without pain or injury. An x-ray revealed a tibial plateau fracture. The computer tomography scanner showed an extremely complex appearance of the fracture associated with complete tibial plateau collapse (Fig. 1) and diffuse oedema next to the knee. The appearance of the fracture and the oedema suggested active CN of the knee.

A brace was fitted to immobilise the knee, and the patient was instructed not to place any weight on her leg.

3. Discussion

To the best of our knowledge, we report for the first time the occurrence of acute CN of the mid-tarsal zone and the knee during rapid normalisation of chronic hyperglycaemia in a patient with type I diabetes complicated by peripheral neuropathy, over a seven-month period.

CN is a non-infectious process involving rapid destruction of osteoarticular structures. It always occurs in a setting of neuropathy, usually in the foot and more rarely in the knee.[6] The physiopathology may be explained in part by the presence of hypervascularisation in contact with nerve endings, with arteriovenous shunts forming at the same time as the symptoms.[7]

The aetiology of CN is not known. The process begins with a so-called "active" phase in which the following are seen: hypervascularisation of the foot,[8,9] activation of inflammation markers and bone remodelling,[10] increased osteoclast activity,[11] activation of the Rank–Rankl pathway (Receptor Activator of Nuclear factor-Kappa B Ligand),[12] and frequently, fatigue fracture proceeding osteoclast activation and osteoarticular destruction.[9] Although an isolated injury occurred in the initial episode, this factor alone was insufficient to account for the onset of CN. According to Jeffcoate,[12] repeated injuries are required to cause episodes of NA in patients presenting with diabetic neuropathy.

Because the nerve endings in the lower limbs contain small fibres, and since NA also involves xerosis (dysfunction of the sweat glands innervated by small fibres), we hypothesised that rapid normalisation of glycaemia could enhance NA since it contributes to painful neuropathy of small fibres.[1]

Cases of CN of the foot have been noticed following the combined kidney-pancreas transplantation[4] and after bariatric surgery.[3] In our patient, HbA1c fell from the added 12% to 7.4% within six months.

There have been other reports in the literature of CN occurring after rapid glycaemia correction. Indeed, rapid normalisation of hyperglycaemia following bariatric surgery is considered a potential risk factor for CN.[3]

A further potential risk factor for the onset of acute CN is chronic corticosteroid use, for example, in kidney-pancreas transplantation.[4] However, in our case, corticosteroids were given for only three days, and three weeks after the patient first noted the presence of oedema on her foot.

The presence of the disorder in the knee has been described,[2,6,13] though only rarely. Questions may be asked about the role of knee surgery a few days before the onset of NA of the knee, but the type of surgery performed in the case described involved only the ligaments. It has in fact been suggested that surgical treatment of osteitis, for example, could trigger an episode of NA.[14]

Finally, we may ponder the contribution of weight loss during pregnancy and after delivery.

In conclusion, this clinical case suggests that **neuroarthropathy** and "Charcot neuroarthropathy" occur during rapid normalisation of

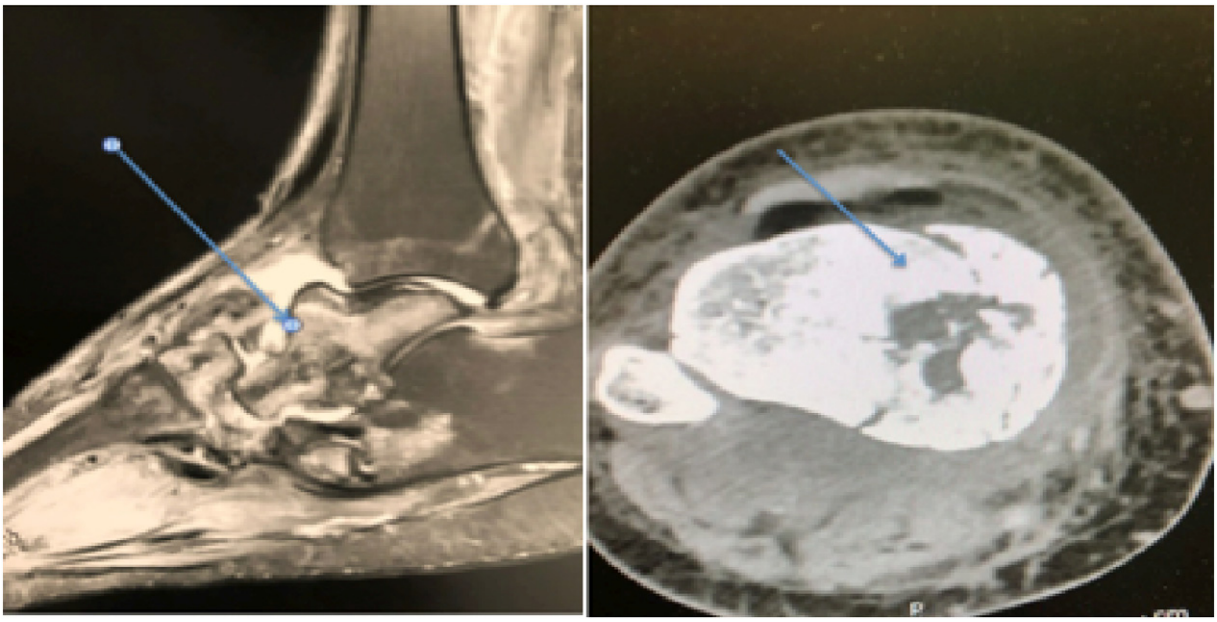

Fig. 1. Mid-tarsal CN and MRI of tibial plateau fracture.

glycaemia in a setting of type I diabetes complicated by peripheral neuropathy. CN may, thus, belong to the clinical signs of small fibre neuropathy already observed in a setting of rapid glycaemic reduction.

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