A Case Report of Peripheral Neuropathy as a Complication of Diabetic Ketoacidosis in a Child with Newly Diagnosed Diabetes Type 1

SCIENCE

Case Studies

A 9-year-old girl with newly diagnosed Type 1 DM, DKA, brain oedema, multifocal vasogenic brain lesions and lower limb paresis was presented for treatment. She had reported polyuria and polydipsia over the past week and a weight loss of 3 kg over the previous month prior to admission. The blood glucose level initially was found to be 1136 mg/dL, and severe acidosis was also present (pH 7.1; BE-25.9). Intravenous fluid therapy and insulin therapy did not show any improvement in her medical and neurological state. Glasgow Coma Scale (GCS) scores depleted from 13 points to 7 points. She experienced agitation and motor restlessness followed by upper limb spasms. Computed tomography scan revealed brain oedema and a hypodense lesion in the left temporal region. An anti-edematous treatment helped improve her medical condition, but she had developed symmetric lower limbs paresis. Brain magnetic resonance imaging (MRI) and nerve conduction studies revealed numerous, diffuse lesions and damaged motor neurons in both lower limbs with dysfunctional both peroneal nerves and the right tibial nerve respectively. She reported improvement in her health after therapeutic regimen intensive physiotherapy.

What will most likely explain the pathogenesis of acute neuropathy in this case?

- Diabetic ketoacidosis
- Peripheral ischemia

Introduction

Neuropathy associated with Diabetic ketoacidosis presents various severe clinical complications. The most common complication is brain oedema, specifically related to central nervous system (CNS) which is prevalent in approximately 0.5-1% of cases with diabetic ketoacidosis (DKA) and has a 20% mortality rate (1,2). Other common less frequent complications are ischemic strokes, hemorrhagic strokes, cerebral vein and sinus thrombosis (3). Neuropathy after DKA is extremely rare.

Medical History

Her past medical history included polyuria and polydipsia over the past week and a weight loss of 3 kg over the previous month with severe dehydration.

Examination and Laboratory Investigations

The laboratory examination included evaluated Blood glucose levels (mg/dL), Osmolarity levels (mOsm/kg H2O), Base excess (mEq/L), Corrected sodium levels (mmol/L), Potassium levels (mmol/L), Phosphate levels (mmol/L), CRP levels (mg/dL), D-dimer levels(ug/L), Fibrinogen levels(g/L). Other investigations made were Computed Tomography Scan, Brain Magnetic Resonance Imaging and lower limb nerve conduction studies.

Management

Treatment included intravenous initial fluid therapy containing 1250 mL 0.9% sodium chloride (NaCl) and 1000 mL of 5% dextrose with 0.9% NaCl (2:1 proportion, sodium concentration-51.34 mEq/L) to restore fluid loss due to excessive dehydration. Then, insulin was infused at a slower rate (0.05 units/kg/hour) to prevent a rapid decrease in glycaemia, but there was no improvement in patient medical condition. After CT scan, an anti-edematous therapy with mannitol 0.3 g/kg/dose, three times a day was introduced for brain oedema; also alpha lipoic acid, vitamins B1, B6 and B12 were added to the therapeutic regimen that helped in improving her medical condition.

Discussion

Diabetic neuropathy is the most common complication of diabetes experienced in approximately 45% of patients with DM2 and 54-59% patients with DM1 (4). It was viewed as an independent entity comprising many types of nerve dysfunction due to various symptoms, clinical courses and pathogenic mechanisms. About 80% of patients with symptomatic DN suffers from various generalised symmetric, chronic polyneuropathy including motor, sensory and autonomic nerve dysfunctions. In most of the cases, DN develops in patients with hyperglycemia (5). Few shreds of the evidence report the occurrence of neuropathy related to newly diagnosed DM1 (6). It can be categorised as acute painful DN, hyperglycemic neuropathy and neuropathy after ketoacidosis. Both symptomatic and asymptomatic changes in nerve function can be seen at the time of DM1 diagnosis.

Previous studies suggested that diabetes mellitus was responsible for mononeuropathy as the onset of neuropathy and motor dysfunction was dependent on the start of DM1 and glycemic control respectively. In this study, the patient suffered from acute motor peripheral neuropathy which can be caused due to DKA. It can be a result of the peripheral ischemia or haemodynamic and metabolic changes linked to the ketoacidosis (7). One hypothesis stated that the procoagulant state occurs during DKA can result in nerve damage through vascular endothelial injury, which is the first line of defence against thrombosis. Endothelial dysfunction results in the activation of coagulation factor and platelet (8,9). The plasma levels of fibrinogen, factors VII, VIII, XI, XII and von Willebrand found to be elevated in DKA. Disrupted anticoagulant mechanisms such as a low protein C level can lead to worsening of a procoagulant state. Impairment of fibrinolysis can occur due to different factors such as more severe degradation of the thrombi or an increased concentration of plasminogen activator inhibitor type 1 (9,10). There was an elevation in d-Dimer levels as indicated by the study, but there is a need for further diagnostic tests. In the present case study, other etiologies of neuropathy, such as hypophosphatemia were also observed and considered during admission to hospital. Hypophosphatemia is generally asymptomatic, but its severity can cause peripheral polyneuropathy that can be both sensory and motor. After normalisation of the phosphate levels, neurological symptoms remains that suggests another alternative mechanism for the pathogenesis of neuropathy. The treatment strategy of DN also included the use of potent antioxidants such as alpha lipoic acid. The efficacy of this therapy was proven in a meta-analysis (10,11).

Learning

Neuropathy can be developed any time after or even before Diabetes mellitus diagnosis. Acute neuropathy after ketoacidosis is rare, but its cause is not apparent yet. It is suggested that patients with DKA need careful monitoring of neurological conditions even after normalisation of glycemic parameters.

References

1. Edge JA, Hawkins MM, Winter DL, Dunger DB. The risk and outcome of cerebral oedema developing during diabetic ketoacidosis. Archives of Disease in Childhood 2001;85:16-22.
2. Dunger DB, Sperling MA, Acerini CL, Bohn DJ, Daneman D, Danne TP, Glaser NS, Hanas R, Hintz RL, Levitsky LL, Savage MO, Tasker RC, Wolfsdorf JI; ESPE; LWPES. ESPE/LWPES consensus statement on diabetic ketoacidosis in children and adolescents. Arch Dis Child 2004;89:188-194.
3. Bialo SR, Agrawal S, Boney CM, Quintos JB. Rare complications of pediatric diabetic ketoacidosis. World J Diabetes 2015;6:167-174.
4. Zilliox L, Russell JW. Treatment of Diabetic Sensory Polyneuropathy. Curr Treat Options Neurol 2011;13:143-159.
5. Tesfaye S, Boulton AJ, Dyck PJ, Freeman R, Horowitz M, Kempler P, Lauria G, Malik RA, Spallone V, Vinik A, Bernardi L, Valensi P; Toronto Diabetic Neuropathy Expert Group. Diabetic Neuropathies: Update on Definitions, Diagnostic Criteria, Estimation of Severity, and Treatments. Diabetes Care 2010;33:2285-2293.
6. Rangel MA, Baptista C, Santos F, Real MV, Campos RA, Leite AL. Acute mononeuropathy in a child with newly diagnosed type 1 diabetes mellitus. J Pediatr Endocrinol Metab 2015;28:341-344.
7. Tracy JA, Dyck PJ. The Spectrum of Diabetic Neuropathies. Phys Med Rehabil Clin N Am 2008;19:1-26.
8. Carr ME. Diabetes mellitus - A hypercoagulable state. J Diabetes Complications 2001;15:44-54.
9. Foster JR, Morrison G, Fraser DD. Diabetic Ketoacidosis-Associated Stroke in Children and Youth. Stroke Res Treat 2011;2011:219706.
10. Ziegler D, Nowak H, Kemplert P, Vargha P, Low PA. Treatment of symptomatic diabetic polyneuropathy with the antioxidant alpha-lipoic acid: a meta-analysis. Diabetic Med 2004;21:114-121.
11. Mijnhout GS, Kollen BJ, Alkhalaf A, Kleefstra N, Bilo HJ. Alpha Lipoic Acid for Symptomatic Peripheral Neuropathy in Patients with Diabetes: A Meta-Analysis of Randomized Controlled Trials. Int J Endocrinol 2012;2012:456279.

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