CASE REPORT

Newly diagnosed type 1 diabetes complicated by ketoacidosis and peripheral thrombosis leading to transfemoral amputation

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SUMMARY

Peripheral vascular thromboembolism is a rarely described complication of diabetic ketoacidosis. We report a 41-year-old otherwise healthy man admitted with ketoacidosis and ischaemia of the left foot. The patient was unsuccessfully treated with thromboendarterectomy, and the extremity was ultimately amputated. The patient had no family history of cardiovascular disease, and all blood sample analyses for hypercoagulability were negative. We recommend an increased focus on peripheral thromboembolism, when treating patients with severe ketoacidosis.

BACKGROUND

Diabetes mellitus is associated with an increased incidence of thromboembolic complications. In type 2 diabetes mellitus there is clear evidence of thrombophilia partly explained by an increased level of *plasminogen activator inhibitor*.¹ It is not certain whether there is an increased risk of peripheral vascular thrombosis/embolism in patients with diabetic ketoacidosis. We present a case of diabetic ketoacidosis in a newly diagnosed individual with type 1 diabetes complicated by peripheral vascular insufficiency.

CASE PRESENTATION

A 41-year-old man was admitted to hospital in a serious medical condition. Besides a history of herniated lumbar disc the patient was healthy. The patient had no history of hypertension, but blood pressure was 156/111 mmHg on admission. During the stay in hospital blood pressure stabilised at around 135/80 mmHg. There was no family history of cardiovascular disease. A few days before admission the patient had episodes of nausea, vomiting and abdominal pain. Additionally, he had polyuria and polydipsia. A few hours before admission, the patient reported acute pain in his left foot and was found to have a pulseless foot without vital signs. On admission an arterial blood gas showed metabolic acidosis (pH 7.02, base excess 24.6, blood glucose 26 mmol/L) and blood ketones (acetone, acetoacetic acid and β -hydroxybutyric acid) were 6.6 mmol/L.

INVESTIGATIONS

The patient was diagnosed with type 1 diabetes mellitus supported by a low C peptide level of 43 (370–1470 pmol/L) and an antigliutamic acid decarboxylase (GAD) antibody titre of 4.7 (ref. 0–1.0). The complete blood count showed high white cell count of

$20.9 \times 10^9/L$ but normal haemoglobin level of 8.4 mmol/L and platelet count of $199 \times 10^9/L$. C reactive protein was below 1.0. Screening for a diversity of systemic inflammatory disorders including vasculitis and systemic lupus erythematosus (eg, antinuclear antibodies, antineutrophil cytoplasmic antibodies, lupus anticoagulant and cardiolipin antibodies) were all negative. Protein S and C levels were normal, antithrombin III level was reduced and the coagulation factors were increased (factor II, VII and X were 1.40 units (0.70–1.30) and factor VIII was 3.89 (0.60–1.30)). APTT (activated partial thromboplastin time) was prolonged to 46 s (27–40). Blood lipids were normal with total cholesterol 2.6 mmol/L, LDL-cholesterol 1.5 mmol/L, HDL-cholesterol 0.8 mmol/L and triglycerides 0.72 mmol/L. The ECG showed sinus rhythm without ischaemia, and an echocardiogram also was found normal. A duplex ultrasonography of the lower limbs showed no blood flow in the arteries of the left crus and foot.

DIFFERENTIAL DIAGNOSIS

Buerger's disease, which is caused by inflammation of the arterial wall, is a relevant differential diagnosis. It mostly appears in smoking men between 20 and 40 years of age, corresponding to the individual in this case who reported smoking 10 cigarettes daily. However, symptoms are mostly less acute in Buerger's disease and the vascular surgeons found no evidence for this condition.

TREATMENT

The patient was treated according to the guidelines for management of diabetic ketoacidosis and subsequently referred to a university hospital. Vascular surgery was performed including thromboendarterectomy in several large arteries in the left leg and medication to provide fibrinolysis was injected in the small arteries in the foot, which were too peripherally located to be accessible to surgery. But sufficient blood flow was not obtained due to peripheral thrombosis, and a below-knee amputation was performed. The amputation related wound did not heal after 1 week of observation, and eventually a transfemoral amputation was performed.

DISCUSSION

Only a few case reports on diabetic ketoacidosis complicated by thrombosis are present in the literature. The fibrinolytic system is disturbed in conditions of metabolic acidosis. Carl *et al*² described

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the haemolytic factors during diabetic ketoacidosis. They found decreased activity of proteins S and C, which are some of the most important inhibitors of the coagulation process. They also found increased activity of von Willebrand factor, which facilitates platelet adhesion.³

Thus, it can be speculated that there is an increased risk of venous and arterial thrombosis and atheromatous plaques are prevailing, related to endothelial factors. In the case report presented here, the coagulation factors were affected in a way which indicated increased activity. Proteins S and C were normal, however, they were analysed 36 h after the initial treatment for ketoacidosis. The level of antithrombin III was reduced, probably related to the use of heparin.

Zipser *et al*⁴ described a similar case report of a newly diagnosed individual with diabetes with ketoacidosis and acute aortoiliac and femoral artery occlusion. The patient was also amputated below the knee, but had a fatal outcome. Lin *et al*⁵ describe a case report of ketoacidosis complicated by acute brachial artery thrombosis in a patient with a diabetes duration of 4 years. The brachial artery was rescued by surgical thrombectomy. Insufficiently regulated diabetes can also cause dyslipidemia with increased risk of atheroma formation and embolism arising from vascular endothelium with disintegrated morphology. Congenital hyperlipidaemia has been described to cause coronary artery disease and acute myocardial infarction in children.⁶

In the case report presented here, the patient was newly diagnosed with diabetes with a short duration of symptoms of the disease. The patient had no history of thromboembolism and an echocardiogram could not identify any cardiac source of the embolism. The patient had sinus rhythm but it cannot conclusively exclude the likelihood of a transient arrhythmia precipitated by ketoacidosis, which could have caused the embolism.⁷ The patient was not influenced by any intercurrent disease, but he was dehydrated because of vomiting during a couple of days. Dehydration in combination with diabetic ketoacidosis increases venous stasis and thereby the risk of deep venous thrombosis according to Virchow's triad. However, it has not been shown to be an independent variable as a cause of venous thrombosis.⁵

The marked peripheral vascular changes resulted in significant oedema of the affected extremity, and even though compartment syndrome was excluded, it was not possible to achieve adequate healing. Abrupt onset of peripheral ischaemic symptoms without any history of claudication mitigated the possibility of Buerger's disease.

We present a case of diabetic ketoacidosis complicated by peripheral thromboembolism, which is a rare complication of diabetic ketoacidosis but can have devastating consequences with limb amputation or even death. We recommend an increased focus on peripheral thromboembolism, including assessment of pulse and general signs of peripheral vascular insufficiency (eg, pallor, pain and coldness), when treating patients with severe ketoacidosis. However, other causes of thromboembolism should be excluded before establishing diabetic ketoacidosis as the cause.

Learning points

- ▶ Diabetic ketoacidosis can promote a prothrombotic state.
- ▶ Peripheral thrombosis/embolism is a rarely described complication of diabetic ketoacidosis, and can have a devastating consequence with limb amputation or death.
- ▶ Other causes of thrombosis including cardiac source, thrombophilia, dyslipidemia should be excluded before determining diabetic ketoacidosis as a causative agent.

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Competing interests None.

Patient consent Obtained.

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