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Gastric Rupture and Necrosis in Prader-Willi Syndrome

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Abstract

Hyperphagia and obesity are common features in individuals with Prader-Willi syndrome (PWS). Demographic and cause of death data from individuals with PWS were obtained through a national support organization. Four reports of unexpected mortality due to gastric rupture and necrosis were found in 152 reported deaths, accounting for 3% of the causes of mortality. Four additional individuals were suspected to have gastric rupture. Vomiting and abdominal pain, although rare in PWS, were frequent findings in this cohort. The physician should consider an emergent evaluation for gastric rupture and necrosis in individuals with PWS who present with vomiting and abdominal pain.

Keywords

Prader-Willi syndrome; gastric necrosis; gastric perforation; vomiting; hyperphagia; mortality

INTRODUCTION

Prader-Willi syndrome (PWS) is a relatively common genetic disorder (1 in 10,000–20,000) characterized by early onset childhood hyperphagia and obesity (1,2). Other clinical findings include mental deficiency, infantile hypotonia, behavioral problems, skin picking, thick saliva, almond-shaped eyes with bitemporal narrowing, cryptorchidism, small hands and feet, and short stature. The management of obesity in PWS is problematic (1,2). However, the recent utilization of growth hormone (GH) therapy, diet and behavior modifications, and group home management have improved body habitus in PWS (3,4,5). Still, individuals with

PWS continue to have excessive appetites and can consume large amounts of food at one time in spite of environmental control. These food seeking behaviors theoretically can lead to life-threatening gastric dilatation with perforation and necrosis (6). Previous reports of suspected incidences are few (6,7), but our study of mortality utilizing data from a parent support group bereavement program has identified four additional individuals and four probable individuals with gastric perforation and necrosis. Their associated clinical history may provide medical providers with insight into signs of pending gastric perforation and necrosis in individuals with PWS.

METHODS

The Prader-Willi Syndrome Association (USA) bereavement program has documented demographic and cause of death data from voluntary familial reporting on individuals with PWS since 1999. In 2004, a multidisciplinary committee was organized consisting of a cardiologist, gastroenterologist, endocrinologist, medical geneticists, and a volunteer patient advocate representative to investigate deaths in PWS and to create a familial-response questionnaire to collect additional information. Request to complete the questionnaire was sent to all families who contacted the bereavement coordinator. Release of medical information was also requested from the families. Institutional Review Board approval was obtained from the University of Utah.

RESULTS

Familial report of cause of death was available in 152 individuals with PWS reported to the coordinator of the Prader-Willi Syndrome Association (USA) bereavement program. A total of 56 families completed and returned the familial-response questionnaires and released medical records, and families reported that autopsies were performed in 31 individuals. Four (3%) of the 152 individuals were reported to have died from gastric rupture and necrosis. In addition, deaths were reported as unexplained in 27 (18%) of the 152 individuals and it is unknown if they had an undiagnosed gastric perforation. Of those who died of gastric rupture and necrosis, cause of death was obtained by familial report in two individuals, and by autopsy and medical records in the other two individuals. All were male. Age at death ranged from 17–49 years. Further, four additional individuals (2 male, 2 female) were suspected to have gastric dilatation and perforation, but without autopsy evidence. Details of each subject are discussed below.

Clinical Summaries

Subject #1, a 17-year-old male, died of sepsis and multisystem organ failure after gastric perforation and necrosis. He had an eating binge during a holiday with subsequent abdominal pain and vomiting one day prior to his death. Parents state that he had never vomited previously. He required a gastric resection due to gastric necrosis and perforation but expired within 24 hours. An autopsy showed microscopic foci of mucosal ulceration extending to full necrosis and perforation. He had been receiving growth hormone therapy and weight was 62.6 kg and body mass index (BMI) was 22 kg/m² at time of death.

Subject #2 was a 24-year-old male with a recent onset of abdominal pain and vomiting before medical intervention. He underwent an exploratory laparotomy which showed gastric perforation and necrosis. A partial gastrectomy was performed. He subsequently developed septic shock leading to multisystem organ failure and death. An autopsy showed transmural gastric necrosis and focal mucosal ulceration of the esophagus. Weight was 81.6 kg and BMI was 27 kg/m² at time of death.

Subject #3 was a 22-year-old male with a report of vomiting and subsequent gastric rupture per parental report. Weight was 53.5 kg at time of death with a reported history of previous weight loss of 38 kg. No further information was available.

Subject #4 was a 49-year-old male with a report of an “ulcer” with gastric rupture and subsequent death per familial report. Weight was 108.9 kg at time of death with a BMI of 50.2 kg/m². No further information was available.

Four other individuals with PWS had suspected gastric rupture and/or necrosis. The first individual was a 22-year-old female who presented to the emergency department with abdominal pain. She was examined, prescribed a laxative, and discharged to home. Later that evening she began to vomit multiple times and was taken to the hospital by ambulance. Attempts to revive her failed. An autopsy reported a markedly distended stomach with a “paper-thin” stomach wall and tear in the anterior stomach wall. The cause of death, however, was reported as secondary to aspiration with discussion that the gastric tear was due to a potentially postmortem event. Her weight at the time of death was 72 kg with a BMI of 30 kg/m². The second individual was a 50-year-old female who died secondary to an upper-gastrointestinal bleed. She presented with hematemesis and an autopsy showed a markedly distended stomach with erosive gastritis and evidence of chronic gastritis. Her weight was 77 kg with a BMI of 36 kg/m² at the time of death. However, she weighed as much as 111 kg ten years earlier. The third individual was a 7-year-old male with abdominal pain and subsequent hematemesis with a rapid and sudden death. The fourth individual was a 49-year-old male who was thought to have died from an upper gastrointestinal bleed, but he was taking coumadin and aspirin for a history of pulmonary embolism. At death his weight was 98kg with a BMI of 38 kg/m².

DISCUSSION

Although episodic hyperphagia, food foraging, and stealing of food may lead to gastric dilatation, the etiology of the gastric perforation and necrosis is still speculative. Acute gastric dilation and its complications, including stomach rupture, have been associated with anorexia nervosa, binge eating disorder, bulimia, acute pancreatitis, and gastric hemorrhage (8). Wharton et al. reported six individuals with PWS who had gastric dilatation, two of whom died (6). They suggested that the associated necrosis was due to acute gastric dilatation after polyphagia (6). In addition, our series suggest that people with PWS are at significant risk of gastric perforation and necrosis. Particularly salient is the observation that gastric perforation/necrosis was the cause of mortality in 3% to 6% of subjects in the cohort of individuals who died who are known to the Prader-Willi Syndrome Association (USA). It is, however, possible that families of individuals with unusual causes of death could be more likely to contact the bereavement program introducing a potential bias.

Approximately a third of individuals with PWS have a weight greater than 200% of their ideal body weight (9,10). The majority of individuals in this study were relatively non-obese compared to what is generally observed in PWS, or had a history of prior weight loss. Previously, Wharton et al. reported that three individuals with PWS with gastric dilatation and necrosis had gradually lost more than 45 kg at an average rate of 1 kg/week after strict dietary programs, and they suggested that alteration in stomach muscle integrity from weight loss may have been a predisposing factor (6). Hence, individuals with PWS with recent weight loss or with a more ideal body weight may be at greater risk for gastric dilatation and perforation. With the advancement of nutritional strategies, group home programs, and growth hormone therapy, individuals with PWS may be more likely to maintain a more ideal body weight, although the underlying pathology leading to consumption of large quantities of food in a short period of time continues to persist. This may predispose subjects with

PWS, particularly those with recent weight loss or absence of obesity, to gastric dilatation and perforation, necessitating wider awareness by medical care providers of this potential complication.

A high threshold for vomiting has been associated with PWS (4), and data from the 54 familial-response questionnaires in our cohort subjectively reported decreased vomiting during viral illnesses in 78% of respondents. Attempts to induce vomiting in individuals with PWS were reported as unsuccessful in 64% in one study (11). The finding of vomiting in the subjects with PWS who presented with gastric perforation and necrosis suggests that vomiting in PWS is a sign of serious underlying pathology.

Decreased sensitivity to pain has also been reported anecdotally in PWS and was a common parental response in our cohort (91%). The complaint of abdominal pain should be considered a further sign for potential gastric perforation. Several family members reported that they thought the occurrence of abdominal pain was extremely unusual, but felt that their concerns were ignored by their physicians as the complaints of abdominal pain were minimal in people with PWS compared to the general population. We think that the presence of abdominal pain and/or vomiting in individuals with PWS likely warrants an abdominal radiograph looking for evidence of perforation and monitoring in an inpatient facility or rapid treatment unit.

Avoiding episodes of binge eating is likely problematic in PWS due to their history of hyperphagia. Of major concern are changes in routine that may expose individuals with PWS to large quantities of food in new environments or in the presence of unusual food sources (e.g., holiday parties). For example, one individual in our study had a bingeing episode during a holiday event, suggesting that close supervision during special occasions (e.g., birthday parties) is important to avoid these episodes.

It is important for physicians working in emergency departments to be aware of this phenomenon in PWS in order to avoid the mistaken diagnosis of viral gastroenteritis, as they are likely to be the first physicians to encounter individuals with PWS with an impending gastric perforation. Reports of a bingeing episode in an individual with PWS with recent weight loss and a relatively normal body weight should alert the physician to an alternative diagnosis. In particular, vomiting and abdominal pain are signs that deserve rapid attention regardless of the intensity of complaint in this subject population in hopes of avoiding morbidity and mortality.

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