The usefulness of biliopancreatic diversion/Scopinaro operation in treatment of patients with Prader-Willi syndrome

Maciej Michalik[1], Agata Frask[2], Pawel Lech[1], Michal Zdrojewski[1], Anna Doboszynska[3]

[1]General and Minimally Invasive Surgery Department, University of Warmia and Mazury, Olsztyn, Poland
[2]General and Vascular Surgery Department, Ceynowa Hospital, Wejherowo, Poland
[3]The Centre for Pulmonary Disease, University of Warmia and Mazury, Olsztyn, Poland

Videosurgery Miniinv 2015; 10 (2): 324–327
DOI: 10.5114/wiitm.2015.49669

Abstract

Prader-Willi syndrome (PWS) is the most common form of obesity with a genetic basis. The short expected survival time due to numerous accompanying diseases and their complications is the reason for research on the maximally efficient method of treatment of obesity in this syndrome. Undertaken attempts of conservative treatment, for example with somatostatin, are ineffective. It seems that the only effective treatment of obesity in this syndrome may be surgical. In this article we present 2 cases of patients with PWS who underwent surgery consisting of biliopancreatic diversion (BPD)/Scopinaro procedure. The BPD/Scopinaro operation in selected cases of disciplined patients with a co-operative family, which we find of key importance, can be considered as one option of treatment of this syndrome in patients with prior neglect of conservative treatment.

Key words: *obesity surgery, biliopancreatic diversion, Prader-Willi syndrome, metabolic syndrome, metabolic surgery.*

Introduction

Prader-Willi syndrome (PWS), described for the first time in 1956 as Prader-Labhart-Willi syndrome, is a genetic disorder with deletion (70% of cases) or no expression of seven genes in chromosome region 15q11-q13 [1]. In around 28% of cases there is mother's heterodisomy of chromosome 15, and it is due to an imprinting mutation [2]. The incidence rate is 410/100 000 live births [3]. The clinical characteristics include muscular hypotony and weak reflex of the infant suckling. In the later stage of development there is hyperorexia followed by obesity, short stature, hypogonadism, psychomotor retardation [4–6], an inclination to tantrums and obsessive-compulsive disorder. Obesity appears in over 80% of untreated patients [7]. About 1/3 of patients with PWS attain a body mass that is twice the ideal body mass [8]. The cause of hyperorexia is not well known. Probably one reason is the high baseline level of ghrelin present both in children and in adults with PWS [1, 9, 10]. Patients develop various behaviors related to eating: compulsive overeating, the search for food and the consumption of material not fit for eating, such as animal fodder and decorative objects resembling food, the theft of money with the aim of purchase of food, escaping from home and searching for food outside the place of residence. These patients tend to die in the fourth decade of life as a result of the development of severe obesity with inadequate body perception together with obesity-related disorders, such as diabetes, apnea, and right heart failure [3]. The short life expectancy of patients with PWS that is due to the numerous diseases and their complications necessitates research on a maximally

Address for correspondence
Pawel Lech MD, General and Minimally Invasive Surgery Department, University of Warmia and Mazury, 44 Niepodleglosci St, 10-045 Olsztyn, Poland, phone: +48 606 889 665, e-mail: lechpawel@op.pl

efficient method of treatment of obesity (metabolic syndrome) in this disorder. Conservative treatment, for example with somatostatin, is ineffective. It seems that the only efficient treatment of obesity and consequential metabolic syndrome may be surgical treatment [11, 12]. The use of restrictive methods is ineffective, and operations such as Roux-en-Y gastric bypass do not bring a good result either. In the literature one can find isolated reports concerning operative treatments of obesity in patients with PWS [13–16].

We present 2 cases of patients with PWS, one of whom underwent Scopinaro's procedure (biliopancreatic diversion – BPD).

Case reports

Case 1

The first patient is a 25-year-old woman with confirmed PWS. Since early childhood one could observe systematic increase in her body mass due to hyperphagia with simultaneous lack of the feeling of satiety and low physical activity. All attempts of conservative management of obesity were ineffective. At the time of hospitalization her body mass was 125 kg and height 150 cm with body mass index (BMI) of 55.5 kg/m^2. In the past the patient had undergone laparoscopic cholecystectomy because of a symptomatic vesicular stone. Prader-Willi syndrome was also diagnosed in the patient's brother, and thus it is one of the rare cases of familial occurrence of this disorder. In July 2013 the patient underwent Scopinaro's biliopancreatic diversion. After the intervention the patient was hospitalized for 1 day in the intensive care unit because of perioperative respiratory insufficiency. She returned home in a good state 4 days after the operation. The patient was re-hospitalized 7 days later because of abdominal pain, weakness, elevated body temperature and elevated inflammatory markers (CRP 387 mg/dl). Subsequently she was diagnosed with cystitis and was discharged 4 days later following conservative management with antibiotics. Six months after the intervention, the patient's weight was 93 kg (BMI 41.3 kg/m^2), and % excess weight loss (%EWL) was 43%. The ideal body mass was calculated according to the formula of Lorenz. After the intervention we did not observe any adverse events. Standard vitamin supplementation and micro- and macronutrients were recommended to the patient. The patient had 3–4 stools daily (with normal consistency), which was acceptable both for the patient and carers. Due to reduction of body mass, improvement in mobility and thus physical activity was possible. In this case the excellent cooperation of the family with attending doctors and the very high level of family care of the patient must be underlined.

Case 2

The second patient was an 18-year-old woman diagnosed with PWS with extremely severe obesity. Neither conservative management nor the intra-gastric balloon procedure reduced the patient's body mass. At admission the body mass was 141 kg, height 148 cm, BMI 64.4 kg/m^2. The patient suffered from poorly controlled obesity-related conditions such as hypertension, diabetes and asthma. Her past medical history showed disruptive behavior disorder necessitating frequent hospital admissions. In 2005, the patient underwent spinal surgery for scoliosis. Her medication list consisted of metformin hydrochloride, captopril, hydroxyzine hydrochloride, fenoterol hydrobromide, ipratropii bromide. She did not receive steroids.

In July 2012, the patient underwent a BPD procedure. After the intervention she stayed 3 days in the intensive care unit because of respiratory insufficiency. Seven days after the intervention she was discharged home in generally good condition, with the standard recommendation of supplementation of vitamins, micro- and macronutrients. At 18 months after the procedure the body mass was 118 kg (BMI 53.9 kg/m^2) with %EWL of 25%. Since the operation the patient has had around 10 loose stools daily. Diseases connected with the metabolic syndrome are better controlled. Since the time of the intervention the patient has been hospitalized three times in the psychiatric hospital because of episodes of aggression. Moreover, the patient refused further care from the obesity service.

Discussion

Prader-Willi syndrome is the most common genetic disorder resulting in severe obesity [7]. Almost all cases of PWS are sporadic, which means that the syndrome is not inherited. Nevertheless, the small number of reported cases shows that familial occurrence is also possible. According to the current knowledge, the risk of PWS in the second child is around 0.1%.

The analysis of behavior of PWS patients suggests that the excessive eating is due not to excessive hunger but probably the lack of satiety sensation. That is the reason for the difficulty in selecting an appropriate and effective operation in these patients.

Diagnosis of PWS includes numerous distinctive criteria. The major criteria include: muscular hypotony during the neonatal period and early childhood, poorly developed suction reflex, problems with feeding requiring special techniques to feed, very fast increase in body mass in the first years of life which causes central obesity, obsession with eating with a continuous search for food, difficulties with self-control, the characteristic facial appearance, hypogonadism with sexual underdevelopment and infertility, considerably retarded psychomotor function and mild to severe delay of intellectual development. Minor criteria include: reduced movements of the embryo, conduct, mood and obsessive-compulsive disorders, obstinacy, the inclination to steal and lie, sleep disorder with periods of apnea, short stature, hypopigmentation of the skin and hair in comparison to healthy family members, small and narrow palms and very small shoulder girdle, esophoria, short-sightedness, secretion of thick and sticky saliva, gathering in corners of mouth, speech articulation disorder, and habitual plucking of the skin. Additional criteria include: high pain threshold, weakened gag reflex, rachioscoliosis and/or kyphosis, osteoporosis, correct neuromuscular findings – muscle biopsy, electromyogram and nerve conduction velocity test [17–30].

The concentration of ghrelin in PWS patients is significantly elevated – three to four times higher in comparison to obese children without PWS. The necessity of surgical management in patients with PWS is due to the numerous diseases accompanying this syndrome. They are much the same as the ones accompanying pathological obesity, e.g. diabetes, arterial hypertension, sleep apnea and cardiorespiratory failure. These comorbidities are responsible for considerably shorter life expectancy. This negative trend can be at least partially reversed by adequate management of PWS-related conditions. As these comorbidities are also directly related to obesity, it is not possible to implement efficient treatment without simultaneous management of excessive body mass. In both presented cases the diagnosis of PWS was confirmed very late despite the genetic character of the disease and symptoms present since birth. In the first case the diagnosis of PWS was made when the patient presented with cholelithiasis, and in the second case when the patient reached the age of twelve. Both patients suffered from super morbid obesity at the presentation with BMI of 64 kg/m^2 and 55 kg/m^2 respectively. Such a delay in the diagnosis and the degree of obesity render all attempts of conservative management ineffective. Treatment of PWS patients requires very close cooperation with their family. Moreover, PWS patients themselves and their families have to be well informed not only about the surgery but also about all other interventions required. This is due to the fact that even such extensive operation as BPD might not be sufficient. Good understanding of possible side effects such as frequent and loose stools is necessary as well.

Certainly, it is difficult to formulate binding conclusions based on the two presented cases. However, use of the biliopancreatic diversion procedure in PWS seems efficient [31]. It provided satisfactory reduction of the excessive body mass, with %EWL of 25–43%, together with improvement of comorbid conditions in presented neglected patients.

Both patients were admitted to the Intensive Care Unit because of perioperative respiratory failure. It has been observed that obese patients suffer from perioperative respiratory insufficiency due to several factors related directly to obesity. First of all, the thick layers of the chest wall cause volume restriction and reduce respiratory muscle efficiency. Secondly, the susceptibility of the alveoli is reduced and thus the respiratory resistance increases. Thirdly, the pressure gradient between the abdomen, the chest and the air changes, causing further impairment of ventilation. That roughly explains why hypercapnia (pCO_2 > 45 mm Hg) is frequent in obese patients with BMI > 30 kg/m^2 with no other identifiable causative factors [32]. Prader-Willi syndrome patients as well as obese patients are at high risk (70%) of sleep apnea [33]. This disorder, identifiable by polysomnography, appears in the form of central and peripheral apnea [34]. Standard treatment for obstructive sleep apnea is usually poorly tolerated [35]. Uncontrolled obesity, especially in the PWS, contributes to respiratory insufficiency, pulmonary hypertension and cardiopulmonary deaths.

Conclusions

It seems that the only effective treatment of obesity and metabolic syndrome in PWS is surgical man-

agement. The BPD/Scopinaro procedure in selected and well-disciplined PWS patients with co-operating families might be a good option.

Conflict of interest

The authors declare no conflict of interest.

References

1. Feigerlova E, Diene G, Conte-Auriol F, et al. Hyperghrelinemia precedes obesity in Prader-Willi syndrome. J Clin Endocrinol Metab 2008; 93: 2800-5.
2. Gunay-Aygun M, Schwartz S, Heeger S, et al. The changing purpose of Prader-Willi syndrome clinical diagnostic criteria and proposed revised criteria. Pediatrics 2001; 108: e92.
3. McCandless SE; The Committee on Genetics. Clinical report-health supervision for children with Prader-Willi syndrome. Pediatrics 2011; 127: 195-204.
4. Goldstone AP, Holland AJ, Hauffa BP, et al. Recommendations for the diagnosis and management of Prader-Willi syndrome. J Clin Endocrinol Metab 2008; 93: 4183-97.
5. Nixon GM, Rodda CP, Davey MJ. Longitudinal association between growth hormone therapy and obstructive sleep apnea in a child with Prader-Willi syndrome. J Clin Endocrinol Metab 2011; 96: 29-33.
6. Clarke DJ, Boer H, Whittington J, et al. Prader-Willi syndrome, compulsive and ritualistic behaviours: the first population-based survey. Br J Psychiatr 2002; 180: 358-62.
7. Delparigi A, Tschöp M, Heiman ML, et al. High circulating ghrelin: a potential cause for hyperphagia and obesity in Prader-Willi syndrome. J Clin Endocrinol Metab 2002; 87: 5461-4.
8. Burman P, Ritzén, Lindgren AC. Endocrine dysfunction in Prader-Willi syndrome: a review with special reference to GH. Endocr Rev 2011; 22: 787-99.
9. Hauffa BP, Haase K, Range IM. The effect of growth hormone on the response of total and acylated ghrelin to a standardized oral glucose load and insulin resistance in children with Prader-Willi syndrome. J Clin Endocrinol Metab 2007; 92: 834-40.
10. Paik KH, Choe YH, Park WH, et al. Suppression of acylated ghrelin during oral glucose tolerance test is correlated with whole-body insulin sensitivity in children with Prader-Willi syndrome. J Clin Endocrinol Metab 2006; 91: 1876-81.
11. Razak Hady R, Dadan J, Golaszewski P, et al. Impact of laparoscopic sleeve gastrectomy on body mass index, ghrelin, insulin and lipid levels in 100 obese patients. Videosurgery 2012; 7: 251-9.
12. Bužga M, Zavadilová V, Holéczy P. Dietary intake and ghrelin and leptin changes after sleeve gastrectomy. Videosurgery Miniinv 2014; 9: 554-61.
13. Grugni G, Guzzaloni G, Morabito F. Failure of biliopancreatic diversion in Prader-Willi syndrome. Obes Surg 2000; 10: 179-81.
14. de Almeida MQ, Cercato C, Rascovski A, et al. Results of biliopancreatic diversion in two patients with Prader-Willi syndrome. Obes Surg 2005; 15: 901-4.
15. Marinari GM, Camerini G, Novelli GB, et al. Outcome of biliopancreatic diversion in subjects with Prader-Willi syndrome. Obes Surg 2001; 11: 491-5.
16. Kobayashi J, Kodama M, Yamazaki K, et al. Gastric bypass in a Japanese man with Prader-Willi syndrome and morbid obesity. Obes Surg 2003; 13: 803-5.
17. Hamilton CR Jr, Scully RE, Kliman B. Hypogonadotropism in Prader-Willi syndrome: induction of puberty and spermatogenesis by clomiphene citrate. Am J Med 1972; 52: 322-9.
18. Crinò A, Schiaffini R, Ciampalini P, et al. Genetic Obesity Study Group of Italian Society of Pediatric endocrinology and diabetology (SIEDP). Hypogonadism and pubertal development in Prader-Willi syndrome. Eur J Pediatr 2003; 162: 327-33.
19. Lindgren AC, Barkeling B, Hagg A, et al. Eating behavior in Prader-Willi syndrome, normal weight, and obese control groups. J Pediatr 2000; 137: 50-5.
20. Aughton DJ, Cassidy SB. Physical features of Prader-Willi syndrome in neonates. Am J Dis Child 1990; 144: 1251-4.
21. Hered RW, Rogers S, Zang YF, et al. Ophthalmologic features of Prader-Willi syndrome. J Pediatr Ophthalmol Strabismus 1988; 25: 145-50.
22. Scardina GA, Fucà G, Messina P. Oral diseases in a patient affected with Prader-Willi syndrome. Eur J Paediatr Dent 2007; 8: 96-9.
23. Wise MS, Zoghbi H, Edwards M, et al. Hyperthermia in infants with Prader-Willi syndrome (Abstract). Am J Med Genet 1991; 41: 528.
24. Bhargava SA, Putnam PE, Kocoshis SA, et al. Rectal bleeding in Prader-Willi syndrome. Pediatrics 1996; 97: 265-267.
25. Dykens EM. Are jigsaw puzzle skills 'spared' in persons with Prader-Willi syndrome? J Child Psychol Psychiatry 2002; 43: 343-52.
26. Miller JL, Couch JA, Schmalfuss I, et al. Intracranial abnormalities detected by three-dimensional magnetic resonance imaging in Prader-Willi syndrome. Am J Med Genet 2007; 143A: 476-83.
27. Wharton RH, Wang T, Graeme-Cook F, et al. Acute idiopathic gastric dilation with gastric necrosis in individuals with Prader-Willi syndrome. Am J Med Genet 1997; 73: 437-41.
28. Stevenson DA, Heinemann J, Angulo M, et al. Gastric rupture and necrosis in Prader-Willi syndrome. J Pediatr Gastroenterol Nutr 2007; 45: 272-4.
29. Holm VA, Cassidy SB, Butler MG, et al. Prader-Willi syndrome: consensus diagnostic criteria. Pediatrics 1993; 91: 398-402.
30. Gunay-Aygun M, Schwartz S, Heeger S, et al. The changing purpose of Prader-Willi syndrome clinical diagnostic criteria and proposed revised criteria. Pediatrics 2001; 108: E92.
31. Karcz WK, Kuesters S, Marjanovic G, et al. Duodeno-enteral omega switches – more physiological techniques in metabolic surgery. Videosurgery Miniinv 2013; 8: 273-9.
32. Piper AJ, Grunstein RR. Obesity hypoventilation syndrome. Am J Resp Critical Care Med 2011; 183: 292-8.
33. O'Donoghue FJ, Camfferman D, Kennedy JD, et al. Sleep-disordered breathing in Prader-Willi syndrome and its association with neurobehavioral abnormalities. J Pediatr 2005; 147: 823-9.
34. Urquhardt DS, Guilliver T, Williams G, et al. Central sleep-disordered breathing and the effect of oxygen therapy in infants with Prader-Willi syndrome. Arch Dis Child 2013; 98: 592-5.
35. Czystowska M, Skoczylas A, Rudnicka A, et al. Obstructive sleep apnea in patient with Prader-Willi syndrome. Pneumonol Alergol Pol 2010; 78: 148-52.

Received: 13.06.2014, **accepted:** 7.01.2015.