Case Report

A rare presentation of type 1 diabetes mellitus: Diabetic ketoacidosis with severe dyslipidaemia and eruptive xanthomas

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Abstract

Diabetic ketoacidosis (DKA) is the most common life-threatening complication of diabetes, especially in type 1 diabetes mellitus (T1DM). Severe dyslipidaemia causing extensive xanthomas is very rarely reported in DKA. We report the case of a 30-year-old male with T1DM who presented with features of ketoacidosis and had extensive eruptive xanthomas. Blood samples drawn on admission showed excessively lipemic serum and marked dyslipidaemia after analysis. The patient was treated with insulin, rehydration and statins with good clinical outcome. The present case highlights the importance of serial monitoring of lipids and early lipid-lowering therapy in DKA presenting with severe dyslipidaemia, especially when occurring with cutaneous symptoms.

Keywords: Diabetic ketoacidosis, dyslipidaemia, statins, xanthomas

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INTRODUCTION

Diabetic ketoacidosis (DKA) is an acute life-threatening complication of diabetes defined by the triad of hyperglycaemia, ketonemia/ketonuria and metabolic acidosis.[1] It accounts for about 30% of first presentations in newly diagnosed T1DM.[2] Mild hyperlipidaemia occurring in association with DKA is common.[3] However, DKA complicated by severe dyslipidaemia resulting in extensive eruptive xanthomas has been rarely described in T1DM. We report the case of a young adult diagnosed with T1DM for 7 months with poor glycaemic control presenting with the triad of DKA, severe dyslipidaemia and eruptive xanthomas.

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CASE REPORT

A 30-year-old male presented with abdominal pain, vomiting and confusion for 2 days duration. His partner also provided additional history of polyuria and polydipsia preceding his presenting symptoms. There were no fever or risk factors for dyslipidaemia. He was diagnosed with T1DM 7 months earlier and was on premixed insulin however with poor adherence. Family history was negative for diabetes and hyperlipidaemia.

On arrival at the emergency department, he was severely dehydrated and had rapid shallow breathing

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(Kussmaul breath) with acetone breath. Further, systemic examination revealed a heart rate of 112 beats/min, blood pressure of 90/60 mmHg, temperature of 37.2 °C, respiratory rate of 44 cycles/min and oxygen saturation of 97%. Glasgow Coma Scale was 13. The chest was clear on auscultation with equal air entry bilaterally. Abdomen was soft and tender with no palpable organomegaly or masses. He had crops of red-yellow papules on the extensor surfaces of his elbows, hands and knees (Figure 1). Anthropometric measurements were as follows: height 1.7 m, weight 55 kg and body mass index 20 kg/m^2. Other examinations were unremarkable.

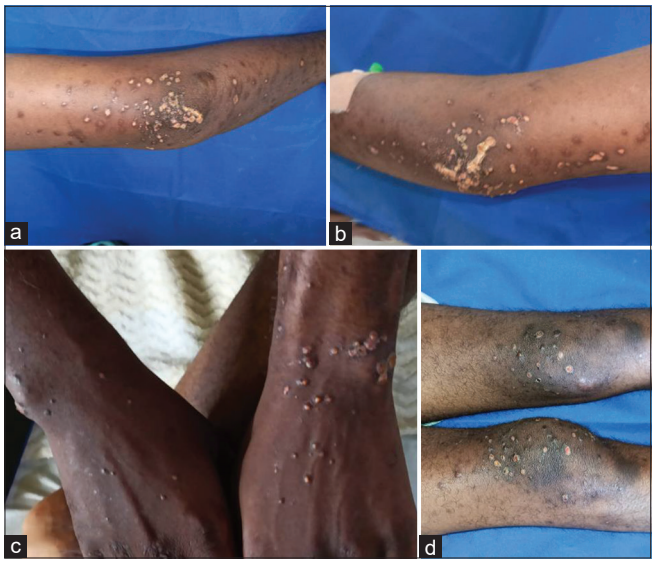

Figure 1: Clinical photographs showing eruptive xanthoma affecting extensor surfaces of the elbows (a and b), hands (c) and knees (d)

Blood samples drawn for laboratory examination appeared grossly lipemic (Figure 2). Serum chemistry analysis revealed abnormal values for triglyceride (75.6 mmol/L, reference range 0.4–1.52 mmol/L), total cholesterol (28.2 mmol/L, reference range 0–5.2 mmol/L), high-density lipoprotein (HDL) cholesterol (0.1 mmol/L, reference range > 0.9 mmol/L) and low-density lipoprotein (LDL) cholesterol could not be estimated using the Friedewald formula (the Friedewald formula is inaccurate at extremely high triglyceride and total cholesterol levels).[4] Serum sodium level was (160 mmol/L, reference range 136–148 mmol/L), potassium (1.9 mmol/L, reference range 3–5 mmol/L), chloride (125 mmol/L, reference range 98–110 mmol/L), bicarbonate (10 mmol/L, reference range 20–30 mmol/L), urea (12.3 mmol/L, reference range 2.1–7.1 mmol/L) and serum creatinine (29umol/L, reference range 64–104 umol). Uric acid level was 5000umol/L (reference range 204–410 umol/L). Random blood glucose check using a meter was (21.3 mmol/L, reference

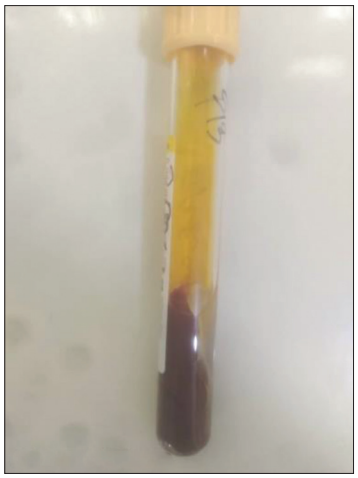

Figure 2: Lipaemic serum due to severe hyperlipidaemia

range 7.8–10 mmol/L). Calculated serum osmolality was (329 mOsm/kg, reference range 275–286 mOsm/kg) and his urinalysis showed 3+ of ketones and glucose. Initial glycosylated haemoglobin was 15% (reference range <6%) and he had a positive anti-glutamic acid decarboxylase 65 antibody. Abdominal ultrasound was unremarkable. Skin biopsy showed infiltration of the papillary dermis with foamy macrophages with overall features in keeping with eruptive xanthomas.

He was admitted and rehydrated with intravenous fluid alongside insulin infusion according to the standard protocol for DKA. He was also commenced on statins and xanthine oxidase inhibitor. The patient was started on statin to treat hyperlipidaemia consisting of hypercholesterolaemia and hypertriglyceridemia. This is because the levels of cholesterol and triglyceride were extremely high coupled with the presence of eruptive xanthomas. Considering most of the guidelines, it is recommended to commence treatment with statin in a situation of combined hypercholesterolaemia and hypertriglyceridemia, fibrates may be added later. In this case, since the patient was responding to rehydration, insulin and statin; there was no need to add fibrates. The xanthomas, hyperlipidaemia, hyperuricaemia and electrolyte values improved with the pharmacologic treatment and resolution of DKA (Figure 3). He was discharged on premixed insulin with good blood glucose control after 16 days on admission. The laboratory parameters during the course of admission can be seen in Table 1.

DISCUSSION

Impaired lipid metabolism in diabetes has been described in the literature for many years. The most common forms of dyslipidaemia in diabetes include elevated triglyceride, total cholesterol and LDL cholesterol levels.[5] Although approximately 30%–50% of patients with DKA may

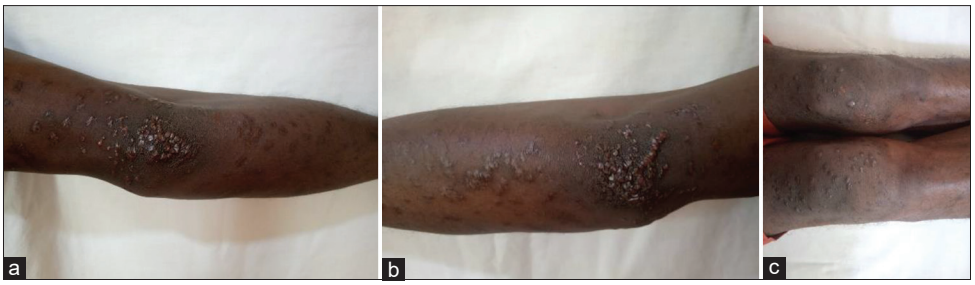

Figure 3: Clinical photographs showing healed eruptive xanthoma lesions over elbows (a and b) and knees (c) following resolution of DKA and hyperlipidaemia

Table 1: Serial serum lipid profiles and electrolytes/urea/creatinine of the patient

Serum analytes	Reference ranges	Day 1	Day 3	Day 6	Day 10	1 month follow-up
Triglyceride (mg/dL)	<150	6696	1943	797	83	2.7
Total cholesterol (mg/dL)	<200	1090	580	259	415	192
Low-density lipoprotein (LDL) cholesterol (mg/dL)	<110		189	27	349	76
High-density lipoprotein (HDL) cholesterol (mg/dL)	>40	3.9	5.8	73	39.8	112
Serum uric acid (mg/dL)	4.0-8.5	>84.1	65.3	30.0	4.7	
Serum sodium (mEq/dL)	136-148	165	156	160	138	
Serum potassium (mEq/dL)	3-5	1.9	4.2	5.6	3.6	
Serum chloride (mEq/dL)	98-110	123	78	178	106	
Serum bicarbonate (mEq/dL)	20-30	<10	13	20	20	
Serum urea (mg/dL)	5.0-20	73.8	57	43.8	12.6	
Serum creatinine (mg/dL)	0.6-1.2	0.33	0.63	0.52	0.45	
Serum calcium (mEq/dL)	2.1-2.6	5.16	3.22	2.36	1.99	
Serum phosphate (mEq/dL)	0.87-1.45	>10	7.84	4.73	1.12	
Blood glucose (mg/dL)	140-180	383.4	204	163	142	121
Glycosylated haemoglobin (%)	<6.0	8.1		7.8		6.5
Serum osmolality (mOsm/Kg)	275-286	329	320	312	294	282

have associated hypertriglyceridemia, severe dyslipidaemia resulting in eruptive xanthomas is a rare occurrence in DKA.[6]

The mechanism of dyslipidaemia in DKA and T1DM is triggered by insulin deficiency. In lipid metabolism, insulin promotes lipogenesis and inhibits both lipolysis and ketogenesis. However, in conditions of severe deficiency, lipolysis is activated in the adipocytes leading to the release of free fatty acids which are taken up by the liver to produce triglyceride-rich lipoproteins.[3,7] The activity of lipoprotein lipase, an extracellular enzyme responsible for the catabolism of triglycerides is also decreased resulting in poor clearance of triglyceride-rich lipoproteins (very LDL [VLDL] and chylomicrons) from the plasma and causing hypertriglyceridemia.[8] Elevated triglyceride-rich lipoprotein levels, in turn, lead to an increase in cholesteryl ester transfer protein-mediated transfer of triglycerides to HDL and LDL forming both triglyceride-rich HDL and LDL which are then further hydrolysed by hepatic lipase resulting in low plasma levels of HDL cholesterol levels and increase production of small dense LDL cholesterol which is highly atherogenic.[3,7,9] However, it is important to state that in addition to insulin deficiency, the occurrence of severe dyslipidaemia may have also been aggravated by an underlying genetic predisposition to dyslipidaemia.

High levels of circulating lipids (cholesterol and triglycerides) can result in diverse clinical manifestations due to abnormal deposition in various tissues. Deposition in the skin leads to eruptive xanthomas commonly on the extensor surfaces of the extremities and buttocks. Eruptive xanthomas occurs almost only in the presence of hyperlipidaemia (mixed hypercholesterolaemia and hypertriglyceridemia in the index case) and has a prevalence of 18 cases in 100,000 people, making it a rare presentation.[6,10]

Furthermore, hyperlipidaemia has been reported by various studies to be associated with hyperuricaemia which is in keeping with our findings.[11,12] In a different vein, severe dyslipidaemia has been shown to interfere with the measurements of other laboratory parameters accurately.[13] This may have contributed to the extremely low potassium levels, even though some potassium depletion occurs as a result of DKA. Pseudohyponatremia was not observed in our case, most likely due to the overriding effect of severe dehydration causing hyperchloremic hypernatremia.

The management of DKA with severe dyslipidaemia includes adequate rehydration and continuous infusion

of insulin according to the DKA management protocol because the underlying mechanism of dyslipidaemia is insulin deficiency. However, in the presence of severe hyperlipidaemia with accompanying eruptive xanthomas, early therapy with lipid-lowering agents may hasten the healing of cutaneous lesions and also significantly reduce the risk of more grievous complications like pancreatitis as well as long-term cardiovascular risk.[14,15] This was the experience in the case of our patient.

The weakness of our case was that an appropriate genetic study could not be performed in the patient and first-degree relatives to detect the presence of a coexisting genetic predisposition to severe dyslipidaemia. DKA patients can also present with features of severe hyperlipidaemia such as eruptive xanthomas. Early recognition and treatment of the accompanying severe dyslipidaemia are important to ensure quick healing of these cutaneous lesions and avert long-term cardiovascular complications.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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