Cerebellar Tonsillar Herniation in Sudden Death of An Adolescent Anorexia Nervosa Patient: A Case Report.

Tasuku Kitajima (✉ tkita@dokkyomed.ac.jp)

Dokkyo Medical University Saitama Medical Center: Dokkyo Ika Daigaku Saitama Iryo Center
<https://orcid.org/0000-0003-3333-7139>

Ryoko Otani

Dokkyo Medical University Saitama Medical Center: Dokkyo Ika Daigaku Saitama Iryo Center

Naho Matsushima

Dokkyo Medical University Saitama Medical Center: Dokkyo Ika Daigaku Saitama Iryo Center

Naoki Matsubara

Dokkyo Medical University Saitama Medical Center: Dokkyo Ika Daigaku Saitama Iryo Center

Takeshi Inoue

Dokkyo Medical University Saitama Medical Center: Dokkyo Ika Daigaku Saitama Iryo Center

Akiko Fujii

Dokkyo Medical University Saitama Medical Center: Dokkyo Ika Daigaku Saitama Iryo Center

Shinichi Ban

Dokkyo Medical University Saitama Medical Center: Dokkyo Ika Daigaku Saitama Iryo Center

Ryoichi Sakuta

Dokkyo Medical University Saitama Medical Center: Dokkyo Ika Daigaku Saitama Iryo Center

Research Article

Keywords: anorexia nervosa, refeeding syndrome, tonsillar herniations, autopsy, sudden death

Posted Date: October 12th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-951351/v1>

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Version of Record: A version of this preprint was published at Eating and Weight Disorders - Studies on Anorexia, Bulimia and Obesity on February 16th, 2022. See the published version at <https://doi.org/10.1007/s40519-022-01377-8>.

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 cerebral herniations in patients with anorexia nervosa.

Case presentation: A 17-year-old adolescent girl with neuropathy and autism spectrum disorder was admitted to the pediatric ward for extreme weight loss. 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.

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, and potentially fatal impacts on the body, such as growth retardation, refeeding syndrome (RS), and sudden death [2, 3]. The mortality associated with AN has been reported to be approximately 5~15%, and in addition to suicide, many patients die from physical complications associated with poor nutrition and refeeding[4–7].

The risk of sudden death must always be kept in mind, as the risk of sudden death is reported to be 12 times greater than that of healthy women [8]. Patients with AN are at risk of sudden death even if not in the acute phase, but when the risk of RS, which can result in electrolyte abnormalities and other problems, is high especially during undernutrition, and special attention should be given to sudden changes in condition [2, 8–12]. Fatal arrhythmias caused by complications, such as QTc prolongation, are thought to be the most common cause of sudden death, but there is no clear evidence that subsequent fatal arrhythmias are a direct cause of death [3].

Here, we describe the case of a 17-year-old adolescent who had a sudden change in condition during the night on 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. This case report may stimulate future research to examine safer physical monitoring methods in severely malnourished AN patients.

Case Presentation

This case involves a 17-year-old female with severe AN of approximately 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. One day, 11 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 during the course.

At the time of admission, she was 151.0 cm tall and 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; Cr, 0.35 mg/dL), elevated liver enzymes (AST, 1033 IU/L; ALT, 971 IU/L; LDH, 1056 IU/L; γ GTP, 145 IU/L) and mild hypokalemia (Na, 143 mmol/L; K, 3.3 mmol/L; P, 3.9 mg/dL; Mg, 2.5 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) (Figure 1). 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 intravenous fluids was initiated (fluid volume, 45 ml/kg/day; glucose, 4.7%; 180 kcal/kg/day=8.4 kcal/kg/day; K, 30 mEq/day; P, 10 mEq/day; VitB₁, 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. At night, based on medical staff and the mother's point of view, she appeared to be asleep, but after 8 hours 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 hours postmortem with the consent of the parents. The brain showed marked edema with a gain of weight (1540 g), narrowing of the ventricles, and herniation of cerebellar tonsils (Figure 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. 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 strong 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, such as those with severe AN, and has implications for the future monitoring of patients during refeeding. 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 may have been cardiogenic or neurogenic with cerebral edema resulting in tonsillar herniation. Both heart damage and cerebral edema could be the cause of death or the result of some conditions.

The patient's ECG at the time of admission suggested that she had suffered some cardiac damage. Turillazzi et al reported that "colliquative myocytolysis" is a possible histological hallmark of congestive heart failure in underweight AN patients [13]. In our case, there were no similar findings on cardiac histology. Although the patient had mild QTc prolongation on admission, we did not find further prolongation of the QTc on posthospitalization ECG monitoring, and it is questionable whether this directly led to lethal arrhythmia and sudden death.

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, 9–12]. Many published guidelines recommend an initial calorie level of 10 kcal/day for high-risk patients and 5-10 kcal/day for very high-risk patients to prevent RS [2, 9–12, 14]. Although the initial calories in the present case were within the recommended range, it is possible that the patient had a sudden change due to fatal arrhythmia.

On the other hand, the autopsy findings of this case showed unexpectedly massive general cerebral edema and tonsillar herniation. 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 [13]. 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 [14]. The initial calorie levels in the present case were within the optimal range and cannot be considered a similar factor.

In our case, the patient drank 700 ml of water in the 6 hours after admission. 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 [15–17]. Similar abnormalities in

sodium and water regulation have been reported in a rare case of cerebral edema associated with hyponatremia and subsequent cerebral herniation in a marathon runner, and water intoxication may have affected the development of cerebral edema in this case [18]. Although various guidelines for the prevention of refeeding syndrome do not provide definitive fluid restriction, further study may be needed in the future for extremely high-risk patients [2, 9–12].

The most common cause of sudden death in AN, with the exception of 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, 3, 8, 19, 20]. However, few patients show evidence of arrhythmia, and fewer patients undergo autopsy. Therefore, it is not clear whether the arrhythmia is caused by electrolyte abnormalities or whether it is preceded by other fatal states, such as intracranial hypertension, respiratory arrest from cerebral herniation, and arrhythmia from hypoxia. In some cases, patients with severe AN may not respond to calls due to psychological resistance, and it is not easy to ascertain their state of consciousness, especially when they are asleep. Therefore, it is assumed that in many cases, as in this case, it may be difficult to determine whether the patient had a sudden disturbance of consciousness before the arrhythmia.

Accurate monitoring of intracranial pressure requires an invasive procedure and, given the rare frequency, should not be performed in malnourished patients without impaired consciousness [21]. 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 prevent sudden death. 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.

Conclusions

The findings in this 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 as well as to elucidate the links between sudden death associated with refeeding and tonsillar herniation.

List Of Abbreviations

AN – Anorexia Nervosa

RS – Refeeding Syndrome

ECG - Electrocardiogram

BMI – Body Mass Index

Declarations

Ethics approval and consent to participate

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).

Consent for publication

We give consent for the publication of our paper.

Availability of data and materials

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

Competing interests

We declare no competing interests.

Funding

This work was supported by JSPS KAKENHI Grant Number JP18K02797.

Author's contributions

Tasuku Kitajima – data collection, analysis, manuscript.

Ryoko Otani – data collection, analysis, manuscript.

Naho Matsushima – data collection and interpretation.

Naoki Matsubara – data collection and interpretation.

Takeshi Inoue – data collection and interpretation.

Akiko Fujii – analysis of autopsy and pathological data.

Shinichi Ban – analysis of autopsy and pathological data, supervision.

Ryoichi Sakuta – interpretation, supervision.

All authors read and approved the final manuscript.

Acknowledgments

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Figures

Figure 1

ECG performed on admission Sinus bradycardia (51 bpm), abnormal Q waves at V1-2, negative T waves at V1-4 and mild QTc prolongation (QTc=452 ms).

Figure 2

Gross examination of the postmortem brain a. Frontal cross sections of the cerebrum. Increased brain weight (1540 g) and narrowing of the ventricles are findings of cerebral edema. b. Gross appearance of the cerebellum. The arrow indicates cerebellar tonsillar herniation.