CASE REPORT

Cerebellar tonsillar herniation in sudden death of an adolescent anorexia nervosa patient: a case report

Tasuku Kitajima1 · Ryoko Otani1 · Takeshi Inoue1 · Naho Matsushima1 · Naoki Matsubara1 · Akiko Fujii2 · Shinichi Ban2 · Ryoichi Sakuta1

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Abstract
Background  Anorexia nervosa not only results in severe malnutrition but also carries a high risk of sudden death. Although fatal arrhythmias are the most common cause of sudden death, it is often unclear what exactly causes them. To the best of our knowledge, there have been no reports of cerebellar tonsillar herniations in patients with anorexia nervosa.

Case presentation  A 17-year-old girl with anorexia nervosa and autism spectrum disorder was admitted to the pediatric ward for extreme weight loss. Since she refused to take oral nutrition or tube feeding, we started continuous intravenous fluids. Eight hours after admission, she suddenly went into cardiopulmonary arrest and died despite resuscitation. A postmortem autopsy revealed the unexpected findings of generalized severe cerebral edema and cerebellar tonsillar herniation.

Conclusion  Intracranial hypertension may need to be considered when the condition of patients with anorexia nervosa suddenly worsens during refeeding periods. Postmortem autopsy and autopsy imaging are recommended to determine the exact cause of sudden death.

Level of evidence  Level IV: Evidence obtained from multiple time series analysis such as case studies. (NB: Dramatic results in uncontrolled trials might also be regarded as this type of evidence).

Keywords  Anorexia nervosa · Cerebral edema · Tonsillar herniations · Autopsy · Sudden death

Abbreviations
AN  Anorexia Nervosa
RS  Refeeding Syndrome
ECG  Electrocardiogram
BMI  Body Mass Index

Background
Anorexia nervosa (AN) is a disease characterized by the restriction of energy intake relative to requirements based on low body weight, abnormal eating attitude, and distortion of body shape perception and cognition [1, 2]. Malnutrition associated with AN has acute, chronic, irreversible and potentially fatal impacts on the body, such as growth retardation, refeeding syndrome (RS), and sudden death [2–4]. Malnutrition also causes significant irreversible changes, such as loss of bone density [3]. The mortality associated with AN has been reported to be 5–15%, and in addition to suicide, many patients die from physical complications associated with poor nutrition and refeeding [3, 4].

The risk of sudden death of patients with AN is reported to be higher than that of healthy women and special attention should be given to sudden changes in the patient’s condition [2, 5]. Arrhythmias lead by QTc prolongation were thought to be the most common cause of sudden death, but contrary to what was thought in the past, a recent large cohort study reported that QTc prolongation is not intrinsic to AN [3, 6], and there is no clear evidence that subsequent arrhythmias are a direct cause of death [3].

Here, we describe the case of a 17-year-old girl who suddenly went into cardiopulmonary arrest during the night of the day admitted to the hospital due to malnutrition with AN and whose postmortem findings were marked by significant cerebral edema and cerebellar tonsillar herniation.
To the best of our knowledge, there have been no reports suggesting an association between edema and herniation of the brain and the sudden death of the patients with AN or RS and monitoring with special attention to this aspect of the disease is not usually done.

**Case presentation**

This case involves a 17-year-old female with severe AN of 2 years and a history of autism spectrum disorders from her childhood before developing AN. She started dieting when she was 14 years old in a junior high school and was diagnosed and treated in an inpatient program twice. At the time of her second discharge from the hospital, she was 153.6 cm tall, weighing 35.9 kg (BMI: 15.2 kg/m²; BMI-SDS: −2.76), and continued outpatient treatment. A few months later, she started losing weight and refused to go to the hospital. Eleven months after discharge, she fainted at home and was transported to our hospital after being rushed to the nearest doctor. No episodes of binge eating or purging behavior were observed from AN onset.

At the time of admission, she was 21.4 kg in weight, with a BMI of 9.4 kg/m² (BMI-SDS: −11.92). Vital signs were as follows: temperature, 35.4 °C; heart rate, 124 bpm; blood pressure, 98/54 mmHg; and respiratory rate, 18/min. Physical examination revealed multiple purpuras on the abdomen as well as marked emaciation. Blood tests showed elevated blood urea nitrogen (blood urea nitrogen, 36.4 mg/dL;Creatinine, 0.35 mg/dL.), elevated liver enzymes (AST, 1033 IU/L; ALT, 971 IU/L; LDH, 1056 IU/L; GGT, 145 IU/L) and mild hypokalemia (Sodium, 143 mmol/L; Potassium, 3.3 mmol/L; Phosphate, 3.9 mg/dL; Magnesium, 2.5 mg/dL). Her blood glucose level was 76 mg/dl. ECG showed sinus bradycardia (51 bpm), abnormal Q waves at V1-2, negative T waves at V1-4, and mild QTc prolongation (QTc = 452 ms) (Fig. 1). Contrary to the heart rate in the sitting position immediately after admission, the heart rate was bradycardic on the resting ECG. Echocardiography was not performed at the time of admission and planned to be performed by a cardiologist the next day. Chest radiographs showed a cardiothoracic ratio of 41% with no signs of pneumonia or pulmonary congestion. Abdominal radiographs showed dilation of the entire colon, a finding suggestive of paralytic ileus. On admission, refeeding with continuous intravenous infusion was initiated (fluid volume, 45 ml/kg/day = 40 ml/hr; glucose, 4.7% = 180 kcal/day = 8.4 kcal/kg/day; Na⁺, 50 mEq/L; K, 40 mEq/L; P, 20 mEq/L; thiamine, 100 mg/day). The patient was admitted to the general pediatric ward, where ECG continuous monitoring was performed, and the parents were escorted to the same room to watch over the patient.

After admission, she was able to speak smoothly with no change in her state of consciousness. She complained of thirst and drank a total of 700 ml of water. She was put on a plan to limit her water consumption if she drank more than 1–2 L/day. She was conscious and talking normally until 7 h after she was admitted, then, based on medical staff and the mother’s point of view, she appeared to be asleep and opened her eyes when called. Five hours after admission, blood pressure was 85/66 mmHg and respiratory rate was 18/min, and heart rate on ECG continuous monitoring was 50–60 bpm. After 8 h of hospitalization, she suddenly went into cardiac arrest, did not respond to resuscitation, and died.

A postmortem examination of the ECG continuous monitor just before cardiac arrest showed frequent premature atrial contractions followed by asystole. Blood samples could not be collected during resuscitation due to technical problems. The autopsy was performed 37 h postmortem with the consent of the parents. The brain showed marked edema with a high weight (1540 g), narrowing of the ventricles, and herniation of cerebellar tonsils (Fig. 2). No obvious neuronal degeneration or other specific findings were noted by microscopic examination. The lungs (310 g: 310 g) presented edema, congestion, and focal pneumonia with foreign body giant cells suggestive of aspiration. There was erosion in the esophagus due to reflux. Severe atrophy of the heart (130 g), liver (450 g), spleen (45 g), and adrenal glands (4.1 g: 3.6 g) was confirmed with loss of the adipose tissue. Microscopic examination revealed congestive findings...
in the liver and lungs. Microscopic examination of the liver showed no extensive necrosis of hepatocytes as seen in acute liver failure. Bone marrow was markedly hypocellular with gelatinous degeneration.

**Discussion**

We present a case of severe AN with sudden death early in the refeeding phase, with findings of cerebellar tonsillar herniation and much cerebral edema on autopsy. To the best of our knowledge, this is the first report of the development of cerebellar tonsillar herniation associated with sudden death in a patient with AN. This report is significant, because it highlights the severity of the markedly malnourished patient and has implications for the future monitoring of patients with severe AN. Here, we discuss the cause of death in our case and the cause of the cerebral edema that led to cerebellar tonsillar herniation.

Based on the clinical course and autopsy findings, the direct cause of death in this case is cerebral edema resulting in tonsillar herniation.

It is known that when refeeding severely undernourished patients, electrolytes are transferred into the cells due to an increase in insulin concentration caused by elevated blood glucose levels, resulting in a decrease in serum phosphorus, potassium, and magnesium levels, and this condition is known as refeeding syndrome [2, 5]. Published guidelines recommend an initial calorie level of 10 kcal/kg/day for high-risk patients and 5–10 kcal/kg/day for very high-risk patients to prevent RS [2, 5]. Since we do not have biochemical data at the time of the sudden change in our case, we cannot determine whether refeeding syndrome had occurred or not. Nevertheless, considering that the patient had been started on refeeding with only a few calories, it is unlikely that this condition was caused by refeeding syndrome.

There have been no reports of patients with AN developing cerebral edema leading to tonsillar herniation. One autopsy case of AN with extensive cerebral edema following congestive heart failure was reported, but the direct cause of death in this reported case was attributed to pulmonary congestion associated with congestive heart failure [7]. Sundström et al. reported a case in which the patient suffered from a disturbance of consciousness during the refeeding period from prolonged malnourishment due to causes other than AN, and intracranial pressure monitoring (ICP) showed a marked increase in intracranial pressure. In their case report, the initial calorie level was 1800 kcal/day, which was higher than recommended and suggested to be a risk factor for cerebral edema [8]. The initial calorie levels in the present case were within the optimal range and cannot be considered a similar factor.

It is known that the regulatory systems related to sodium and water, such as ADH secretion and the renin–angiotensin–aldosterone system, are impaired in those with weight loss due to AN [9]. In our case, the patient drank 700 ml of water in the 6 h after admission, which may have been a factor in the development of cerebral edema due to water intoxication leading to hyponatremia, although various guidelines do not provide clear criteria for water restriction or do not recommend it [2, 5].

Various guidelines do not recommend the use of intravenous fluids for patients with AN [2, 5]. However, when a patient refuses food or tube feeding, emergency continuous infusion is used commonly. Hypotonic maintenance infusion was used in our case, but several recent systematic reviews and guidelines on maintenance infusions in children have reported that the use of isotonic solutions reduces the incidence of hyponatremia [10]. Although blood tests could not be performed in our case, it is possible that hyponatremia was a factor in the development of cerebral edema. We should have monitored more carefully the development of hyponatremia after starting hypotonic infusion. We may also need to use maintenance infusion of isotonic fluids in similar cases with AN.

The most common cause of sudden death in AN, except for suicide, is fatal arrhythmia, and for this reason, during refeeding, attention has been given to monitoring...
biochemical tests and continuous ECG monitoring with an emphasis on arrhythmia [2]. However, some deaths that are thought to be sudden deaths due to arrhythmia may include cases of sudden changes due to cerebral edema. Accurate monitoring of intracranial pressure requires an invasive procedure and given the rare frequency, should not be performed in malnourished patients without impaired consciousness. However, given the risk of impaired consciousness and respiratory arrest even in the absence of arrhythmias, it may be worthwhile to study the necessity of repeated conscious status checks and continuous/nocturnal SpO2 monitoring in the acute phase of severely malnourished patients to recognize sudden change of consciousness at an early stage. In addition, in the unfortunate event of sudden death in patients with AN, autopsy and autopsy imaging may help to determine the frequency of massive cerebral edema in such situations.

**Strength and limits**

Many reports do not examine the cause of death of AN patients by autopsy, and this report is valuable as a report of autopsy cases. However, it is important to note that this is a report of only one case. In addition, the absence of blood tests at the time of the sudden change is an important limitation.

**What is already known on this subject?**

There are few reports of autopsy results in patients with anorexia nervosa who died during refeeding, and there have been no reports of cases with cerebellar tonsillar herniation.

**What this study adds?**

This report describes a rare but serious complication that can occur in patients with AN who are extremely undernourished.

**Conclusions**

The findings in our patient, which showed that massive general cerebral edema and cerebellar tonsillar herniation can occur during refeeding in AN patients with severe emaciation, provide important material for future research on how to monitor and observe extremely high-risk patients. We recommend that autopsy or autopsy imaging be performed to examine the exact cause of sudden death in patients with eating disorders.

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**Authors’ contributions** TK—data collection, analysis, manuscript. RO—data collection, analysis, manuscript. TI—data collection, interpretation and manuscript. NM—data collection and interpretation. AF—analysis of autopsy and pathological data. SB—analysis of autopsy and pathological data, supervision. RS—interpretation, supervision. All authors read and approved the final manuscript.

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**Data availability** No data or materials were generated during our study; we performed a retrospective analysis of the patient’s medical records.

**Declarations**

**Ethical approval** The patient’s parents consented for the use of medical data, including pictures of the autopsy in our paper. Consent of the ethics committee of Dokkyo Medical University Saitama Medical Center was also obtained (No. 21025).

**Informed consent** We give consent for the publication of our paper.

**Conflicts of interest** We declare no competing interests.

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