

Short Communication

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. *JPGN* 45:272–274, 2007. **Key Words:** Prader-Willi syndrome—Gastric necrosis—Gastric perforation—Vomiting—Hyperphagia—Mortality. © 2007 by European Society for Pediatric Gastroenterology, Hepatology, and Nutrition and North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition

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 use of growth hormone therapy, diet and behavior modifications, and group home management has improved body habitus in PWS (3–5). Still, individuals with PWS continue to have excessive appetites and can consume large amounts of food at one time despite

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, which used data from a parent support group bereavement program, has identified 4 additional individuals with gastric perforation and necrosis and 4 individuals with suspected gastric rupture and/or necrosis. Their associated clinical history may provide medical providers with insight into signs of pending gastric perforation and necrosis in individuals with PWS.

MATERIALS AND 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, a gastroenterologist, an 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. A request to complete the questionnaire was sent to all families who contacted the bereavement coordinator. Release of medical information was also requested from the

Received January 5, 2007; accepted March 9, 2007.

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Supported by a grant from the Prader-Willi Syndrome Association (USA) and also supported in part by grants from NIH RR-00064, NIH K23 NS052500, and the Children's Health Research Center and Clinical Genetics Research Program at the University of Utah.

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 of gastric rupture and necrosis. In addition, deaths were reported as unexplained in 27 (18%) of the 152 individuals, and it is unknown whether they had an undiagnosed gastric perforation. Of those who died of gastric rupture and necrosis (all male), cause of death was obtained by familial report in 2 individuals and by autopsy and medical records in the other 2 individuals. The ages at death ranged from 17 to 49 years. Furthermore, 4 additional individuals (2 male, 2 female) were suspected to have gastric dilatation and perforation, but without autopsy evidence. The details of each individual are discussed below.

Clinical Summaries

The first individual, a 17-year-old adolescent boy, 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 1 day before his death. His parents stated that he had never vomited previously. He required a gastric resection because of 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; his weight was 62.6 kg and his body mass index (BMI) was 22 kg/m² at the time of death.

The second individual was a 24-year-old man 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 experienced septic shock, leading to multisystem organ failure and death. An autopsy showed transmural gastric necrosis and focal mucosal ulceration of the esophagus. His weight was 81.6 kg and his BMI was 27 kg/m² at the time of death.

The third individual was a 22-year-old man with a report of vomiting and subsequent gastric rupture according to the parental report. His weight was 53.5 kg at the time of death, with a reported history of previous weight loss of 38 kg. No further information was available.

The fourth individual was a 49-year-old man with a report of an "ulcer" with gastric rupture and subsequent

death according to the familial report. His weight was 108.9 kg at the 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 woman who presented at the emergency department with abdominal pain. She was examined, prescribed a laxative, and discharged. Later that evening she vomited 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 a tear in the anterior wall of the stomach. 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 woman 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 had weighed as much as 111 kg 10 years earlier. The third individual was a 7-year-old boy with abdominal pain and subsequent hematemesis, with a rapid and sudden death. The fourth individual was a 49-year-old man who was thought to have died of an upper gastrointestinal bleed, but he was taking coumadin and aspirin for a history of pulmonary embolism. At death his weight was 98 kg, with a BMI of 38 kg/m².

DISCUSSION

Although episodic hyperphagia, food foraging, and stealing food may lead to gastric dilatation, the cause 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 (6) reported 6 individuals with PWS who had gastric dilatation, 2 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 for gastric perforation and necrosis. Particularly salient is the observation that gastric perforation/necrosis was the cause of mortality in 3% to 6% of individuals in the cohort of those who died who were 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 >200% of their ideal body weight (9,10). The majority of individuals in this study were relatively nonobese, compared with what is generally observed

in PWS, or had a history of previous weight loss. Previously, Wharton et al (6) reported that 3 individuals with PWS with gastric dilatation and necrosis had gradually lost >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 body weight closer to the ideal 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 body weight closer to the ideal, although the underlying pathological condition leading to the consumption of large quantities of food in a short time continues to persist. This may predispose individuals 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 1 study (11). The finding of vomiting in the individuals with PWS who presented with gastric perforation and necrosis suggests that vomiting in PWS is a sign of a serious underlying pathological condition.

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

Avoiding episodes of binge eating is likely problematic in PWS patients because of 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 (eg, holiday parties). For example, 1 individual in our study

had a bingeing episode during a holiday event, suggesting that close supervision during special occasions (eg, 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 to avoid the mistaken diagnosis of viral gastroenteritis, because 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 deserve rapid attention regardless of their intensity in this population, in the hope of avoiding morbidity and mortality.

Acknowledgment: The authors thank Amy Watkins for her help in coordinating the study.

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