CASE REPORT

Infantile hypertrophic pyloric stenosis in twins

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SUMMARY

Infantile hypertrophic pyloric stenosis (IHPS) is a common surgical cause of vomiting, which requires surgery in infant. There is the complete or partial obstruction of pylorus due to hypertrophy of circular muscle of the pylorus leading gastric outlet obstruction. The occurrence of IHPS in dizygotic twins is rarer and the theory of genetic origin alone does not explain it. Recent literature points to the association of bottle feeding in singletons to be a major aetiological factor for this condition. Here, we present a rare case of dizygotic twins who were bottle-fed and were affected with IHPS. We review the literature and focus on the question of whether this condition in twins supports a genetic or environmental origin of IHPS.

BACKGROUND

An association of occurrence of infantile hypertrophic pyloric stenosis (IHPS) is seen in twins, with concordance among monozygotic twins of 0.25–0.44 and in dizygotic twins of 0.05–0.10. The occurrence of IHPS in dizygotic twins is rare as compared to monozygotic twins. The theory of genetic origin alone does not explain it. Recent literature points to the association of bottle feeding in singletons to be a major aetiological factor for this condition. We present a rare case of dizygotic twins who were bottle-fed exclusively and were affected with IHPS and review the literature and focus on the question of whether this condition in twins supports a genetic or environmental origin of IHPS.

CASE PRESENTATION

Dizygotic male twins presented to our facility on 45th day of life, with complaints of non-bilious vomiting after feeds. They were born to a G2 P2 mother at gestation age of 38 weeks by normal delivery out of consanguineous marriage. The twins were exclusively bottle-fed. No family history of IHPS was found on either maternal or paternal side. The body weights at birth and body length at birth of twin A1 were 2080 g and 48 cm, respectively. The body weight and body length at birth of twin A2 were 1804 g and 46 cm, respectively. Both the babies cried immediately after birth and passed meconium within 10 h after birth. There is no history of jaundice in both the twins. Physical examination revealed decreased activity, dry lips and mucosal surface and sunken eyes. Baby A1 had a weight palpable mass in right upper quadrant during sleep. No such mass could be palpated in baby A2 but a visible gastric peristalsis could be seen in both twins. No other abnormality was noted (figure 1).

INVESTIGATIONS

Haemograms of both the babies were within normal range. Biochemistry of baby A1 revealed serum urea (104 mg/dl), creatine (1.6 mg/dl), Na⁺ (126 meq/l), K⁺ (2.9 meq/l), chloride (98 meq/l), aspartate amino transferase (AST) 120 U/l. Lab values of baby A2 showed blood urea (88 mg/dl), creatine (1.2 mg/dl), Na⁺ (124 meq/l), K⁺ (3.2 meq/l), chloride (99 meq/l), AST 90 U/l. Plain x-ray abdomen finding showed a dilated stomach with paucity of air in the intestines. A contrast study was not done. Ultrasonographic (USG) findings of baby A1 revealed pyloric canal length of 19.4 mm, wall thickness 8 mm and diameter of 16 mm in epigastric region. A hypoechoic target of 21 mm in length, 7 mm is thickness and 15 mm in diameter was seen in right upper quadrant of abdomen in baby A2.

TREATMENT

Diagnosis of IHPS was confirmed after investigations. After preoperative stabilisation, hydration and correction of electrolyte imbalance, both babies underwent Fredet-Ramsted's pyloromyotomy. Nasogastric tube was removed on first post-operative day (POD) in both babies. Both were fed on formula feeds on first POD evening and were discharged from hospital on fourth POD. No family history of IHPS was found on either maternal or paternal side. Their disease is assumed to be gene related, but no further genetic study was performed in these patients.

OUTCOME AND FOLLOW-UP

Patients were feeding normally and gained weight appropriate for age on follow-up, visits with normal developmental milestones. No family history of IHPS was found on either the maternal

Figure 1 Infantile hypertrophic pyloric stenosis in twins.

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or paternal side. Their disease is assumed to be gene related, but no further genetic study was performed in these patients.

DISCUSSION

IHPS is the most common condition in infancy requiring surgery with incidence of 1.5–3/1000 live-births globally.^{1–5} But the incidence of IHPS is lower in the Indian patients with a frequency that is one-third to one-fifth as compared to white population also it has been observed that there is less incidence of haematemesis in an Indian study.^{6–7} Clinically, patients with IHPS usually present with gradual onset of worsening non-bilious projectile vomiting beginning between 4 and 6 weeks of age. Typical clinical feature is baby is hungry after vomiting and eager to feed, only to vomit again. Signs of dehydration may be present in the case of repeated vomiting. Visible peristalsis may be observed in upper abdomen. Classic laboratory findings reveal hypochloraemic, hypokalaemic, metabolic alkalosis with paradoxical aciduria. In our babies, hyponatraemia, hypokalaemia, hypochloraemia and elevated level of serum AST were noted.

USG findings of increased pyloric muscle thickness and pyloric canal length, increased transverse diameter of the pylorus and calculation of pyloric muscle volume are used to diagnose pyloric stenosis, but among these criteria, thickening of the pyloric muscle and elongation of the pyloric canal are the most useful. The thickness at which muscle is considered hypertrophied is 3 mm or greater.⁸ Pyloric canal length of 1.5 cm is considered diagnostic of pyloric stenosis when seen in conjunction with thickened pyloric muscle.

The exact aetiology of IHPS is not known. Detailed review of the literature considers both genetic as well as environmental factors in the aetiopathogenesis of IHPS. Several features that argue for a hereditary component of IHPS are as: (1) male predominance³; (2) familial aggregation in first and second degree relatives; (3) high incidence in the children of affected parents^{3–9}; (4) high incidence rates in monozygotic twins; (5) similar degree of aggregation in dizygotic twins and (6) higher risk ratio for developing IHPS in multiple birth. However, the condition does not follow classic Mendelian mode of inheritance, which has led researchers to propose other inheritance models. In 1961, Carter and Evans³ proposed the multifactorial threshold (MFT) model of inheritance, which suggests that IHPS has a polygenic inheritance involving multiple genes; it disapproves the genetic aetiology from being autosomal recessive or sex-linked recessive.^{3–9–10} Owing to the male predominance in IHPS,^{3–4–11} the MFT model proposes that the disease has sex-modified inheritance,³ so females are protected from developing the disease. The MFT model assumes that the risk of developing IHPS is determined by the additive effect of numerous genetic and environmental factors. Alternatively, single major locus model has also been suggested, which proposes the involvement of one gene subject to random environmental modifications.¹² Both these models consider the environmental effect on genes as significant. Various studies in twins have shown a higher concordance rate in monozygotic twins than dizygotic twins; however, within monozygotic twins, approximately 50% are not diseased.³ This inconsistency in inheritance is not justified by Mendelian genetics, but confirmed by MFT model. Carrying the genes only increases the risk for IHPS development, but environmental factors are required for disease to manifest.^{3–9–10}

As all cases of IHPS cannot be explained by genetic inheritance theory, environmental factors have also been proposed in its aetiology. Maternal smoking is considered a recognised risk

factor for development of IHPS.¹³ Some perinatal factors like sex ratio imbalance, parity and birth weight are strongly associated with IHPS.¹⁴ Researchers have further hypothesised that mucosal thickening is the primary event initiating the antro-pyloric changes in patients with IHPS.¹⁵ Hyperacidity along with immature gut epithelium in early weeks of life could also contribute to mucosal thickening.¹⁵ Infectious agents such as *Helicobacter pylori* have also been considered as potential aetiological agents.¹⁶ Peptic ulcer disease in adults who were treated for IHPS in infancy also points to HP infection. IHPS is also considered to be induced by prostaglandins therapy for patients with patent ductus arteriosus.¹⁷

A large population-based cohort study based on the Danish national birth cohort by Krogh *et al*¹⁸ demonstrated that bottle-fed infants had a 4.6-fold increased risk of developing pyloric stenosis compared with infants who were not bottle-fed.

Despite numerous studies, the aetiology of IHPS is still not fully understood. As monozygotic twins share an identical genetic pattern, they also share genetic anomalies, like IHPS gene or mutation. If the gene is modified by environmental factors, both monozygotic or dizygotic twins also bear the same perinatal conditions, which justifies the increased concordance rates in twins. Presently, the genetic predisposition acting in conjunction with environmental factors is considered the widely accepted explanation.

Learning points

- Infantile hypertrophic pyloric stenosis (IHPS) is the most common surgical cause of vomiting in infancy.
- Both genetic and environmental factors play a role in the aetiology of IHPS.
- Regardless of a genetic or an environmental origin of IHPS, the diagnosis of IHPS in one twin favours evaluation of the other asymptomatic twin.
- Bottle-fed infants have higher risk of developing the IHPS so exclusive breast feeding should be encouraged.
- Presently, the genetic predisposition acting in conjunction with environmental factors is considered the widely accepted explanation in the aetiology of IHPS.

Competing interests None.

Patient consent Obtained.

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