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Case report

Sudden death of a 15-year-old girl due to fulminant type 1 diabetes mellitus—Diabetic ketoacidosis induced cerebral edema?

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ABSTRACT

Sudden death from fulminant type 1 diabetes mellitus is uncommon in forensic practice. Here we report the sudden death of a 15-year-old girl who presented with vomiting, fever and abdominal pain and died unexpectedly. Postmortem examination showed severe pancreatic islet destruction, cerebral edema and lipid vacuolization of the epithelium of the renal proximal tubules and liver cells. The biochemical analysis in reserved heart blood and vitreous fluid indicated the elevated levels of glucose and ketone bodies and lower glycosylated hemoglobin and C-peptide. The cause of death was attributed to fulminant type 1 diabetes mellitus which led to diabetic ketoacidosis-associated cerebral edema. This report suggested that the histological examination of the pancreas, liver and kidney, insulin immunohistochemistry, as well as biochemical analysis could be useful for the diagnosis of diabetes related death.

1. Introduction

Type 1 diabetes, previously called insulin-dependent diabetes mellitus (IDDM) or juvenile-onset diabetes, usually develops in childhood or adolescence. There is a significantly higher mortality rate among children with type 1 diabetes compared with the general population of the similar age and sex.[1–3] In this group, the leading death mechanism was diabetic ketoacidosis (DKA), with cerebral edema accounting for two-thirds or more among all DKA deaths.[1,4–6] Also, DKA may be the first manifestation of type 1 diabetes in a minority of patients.

Fulminant type 1 diabetes (FTD1M) is a recently discovered subtype of type 1 diabetes which is classified not as autoimmune (type 1A) but as idiopathic (type 1B) diabetes. This disease is characterized by sudden onset and extremely rapid progression. The morbidity under 20 years of age is 8.7% in FTD1M patients of all ages according to Hanafusa's article.[7] Compared to type 1A diabetes, β cells are significantly reduced in fulminant type 1 diabetes. To date, most reports about this disease are from Japan. Although it is recognized that the death from FTD1M is inevitable if without timely treatment, but sudden and unexpected death from FTD1M is rarely reported and the death mechanism of this disease is not fully clarified. The cardiac arrest was thought to be one possible mechanism.[7] Here we described the unexpected death of a 15-year-old girl who was demonstrated to have FTD1M, DKA and lethal cerebral edema in the postmortem examination.

2. Case presentation

2.1. Case history

A 15-year-old Han Chinese girl went to see a doctor with a chief complaint of vomiting, fever and abdominal pain for about 24 h one day in the afternoon of early August in Fujian province. She was diagnosed with acute gastritis. She was prescribed injections of amikacin and alidine, the tablets of cidomycin, berberine and anisodamine. The symptoms were not relieved obviously. She still suffered from abdominal pain and weakness until she was found dead in bed at 4 am the next morning. Her relatives requested a forensic autopsy. Her family history was negative for diabetes mellitus and she had no relevant remarkable known medical history. And according to the supplemented memory from her relatives, the girl complained of fatigue, thirst and loss of appetite for some days, but without obvious weight loss. The relatives neglected it.

2.2. Autopsy findings

The body was preserved at room temperature (about 30 °C–26 °C) until a forensic autopsy was performed after 6 h since death.

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The body was that of a well-nourished girl. A punctiform abrasion was seen in the nasolabial groove. The needle puncture marks were seen on each lateral gluteal region. Multiple petechiae were seen in the epicardium. The heart weighed 190 g, and the brain weight was 1420 g. The cerebral gyri were flattened accompanied by shallower cortical sulci, and cerebellar tonsillar herniation was found. The liver weighed 1060 g and was yellow and greasy.

2.3. Histological, toxicological and biochemistry examination

Microscopically, slides of the brain showed extensive and severe edema. The granular layer of the cerebellum was remarkably swollen (Fig. 1). The hepatocytes and the epithelial cells of the renal proximal tubule were filled with vacuoles (Fig. 2), which were confirmed by Oil Red O stain to be lipid droplets, but PAS stain negative (Supplementary figure). The pancreatic islets were seriously damaged, and intact islets were hardly seen. Islet fibrosis was observed and the islet cells were notably reduced. The islets and stroma of the pancreas were infiltrated by dispersed lymphocytes. In contrast to the normal pancreas, insulin-positive cells were hardly detected by immunohistochemistry (Fig. 3). 190 insulin-positive islets were seen in fifty 10 × 10 visual fields for control pancreas, but no insulin-positive islets were seen in the reported case in the same fields. Other organs were unremarkable on gross or microscopic examination.

The heart blood and the vitreous fluid were collected at autopsy and sent to the lab for biochemistry analysis after autopsy. Then the blood sample and the vitreous fluid were centrifuged. The mild hemolysis was observed. The plasma and the supernatant of vitreous fluid were stored at −20 °C. The toxicology analysis revealed no positive findings. The traces of the prescribed drugs were present. The levels of the glucose and β-hydroxybutyrate were tested after 1 week of storage. The blood plasma glucose and β-hydroxybutyrate (the major component of the ketone bodies) were 12.4 mmol/L (ref: <6.1 mmol/L) and 6.3 mmol/L (ref: <0.3 mmol/L) respectively. The levels of glucose and β-hydroxybutyrate in the vitreous fluid were 14.2 mmol/L and 7.8 mmol/L. Since FT1DM was suspected highly, the other relevant biochemistry analysis was performed about 1.5 years after storage at −20 °C. Plasma HbA1c was 5.0% and C-protein was 0.05 nmol/L. The Abs of GAD and ICA were negative. Plasma amylase was 312 U/L (ref: 18–72 U/L).

3. Discussion

FTD1M was termed in 2000. The clinical diagnosis criteria for FTD1M were already well-established[7,8]: 1) development of ketosis within about one week after the onset of diabetic symptoms (average 4.4 days), 2) high blood glucose and near normal HbA1c (blood glucose more than 16.0 mmol/l and HbA1c less than 8.5% on the first examination), 3) virtually no C-peptide secretion (urinary C-peptide less than 10 μg/day or fasting serum <0.10 nmol/l). Except these indispensable features, the other clinical features are often seen: 1) absence of islet-related autoantibodies, such as ICA, GADAb, IAA, or IA-2Ab, 2) elevated serum pancreatic enzyme levels, 3) flue-like or gastrointestinal prodromal symptoms, 4) frequently pregnancy related. At postmortem, diagnosis of FTD1M is difficult because the disease is abrupt onset and the typical symptoms of diabetes are not obvious, moreover, the glucose and ketone levels of the blood and vitreous fluids were affected by postmortem changes and have remained undetected at routine postmortem examinations. In the case reported, the clinical manifestation of abdominal pain, nausea and vomiting is easily misdiagnosed as acute gastritis or acute pancreatitis if without the blood biochemistry. However, the acute pancreatitis was not being considered because the absence of neutrophils infiltration, necrosis of pancreas parenchyma and fat tissue, and hemorrhage as well in spite of elevated pancreatic enzyme levels. Severe islet destruction and insulitis were observed in the case, almost no remaining insulin-positive β cells could be seen by the histology and immunohistochemistry. Therefore, FTD1M was highly suspected combined with the clinical symptoms of the deceased.

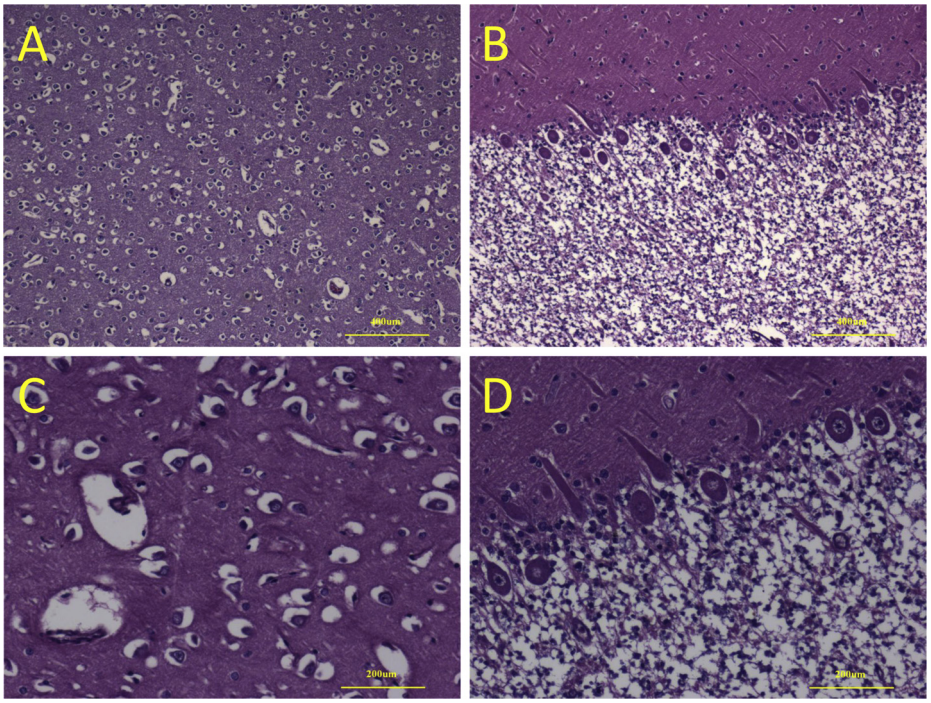

Fig. 1. Severe edema in the brain. A: perivascular, pericellular and interstitial edema in cerebrum. B: remarkable edema in the granule layer of cerebellum. C and D were the higher magnification of A and B. HE stain. Bars represent 400 μm in A and B, 200 μm in C and D.