Rare disease

Pregnancy outcome in a woman with prune belly syndrome

R Tyler Hillman,¹ Matthew James Garabedian,² Robert J Wallerstein³¹Stanford University, School of Medicine, Palo Alto, California, USA²Department of Obstetrics & Gynecology, Santa Clara Valley Medical Center, San Jose, California, USA³Department of Pediatrics, Santa Clara Valley Medical Center, San Jose, California, USA

Correspondence to Dr Matthew James Garabedian, Matthew.Garabedian@hhs.sccgov.org

Summary

Prune belly syndrome is a rare congenital syndrome that primarily affects male fetuses. Affected men are universally infertile; however, there is a paucity of information published on the reproductive potential of affected women. Pregnancy outcomes in affected women have not been described in the literature. We describe the case of pregnancy in an affected woman. Her pregnancy progressed without complication. Her fetus had no stigmata of the syndrome. Her labour and delivery were, however, complicated by a prolonged second stage of labour and need for vacuum-assisted vaginal delivery.

BACKGROUND

Prune belly syndrome (PBS) is a rare congenital abnormality conventionally characterised by a triad of absent abdominal musculature, urinary tract ectasia and cryptorchidism.¹ The overall incidence is estimated to be 1 in 40 000 live births, with approximately 95% of PBS cases occurring in males, with an incidence of 1.1 per 100 000 in women.¹ The aetiology of PBS remains obscure, although evidence suggests a genetic contribution in some cases. Regardless of sex, the severity and associated phenotypic features of the disorder vary extensively. Notably, men with PBS are universally infertile without the use of assisted reproductive technologies. To date there have been no documented cases of fertility in a female patient with PBS, yet normal menstrual cycles have been described in such patients.² Here, we report a case of a woman with PBS who naturally conceived and gave birth to a healthy female infant.

CASE PRESENTATION

A 25-year-old gravida 1, para 0 woman with PBS presented to our institution for routine prenatal care. The patient was born at term by uncomplicated spontaneous vaginal delivery and weighed 7 lb 9 oz at birth. Immediately following delivery, the patient was noted to have loose, wrinkled abdominal musculature and a presumptive diagnosis of PBS was made. External genitalia were reportedly normal. A full workup for urinary tract abnormalities was initiated. Intravenous pyelogram and renal ultrasound performed shortly after birth showed no evidence of reflux or obstruction. Over the next 5 years of life, the patient was hospitalised four times for recurrent bouts of pneumonia and otitis media, resulting in failure to thrive. Since birth, she has had multiple urinary tract infections (UTI). She reported no history consistent with infertility. Family history was significant for a maternal grandfather with unspecified kidney disease, as well as a first cousin on the maternal side who was born with underdeveloped kidneys.

INVESTIGATIONS

At the patient's first prenatal visit, a dating ultrasound was performed that revealed a normal intrauterine pregnancy with an estimated gestational age of 9 3/7 weeks, consistent with the last menstrual period. She was enrolled in routine prenatal care. The prenatal labs were unremarkable. Her medications during the pregnancy included an albuterol inhaler and loratadine, as well as nitrofurantoin for a first trimester pan-sensitive *Escherichia coli* UTI. She had normal renal function, with serum creatinine of 0.6 mg/dl.

TREATMENT

The patient received genetic counselling. It was discussed that there is a genetic predisposition to PBS, but no specific mode of inheritance or genetic marker is available for testing. In addition, a precise estimate of risk to the fetus was unknown, but thought to be low based on ultrasound findings. Second trimester ultrasonography revealed a singleton female fetus with normal anatomy and size appropriate for gestational age.

OUTCOME AND FOLLOW-UP

The remainder of the pregnancy was notable for a 56 lb weight gain but was otherwise unremarkable. At 40 5/7 weeks gestation, the patient delivered a 2975 g female infant with Apgar scores of 9 and 9 at 1 and 5 min, respectively. Delivery was accomplished with vacuum assistance, indicated for prolonged second stage of labour secondary to diminished maternal pushing forces. No anatomical abnormalities were noted upon physical examination of the infant and both mother and infant were discharged home after an uncomplicated postpartum stay. At the 1-month postpartum clinic visit, the patient had no specific complaints. Physical examination was remarkable for deficient abdominal musculature. Pelvic examination revealed a normal sized uterus with normal adnexa. She experienced an uncomplicated postpartum course.

DISCUSSION

PBS is a rare condition, with an estimated incidence of approximately 1 in 40 000 live births. The 95% male predominance of the syndrome makes cases in women especially uncommon. Although the specific aetiology of PBS is unknown, several lines of evidence suggest it has a genetic contribution. For example, PBS is more common in populations with high rates of consanguinity, a familial form with X linked recessive and autosomal recessive inheritance has been described.³ In addition, specific chromosomal deletions have been identified in some patients with PBS. Case reports of interstitial deletions in 17q12 have been observed in two patients with PBS, but not all genetic variations identified in this region lead to the PBS phenotype.^{4–6} The constellation of defects in PBS reflects abnormal development of multiple structures that are derived from the lateral plate mesoderm, including the abdominal musculature and urinary tract. One longstanding model of PBS pathogenesis cites permanent or transient urethral obstruction as the proximal insult, which in turn results in bladder and urethral distension. It is thought that this urinary tract ectasia may physically obstruct the development of abdominal wall musculature and impede testicular descent.^{7–8} A second model of PBS posits that the condition represents a selective arrest of lateral plate mesoderm differentiation, from which the urogenital tract and abdominal wall musculature share a common origin.⁹

The classical PBS triad of absent abdominal musculature, urinary tract ectasia and bilateral cryptorchidism belies a heterogeneous disorder with numerous phenotypic associations.⁹ However, PBS is a syndrome, with case reports describing myriad specific associations, including genital malformations, pulmonary hypoplasia, hemivertebrae, congenital cardiac defects and a variety of gastrointestinal manifestations.^{1–9} The heterogeneity of PBS has engendered proposals to either subclassify the syndrome based upon severity and phenotypic associations,¹⁰ or to expand the definition of PBS so as to capture the heterogeneity of the condition in a better manner.⁹ Classification of PBS along an axis of severity has not been routinely adopted and the epidemiological and aetiological implications of PBS subclassification remain incompletely understood.¹⁰

Most patients with PBS require multiple surgeries to correct urogenital abnormalities, to remove loose abdominal skin or to treat cryptorchidism. Our patient did not require any corrective surgeries related to PBS. In fact, the absence of abdominal musculature was the major manifestation of PBS in this individual, although the lifetime of recurrent UTI does suggest urinary stasis or incomplete bladder emptying. The spectrum of severity of PBS has been categorised with 40% of individuals with PBS having incomplete or mild manifestation of external features, normal renal function and a mild uropathy.¹ A review of several cases of female PBS noted a substantial fraction of patients presented with isolated deficiency of abdominal wall musculature.¹¹ It is unclear as to whether this incomplete form of PBS is relatively more frequent in women than in men, but it possibly represents a pathological mechanism that is similar to that of conventional PBS. Despite the overall mild presentation of PBS in our patient, she did experience

repeated bouts of pneumonia and UTI that were likely the result of her condition. Respiratory tract complaints are common among children with PBS, possibly due to an impaired cough mechanism resulting from absent abdominal musculature. Frequent UTI is common from incomplete bladder emptying, urinary stasis and urinary reflux.

Understanding the reproductive potential in men and women with PBS is important for the care of these patients and provides an important clue about the developmental underpinnings of this poorly understood condition. Men with PBS are universally infertile,¹ yet this is probably not the result of gonadal dysfunction as these patients do not typically require testosterone replacement therapy and cases of fertility via intracytoplasmic sperm injection have been reported in the literature.¹² Although women with PBS often have Müllerian abnormalities, including vaginal atresia and bicornuate uterus, the majority of these patients have functionally and histologically normal ovaries.² Gonadal tissue is derived from intermediate mesoderm. The presence of normal gonads in these patients suggests that PBS is primarily a defect in lateral plate mesoderm morphogenesis. Consequently, gonadal dysfunction therefore might not be a necessary consequence of the PBS sequence in female patients and fertility may be possible, especially when the phenotype is mild.

In our case, pregnancy, labour and delivery were relatively uncomplicated. The vacuum-assisted vaginal delivery for a prolonged second stage of labour, however, does suggest that affected women may be at increased risk of operative vaginal delivery.

Learning points

- ▶ Prune belly syndrome (PBS) is a rare syndrome, primarily affecting male fetuses.
- ▶ Infertility is frequently a complication of PBS, but very little is known about the reproductive potential of affected women.
- ▶ An incomplete phenotype has been described in which not all components of the classic triad of absent abdominal musculature, urinary tract ectasia and bilateral cryptorchidism have been described. Affected women appear to have normal gonads.
- ▶ While genetic predisposition to PBS has been described, the exact mode of inheritance remains poorly understood.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. Hassett S, Smith GH, Holland AJ. Prune belly syndrome. *Pediatr Surg Int* 2012;**28**:219–28.
2. Reinberg Y, Shapiro E, Manivel JC, et al. Prune belly syndrome in females: a triad of abdominal musculature deficiency and anomalies of the urinary and genital systems. *J Pediatr* 1991;**118**:395–8.
3. Ramasamy R, Haviland M, Woodard JR, et al. Patterns of inheritance in familial prune belly syndrome. *Urology* 2005;**65**:1227.e26–7.e27.

4. **Haeri S**, Devers PL, Kaiser-Rogers KA, *et al*. Deletion of hepatocyte nuclear factor-1-beta in an infant with prune belly syndrome. *Am J Perinatol* 2010;**27**:559–63.
5. **Murray PJ**, Thomas K, Mulgrew CJ, *et al*. Whole gene deletion of hepatocyte nuclear factor-1 β gene in a patient with the prune-belly syndrome. *Nephrol Dial Transplant* 2008;**23**:2412–5.
6. **Granberg CF**, Harrison SM, Dajusta D, *et al*. Genetic basis of prune belly syndrome: screening for *HNF1 β* gene. *J Urol* 2012;**187**:272–8.
7. **Terada S**, Suzuki N, Uchida K, *et al*. Etiology of prune belly syndrome: evidence of megalocystic origin in an early fetus. *Obstet Gynecol* 1994;**83**:865–8.
8. **Gonzalez R**, Reinberg Y, Burke B, *et al*. Early bladder outlet obstruction in fetal lambs induces renal dysplasia and the prune-belly syndrome. *J Pediatr Surg* 1990;**25**:342–5.
9. **Smolkin T**, Soudack M, Goldstein I, *et al*. Prune belly syndrome: expanding the phenotype. *Clin Dysmorphol* 2008;**17**:133–5.
10. **Woodard JR**. The prune belly syndrome. *Urol Clin North Am* 1978;**5**:75–93.
11. **Rabinowitz R**, Schillinger JE. Prune belly syndrome in the female subject. *J Urol* 1977;**118**:454–6.
12. **Kolettis PN**, Ross JH, Kay R, *et al*. Sperm retrieval and intracytoplasmic sperm injection in patients with prune-belly syndrome. *Fertil Steril* 1999;**72**:948–9.

Copyright 2012 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit

<http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Hillman RT, Garabedian MJ, Wallerstein RJ. Pregnancy outcome in a woman with prune belly syndrome. *BMJ Case Reports* 2012;10.1136/bcr-2012-006490, Published XXX

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow