Infantile Hypertrophic Pyloric Stenosis, A Mendelian Inheritance or Multifactorial Influence: A Case Report

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Abstract
Background: Infantile hypertrophic pyloric stenosis (IHPS) is one of the surgical causes of “protracted vomiting in early infancy”. This condition is characterized by abnormal thickening of the muscular wall of the pylorus, hence it is the commonest cause of gastric outlet obstruction in infant. Males (especially first-borns) are affected approximately 4 to 6 times as often as females. The offspring of a mother and, to a lesser extent, the father who had pyloric stenosis are at higher risk for pyloric stenosis and it develops in approximately 20% of the male and 10% of the female descendants of a mother who had pyloric stenosis. The incidence of pyloric stenosis has been found more in B and O blood groups. Pyloric stenosis is usually presents at 3-4 weeks of life and is more concordant in monozygotic.

Keywords: Pyloric stenosis, newborn.

Case Presentation
A 27 days old male newborn presented to our opd with complaints of fever, and vomiting after feeds and weight loss. Newborn was born to a 19year old primigravida at gestational age of 39+1 weeks by normal vaginal delivery out of non-consanguineous marriage with no history of delayed cry. Newborn passed meconium after 10 hours of birth. Birth weight was 3.1kg. Mother blood group was A+. There was history of previous admission to SNCU with neonatal jaundice at day 4 of life. Total serum bilirubin value was13.0 mg/dl at admission (day 4) and newborn was kept in SNCU for one day for phototherapy. Thyroid profile and G-6-PD levels were normal. TSB levels decreased to 9.0mg/dl after phototherapy by day 5 of life. At discharge, baby weight was 2.810 kg and ofc-35.5cm and length 51cm.
At admission on day 27 of life, on physical examination newborn was irritable and had dry lips and mucosal surface and sunken eyes. There was loss of fat which was generalized including buccal fat. Weight of newborn was 2.5kg at admission. Haemogram of newborn was within normal range. Biochemistry profile of newborn revealed serum urea (94 mg/dl), Creatine (1.7 mg/dl), Na+ (128 meq/l), K+ (3.1 meq/l), chloride (99 meq/l), aspartate amino transferase (AST) 120 U/l and cRP negative. Plain x-ray abdomen finding showed a dilated stomach with paucity of air in the intestines. Ultrasonography (USG) findings of newborn revealed pylorus thickened and elongated with pylorus width measuring 14.0 mm and pylorus length measuring 20mm.

Treatment
Diagnosis of IHPS was confirmed after investigations (usg). After preoperative stabilization, hydration and correction of electrolyte imbalance, newborn was referred to PGIMER, Chandigarh and underwent Fredet-Ramsted’s pyloromyotomy. Post operatively, Nasogastric tube was removed on first postoperative day (POD) and breastfeed was initiated on first POD evening and newborn was 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
Newborn was monitored for weight gain and currently feeding normally and gaining weight appropriately for age on follow-up visits with normal developmental milestones.

Discussion
“IHPS is the most common condition in infancy requiring surgery with incidence of 1.5–3/1000 live-births globally¹”. 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 population². 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
hypocholemaemic, hypokalaemic, metabolic alkalosis with paradoxical aciduria. In our babies, hyponatraemia, hypokalaemia, hypocholemaemia. 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 predominance [3];
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 Evans [3] proposed the multifactorial threshold (MFT) model of inheritance, which suggests that IHPS has a polygenic inheritance involving multiple genes; it disapproves the genetic etiology 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 antropyloric 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” 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 in considered the widely accepted explanation.

References