NEONATAL-ONSET CHRONIC INTESTINAL PSEUDO-OBSTRUCTION SYNDROME WITH *IN UTERO* UROLOGICAL MANIFESTATION AS MEGACYSTIS

Wei-Chih Chen[1], San-Yi Lin[1], Jenn-Jhy Tseng[1,2], Esther Shih-Chu Ho[1,3], Min-Min Chou[1–3]*

[1]*Department of Obstetrics and Gynecology, Taichung Veterans General Hospital,*
[2]*Hung Kuang University, and* [3]*Chung Shan Medical University, Taichung, Taiwan.*

SUMMARY

Objective: We describe a case of neonatal-onset chronic intestinal pseudo-obstruction syndrome (CIPS) with *in utero* urological manifestation as congenital megacystis. Pitfalls in the interpretation of prenatal sonographic appearance, genetic counseling, and differential diagnosis are discussed.

Case Report: A 28-year-old Taiwanese woman, gravida 6, para 3, was referred for further sonographic examination because of a suspected fetal abdominal cyst. Targeted ultrasound at 28 weeks' gestation showed megacystis filling the abdominal cavity. The renal parenchyma appeared normal, and there was no evidence of reflux hydroureteronephrosis. At 38 weeks of gestation, the patient spontaneously delivered a female infant weighing 3,350 g with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively. At the age of 12 days, the infant still required Foley catheterization because of voiding difficulty, so reduction cystoplasty was performed. The infant presented with recurrent episodes of intestinal obstruction thereafter and underwent ileostomy and resections of segmental intestine loops (3 times) in the ensuing years. At the age of 6 years, she is orally fed with partial parenteral infusion support, and the voiding act is satisfactory.

Conclusion: Attention should be given to the prenatal diagnosis of neonatal-onset CIPS when fetal congenital megacystis with unknown etiology is first detected. Whether there is any relationship between the megacystis-microcolon-intestinal-hypoperistalsis syndrome, CIPS, and pure congenital megacystis requires further study. [*Taiwanese J Obstet Gynecol* 2005;44(3):284–287]

Key Words: fetal megacystis, neonatal-onset chronic intestinal pseudo-obstruction syndrome, prenatal diagnosis

Introduction

Chronic intestinal pseudo-obstruction syndrome (CIPS) is a rare disease characterized by repetitive bouts of intestinal obstruction without an actual mechanical obstructive lesion [1–4]. Classification of adult and pediatric forms, based on histopathologic data, into myopathic, neuropathic, and unclassified forms has been attempted [3–5]. CIPS may involve a single segment or multiple segments of the gastrointestinal tract or its entire length, and may involve the urinary tract in some patients [1–5]. CIPS can occur at any age, and the earlier the onset, the more severe the symptoms [2]. The disease may occur sporadically or be hereditary, transmitted by autosomal dominant or recessive genes [3,5,6].

We describe a case of neonatal-onset CIPS with *in utero* sonographic manifestation as megacystis without hydroureteronephrosis. Pitfalls in the interpretation of prenatal sonographic appearance and appropriate postnatal management options are discussed in the light of current literature.

**Correspondence to:* Dr. Min-Min Chou, Division of Maternal–Fetal Medicine, Department of Obstetrics and Gynecology, Taichung Veterans General Hospital, 160, Section 3, Taichungkang Road, Taichung 407, Taiwan.
E-mail: mmchou@vghtc.gov.tw
Received: January 3, 2005
Revised: January 4, 2005
Accepted: January 5, 2005

Case Report

A 28-year-old Taiwanese woman, gravida 6, para 3, was referred for further sonographic examination because of a suspected fetal ovarian cyst. Scanning performed at 28 weeks' gestation revealed a cystic mass measuring 5.2 × 5.2 × 5.1 cm and occupying the lower fetal abdomen. It was thought to be the enlarged bladder; the kidneys appeared normal. Follow-up scans at 32, 34 and 36 weeks showed progressive bladder dilation (Figure). At 38 weeks of gestation, the bladder dimensions were 10.6 × 8.2 × 7.5 cm. Both kidneys remained normal without hydronephrosis. Fetal ureters were invisible. The amniotic fluid volume was normal. Umbilical artery Doppler study revealed normal flow velocity waveforms with a systolic/diastolic ratio of 2.3. No other fetal gross abnormalities were identified.

At 38 weeks of gestation, the patient spontaneously delivered a female infant weighing 3,350 g with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively. The infant's bladder was catheterized immediately after birth; catheterized urine volume was 300 mL, and the total urine output recorded in the first 24 hours was 430 mL. The catheter was left because of voiding difficulty. The blood urea nitrogen concentration was 7 mg/dL, creatinine was 0.6 mg/dL, serum sodium was 144 mmol/L, and potassium was 4.4 mmol/L. Detailed neurologic examination revealed no abnormalities. Tc-99m dimercaptosuccinic acid renal single photon emission computed tomography showed no definite abnormality in either kidney. Voiding cystourethrogram revealed an enlarged urinary bladder with no evidence of vesicoureteric reflux or urethral obstruction. A cystometrogram revealed poor compliance. The curve was initially low and then rose abruptly at the end as if the elasticity of the bladder wall was somehow impaired. The infant underwent reduction cystoplasty at the age of 12 days at the request of the family after counseling. At laparotomy, a markedly distended atonic bladder, measuring 15 × 11 cm, was found. The entire dome was excised circumferentially 4.0 × 4.0 × 0.8 cm above the base, and the bladder volume was reduced to two-thirds of its original size. An indwelling 12-F Foley catheter was left in the bladder for 9 days. A single-contrast lower gastrointestinal series performed at the age of 5 months revealed that barium passed through the entire colon smoothly with no definite obstructive lesions. However, intestinal transit time exceeded 48 hours. Electron microscopy of the excised bladder specimen showed fibrosis with numerous collagen fibers separating smooth muscle cells within smooth muscle bundles. The ganglion cells and nerve plexus of the bladder wall were normal. Rectal biopsy showed the presence of normal ganglion cells.

The patient presented with recurrent episodes of intestinal obstruction and bacterial infection thereafter. She underwent ileostomy and three resections of segmental intestine loops in the ensuing years. She depended on total parenteral nutrition for 2 years after surgical intervention. At the age of 6 years, she is orally fed with partial parenteral infusion support, and the voiding act is satisfactory.

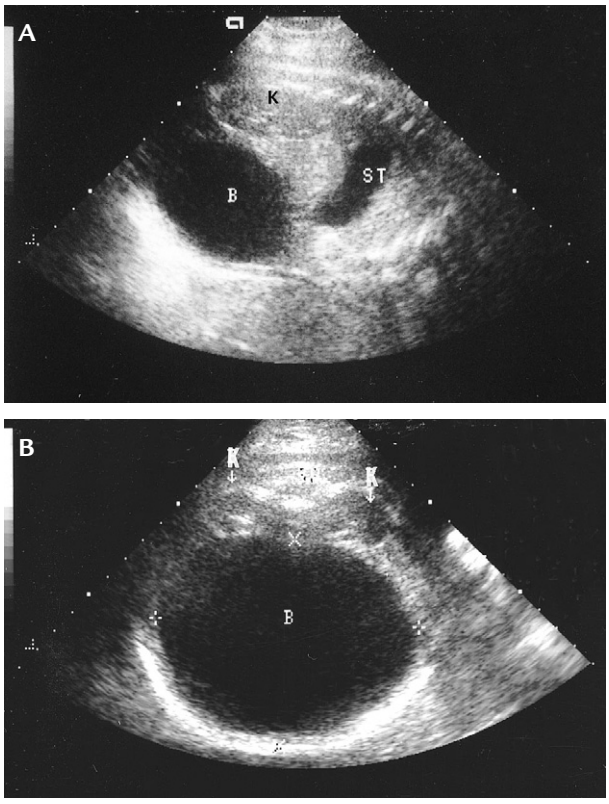

Figure. Fetal congenital megacystis at 30 weeks of gestation: (A) longitudinal scan showing enlarged bladder extending to the upper abdominal cavity; (B) transverse scan of the fetal abdomen at the level of the kidneys showing a grossly distended bladder. Note the absence of hydronephrosis. B = bladder; K = kidney; ST = stomach.

Discussion

Neonatal-onset CIPS represents a particularly difficult clinical challenge. It is a rare and highly morbid syndrome characterized by impaired gastrointestinal propulsion together with symptoms and signs of recurrent bowel obstruction such as bowel distension, nausea and/or vomiting, and bloating in the first 30 days of life [1–3].

The diagnosis of CIPS is mainly clinical and confirmed by endoscopic or radiologic exclusion of mechanical cause as well as by evidence of air–fluid levels in distended bowel loops [4]. However, the early prenatal diagnosis

of CIPS remains challenging because of its unique clinical characteristics and lack of awareness of this disease entity among obstetricians and sonographers. In patients with early-onset CIPS, prenatal diagnosis is possible. However, Faure et al reported that prenatal sonographic signs were present in only 17% of patients [5]. The signs are observed between 21 and 35 weeks of gestation. The most frequent sign is megacystis, followed by polyhydramnios and dilatation of the upper urinary tract. Dilated intestinal loops were observed in only 0.95% of patients (1/105).

The precise nature and cause of the fundamental anomaly producing this syndrome are unknown. Etiologic guesses include a neuropathic origin, mesenchymopathies, and myopathic origin [4]. Although ganglion cells have been reported as normal in the literature, further fundamental molecular, morphofunctional, and electron microscopy studies of the actual function of ganglion cells or, specifically, dysfunction of the neuromuscular junction in this disorder or defects in the smooth muscle and immunohistochemistry α-actin staining have significantly improved our understanding of the mechanisms of CIPS [3,4].

Differential diagnoses include megacystis-microcolon-intestinal-hypoperistalsis (MMIH) syndrome, obstructive uropathies caused by urethral stenosis or atresia in a female infant, posterior urethral valve in a male infant, megacystis-megaureter syndrome, cloacal dysgenesis sequence (CDS), and intra-abdominal cysts such as ovarian cyst and omental cyst. MMIH syndrome consists of the association of a distended unobstructed bladder and a small malrotated colon; it is usually a lethal disorder and most infants die before the age of 6 months [7–9]. Hydroureteronephrosis is present in 88% of patients, and dilated small bowel is present in most cases [7–9]. The ultrasound hallmarks of obstructive uropathy are bladder enlargement, hydroureter, simple hydronephrosis or multicystic dysplastic kidney, and frequent oligohydramnios. The prenatal ultrasound findings of megacystis-megaureter include bilateral hydroureteronephrosis and a large, thin, smooth-walled bladder. CDS is characterized by the presence of a phallic structure and anorectal Mullerian duct and urinary tract malformations. The prenatal sonographic findings include abnormal phallic development, enlarged bladder, dysplastic kidneys, hydroureters, fetal ascites, hyperechogenic bowel (intraluminal colonic calcifications), and oligohydramnios [10].

Whether there is any relationship between the MMIH syndrome, pseudo-obstructive syndrome, and pure congenital megacystis needs further study. The distinction between these disorders may not be possible in some cases on the basis of clinical presentation and laboratory evaluation alone, especially in view of the fact that there may be a spectrum of a more heterogeneous group of nerve and muscle disorders with different clinical presentations and variable severity of underlying pathologic involvement. Therefore, some authors have suggested that the MMIH syndrome and CIPS are part of a spectrum, with the MMIH syndrome representing the most extreme end [9,11]. We suggest that pure congenital megacystis might be at the milder end of the spectrum, with bladder involvement only [6, 12–15]. This finding is interesting in view of the common embryologic derivation of the bladder and hindgut from the cloaca [6].

Until the etiologic cause is identified, treatment must remain largely empirical. Treatment should be conservative, and therapeutic efforts include prokinetic drugs such as cisapride to try to enhance motility, bethanechol, erythromycin, oral antibiotics, surgery, nutritional support, and clean intermittent catheterization to decrease the frequency of recurrent urinary tract infections and aid bladder emptying [1,2,5]. We suggest that surgical intervention in the form of reduction cystoplasty may be required in young infants because this procedure would make the voiding act more effective and, thus, avoid distressing long-term urinary catheterization. Our two unique cases, including this case with elective reduction cystoplasty, have made some significant improvements in therapeutic experience [15]. More cases would be of benefit in confirming the usefulness of this procedure. The prognosis is poor in those who are not able to tolerate oral feeding in the newborn period [2,5].

References

1. Bagwell CE, Filler RM, Cutz E, et al. Neonatal intestinal pseudo-obstruction. *J Pediatr Surg* 1984;19:732–9.
2. Huang YC, Lee HC, Huang FY, et al. Neonatal-onset chronic intestinal pseudo-obstruction syndrome. *Clin Pediatr* 1995; 34:241–7.
3. Anuras S, Mitros FA, Soper RT, et al. Chronic intestinal pseudoobstruction in young children. *Gastroenterology* 1986; 91:62–70.
4. De Giorgio R, Sarnelli G, Corinaldesi R, Stanghellini V. Advances in our understanding of the pathology of chronic intestinal pseudo-obstruction. *Gut* 2004;53:1549–52.
5. Faure C, Goulet O, Ategbo S, et al. Chronic intestinal pseudo-obstruction syndrome: clinical analysis, outcome, and prognosis in 105 children. *Dig Dis Sci* 1999;44:953–9.
6. Bonsib SM, Fallon B, Mitros FA, Anuras S. Urological manifestations of patients with visceral myopathy. *J Urol* 1984;132:1112–6.

7. Young LW, Yunis EJ, Girdany BR, Sieber WK. Megacystis-microcolon-intestinal hypoperistalsis syndrome: additional clinical, radiologic, surgical, and histopathologic aspects. *AJR Am J Roentgenol* 1981;137:749–55.
8. Anneren G, Meurling S, Olsen L. Megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS), an autosomal recessive disorder: clinical reports and review of the literature. *Am J Med Genet* 1991;41:251–4.
9. Puri P, Lake D, Gorman F, O'Donnell B, Nixon HH. Megacystis-microcolon-intestinal hypoperistalsis syndrome: a visceral myopathy. *J Pediatr Surg* 193;18:64–9.
10. Chen CP, Chern SR, Lee CC, Town DD. Isochromosome 18q in a fetus with congenital megacystis, intrauterine growth retardation and cloacal dysgenesis sequence. *Prenat Diagn* 1998;18:1069–74.
11. Ghavamian R, Wilcox DT, Duffy PG, Milla PJ. The urological manifestations of hollow visceral myopathy in children. *J Urol* 1997;158:1286–90.
12. Inamdar S, Mallouh C, Ganguly R. Vesical gigantism or congenital megacystis. *Urology* 1984;24:601–3.
13. Hurwitz A, Yagel S, Rabinovitz R. Hydramnios caused by pure megacystis. *J Clin Ultrasound* 1984;12:110–1.
14. Tomlinson MW, Johnson MP, Gonclaves L, et al. Correction of hemodynamic abnormalities by vesicoamniotic shunting in familial congenital megacystis. *Fetal Diagn Ther* 1996;11: 46–9.
15. Peng HC. Congenital megacystis: a case report. *Zhonghua Yi Xue Za Zhi (Taipei)* 1998;61:235–8.