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Case Report

Paediatrics Section

Acute Painful Neuropathy in a Girl with Type 1 Diabetes: Long Term Follow-Up

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ABSTRACT

Acute Painful Diabetic Neuropathy (APDN) is a reversible neuropathy that occurs in patients with diabetes usually after a fast improvement in glycaemic control. The condition is extremely rare in children with Type 1 Diabetes (T1D). We describe a 12-year-old girl T1D who developed APDN shortly after diagnosis of T1D. Neurological examination, nerve conduction studies showed severe asymmetric lower limb sensorimotor neuropathy. She was treated with carbamazepine and benfotiamine (vitamin B1 analogue), and NSAID analgesics and showed complete recovery 9 months after the onset. The treating physicians should recognize and understand this entity in view of the current recommendations for quick achievement of glycaemic targets in T1D, the need to provide relief from severe pain and to lay emphasis on complete recovery.

Keywords: Benfotiamine, Children, Glycaemic control, Insulin

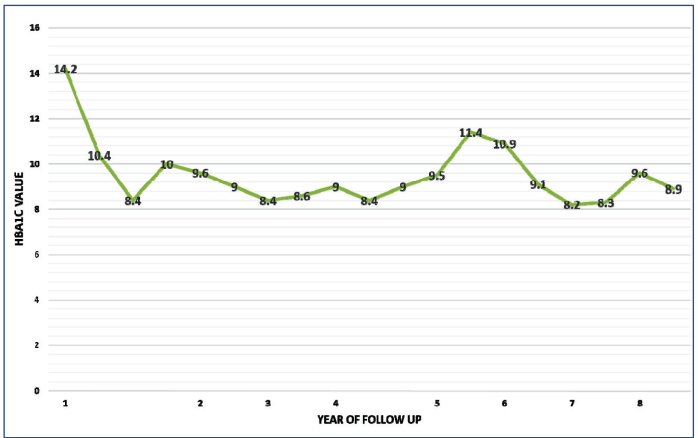
CASE REPORT

A 12-year-old girl was diagnosed as Type 1 Diabetes (T1D) and initiated on premixed insulin. Her glycosylated haemoglobin A1c (HbA1c) at diagnosis was 14.2%. Her compliance and glycaemic control were poor. She belonged to a family of low Socio Economic Status (SES) and both her parents were illiterate. She had not manifested anxiety, depression, and/or posttraumatic stress after the diagnosis of diabetes. She presented to our hospital in Diabetic Ketoacidosis (DKA) one month after diagnosis of T1D. After recovery from DKA, her insulin was titrated to achieve normoglycaemia. Ten days after hospitalisation she started having episodes of hypoglycaemia necessitating a reduction in insulin doses. Repeat HbA1c a month after the initial estimation was 10.4%. During the second week of hospital stay she developed acute onset moderately severe, continuous, burning pain affecting soles and left leg. She described her pain as stabbing and burning in nature. She also perceived contact with bed clothing, socks, shoes or floor as causing extreme discomfort. She could barely move out of bed as a consequence. Her pain only partially and transiently responded to intravenous Tramadol hydrochloride. She had no symptoms in hands or any other neurological complaints.

On examination, her vitals and general physical examination were unremarkable. Her breast development was Tanner stage 2 and pubic hair development was Tanner stage 1. On neurological examination, cranial nerves were normal. There was reduced strength in ankle dorsiflexors (left 3/5 MRC and right 4/5 MRC). Left ankle muscle stretch reflex was absent. Sensory system examination was curtailed by pain, however, revealed impaired touch, pain and temperature sensations below the ankle on the right side and below the knee on the left side. The joint position and vibration sense were impaired at the left great toe and ankle. Postural fall in blood pressure was within normal range. Pulses in the lower limb were normally palpable. A possibility of APDN was considered, and the child was given symptomatic treatment. The nerve conduction studies suggested asymmetric lower limb sensorimotor neuropathy affecting the left more than the right side [Table/Fig-1]. Her insulin was titrated to keep blood glucose levels towards higher side within the target ranges. She was discharged on carbamazepine (8 mg/k/d) and benfotiamine (vitamin B1 analogue) 150 mg twice daily, and NSAID analgesics (for intermittent use). At the three months follow-up the symptoms were static and neurological examination showed similar findings with additional mild wasting of left calf muscles. Gradually over the next few months her pain decreased. Nine months after hospitalisation, she became symptom-free. Over the last eight years of follow-up, she had continued to remain asymptomatic.

Nerve	Side	Distal latency (ms)	Amplitude	Conduction velocity (m/s)
Motor nerve conduction				
Tibial Nerve	Left	Not recordable*		
Peroneal nerve	Left	Not recordable*		
Ulnar nerve	Left	2.5 (<3.3)	12.55 mV (≥2.3)	48.97(≥39.7)
Tibial Nerve	Right	4.38 (<4.94)	2.62 mV*(>5)	36.95 (≥33.01)
Peroneal Nerve	Right	4 (<4.27)	6.37 mV (≥2)	40.93 (≥ 36)
Median Nerve	Right	4.88* (<4.7)	15.22 mV(≥3)	51.89 (≥38.02)
Sensory nerve conduction				
Sural sensory nerve	Left	Not recordable*		
Sural sensory nerve	Right	Not recordable*		
Median sensory nerve	Right	1.7 (<3)	22.06 µv (≥7.8)	42.5(≥35.5)
Ulnar sensory nerve	Left	1.6 (<3)	21.2 µv (≥6)	40.5 (≥37.3)

[Table/Fig-1]: Nerve conduction studies during the period of maximum symptoms[#] *abnormal; numbers in parenthesis are normal ranges/cut-off values for abnormal *Abbreviations*: mV, millivolts; µv, microvolts; m/s, meters/second; ms, milliseconds.



[Table/Fig-2]: HbA1c values at onset and during 8 years of follow up.

Her glycaemic control has, however, remained between fair and poor [Table/Fig-2]. Due to financial constraints and the parents' inability to follow instructions, she was continued on premixed insulin therapy. A written informed consent was obtained from parents for using the patient's details.

DISCUSSION

Unlike the chronic diabetic neuropathy related to suboptimal glycaemic control, APDN typically occurs after a fast improvement in glycaemic control in a patient with poor metabolic control, and shows complete recovery [1,2]. In our patient, this occurred shortly after initial diagnosis of T1D. Such an early onset, however, was described in the very first report on this entity [3].

The exact aetiology of APDN is still unknown. The findings of demyelination and axonal degeneration on nerve biopsy are often non-specific [1,4,5]. Proposed mechanisms include epineurial arterio-venous shunting causing endoneurial ischemia, apoptosis due to sudden glucose deprivation, microvascular neuronal damage due to recurrent hypoglycaemia, insulin-induced reduction in endoneurial oxygen tension due to opening of arteriovenous shunts, ectopic firing of regenerating axon sprouts, ectopic pain from regenerating nerve fibers, activation of microglia with subsequent cytokine production and immunologic reaction to insulin [1,5].

The treatment of APDN is always challenging. Symptomatic relief often requires sedatives and opiates analgesics either alone or in combination with various antiepileptic drugs [1-5]. Percutaneous electrical stimulation to the area of the pain may be beneficial in some cases [4]. Reassurance by the treating physician that severe pain will always provides great relief and is remembered long afterwards by the patient [4]. Psychiatric intervention is required for insomnia and depression [1,5]. In our patient, benfotiamine, a thiamine analogue often used for chronic diabetic neuropathy, in combination with carbamazepine showed good results. However, the possibility that remission was related to the natural course of APDN cannot be excluded. Resolution of symptoms is usually reported to occur between 6 and 12 months of onset [1-6].

The majority of the reports indicate that APDN occurs after a precipitous fall in HbA1c after initiation of insulin therapy [5,6]. In our patient, the drop in HbA1c was 3.8%. However, the recently published largest series defines APDN as an acute onset of neuropathic pain and/or autonomic dysfunction within 8 weeks of a large improvement in glycaemic control specified as a decrease in HbA1c of ≥2% points over 3 months [1]. The estimated absolute risk of developing APDN exceeds 80% with a decrease in HbA1c of >4% points over 3 months [1]. In this context, it may be worthwhile for treating physicians to attempt a slower and gradual reduction in HbA1c when trying to achieve a stricter glycaemic control especially in poorly controlled diabetics to prevent the occurrence of APDN.

In the follow up period, HbA1c remained high in the index patient. The primary reason for this suboptimal glycaemic control was a poor compliance probably as a result of parents' financial and educational status. A change to the newer insulin regimens used in the majority of our patients [7,8] could not be made due to higher costs. Additionally, there was frequent missing of insulin doses, and infrequent blood sugar and HbA1c monitoring, a scenario quite often observed in patients with T1D in our region.

APDN is almost exclusively described in adults and adolescents with diabetes [1,2]. To our knowledge, five children aged 13 to 18 years have been reported in English literature [4-6,9]. Our patient is possibly one of the youngest ever to have developed APDN. Besides, this is the only child to develop APDN out of a total of nearly 800 children with T1D who were initiated on insulin at our hospital over the last 14 years [10].

CONCLUSION

We describe a child with T1D who developed a rare complication of APDN after a fast improvement in glycaemic control. In the face of current recommendations for achieving glycaemic targets quickly, a paradoxical occurrence of APDN should be kept in mind. It is important for the paediatric endocrinologists and neurologists to recognize this rare entity for the need to provide adequate analgesia for relief from severe debilitating pain as well as to emphasize on the complete reversibility.

REFERENCES

[1] Gibbons CH, Freeman R. Treatment-induced neuropathy of diabetes: an acute, iatrogenic complication of diabetes. *Brain.* 2015;138(Pt 1):43-52.
[2] Tran C, Philippe J, Ochsner F, Kuntzer T, Truffert A. Acute painful diabetic neuropathy: an uncommon, remittent type of acute distal small fibre neuropathy. *Swiss Med Wkly.* 2015;145:w14131.
[3] Caravati CM. Insulin neuritis: A case report. *Va Med Mon*. 1933;59:745-46.
[4] Archer AG, Watkins PJ, Thomas PK, Sharma AK, Payan J. The natural history of acute painful neuropathy in diabetes mellitus. *J Neurol Neurosurg Psychiatry.* 1983;46:491-99.
[5] Wilson JL, Sokol DK, Smith LH, Snook RJ, Waguespack SG, Kincaid JC. Acute painful neuropathy (insulin neuritis) in a boy following rapid glycaemic control for type 1 diabetes mellitus. *J Child Neurol.* 2003;18:365-67.
[6] Llewelyn JG, Thomas PK, Fonseca V, King RH, Dandona P. Acute painful diabetic neuropathy precipitated by strict glycaemic control. *Acta Neuropathol.* 1986;72:157-63.
[7] Saini A, Devidayal, Verma S, Bhalla AK. Comparative Efficacy of Once Daily Insulin Glargine with Twice Daily NPH Insulin in Children with Type 1 Diabetes. *J Diabetes Metab.* 2011;2:124.
[8] Dayal D, Sharma S, Sachdeva N, Bhalla AK, Attri SV. Efficacy of insulin detemir compared to insulin NPH on glycaemic control in Indian children with Type 1 Diabetes. *J Diabetology.* 2014;2:2.
[9] Said G, Goulon-Goeau C, Slama G, Tchobroutsky G. Severe early-onset polyneuropathy in insulin-dependent diabetes mellitus. A clinical and pathological study. *N Engl J Med.* 1992;326:1257-63.
[10] Dayal D, Saini AG, Jayashree M, Singhi S, Kumar R, Samprati M, Singh M. Hospital based incidence, patterns of presentation and outcome of Type 1 diabetes: 12 years' data from a tertiary care center in North India. *Int J Diabetes Dev Ctries.* 2015;35:103-07.

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