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INFANTILE HYPERTROPHIC PYLORIC STENOSIS IN DIZYGOTIC TWINS: A RARE CASE REPORT.

Neonatology

Karuna Kawhale Registrar, Department of Neonatology, Indraprastha Apollo Hospital, New Delhi

Sujeet Chowdhary Senior Consultant, Director of the pediatrics department, Indraprastha Apollo Hospital, New Delhi.

Vidya Gupta Senior Consultant, Paediatrics & Neonatology, Indraprastha Apollo Hospital, New Delhi.

Saroja Balan* Senior Consultant, Paediatrics & Neonatology, Indraprastha Apollo Hospital, New Delhi. *Corresponding Author

ABSTRACT

Infantile hypertrophic pyloric stenosis (IHPS) is an uncommon condition affecting neonates three to eight weeks after birth which is caused by hypertrophy of the circular muscle of the pylorus of the stomach leading to gastric outlet obstruction. Various litterateurs have discussed the incidence and variability of presentation of IHPS. The occurrence of IHPS is rare in dizygotic twins, especially of different sexes and the genetic predisposition alone does not explain it. Recent litterateurs have focused on the etiology of both genetic and environmental associations contributing to this condition. Here we present a rare case of Dizygotic twins of opposite sex presenting with IHPS together with a review of literature focusing on the theories aiming to explain the etiology and the mechanism contributing to the development of IHPS. In this study, we aim to identify the factors which lead to similar presentation and severity of IHPS despite being dizygotic twins of the opposite sexes.

KEYWORDS

Infantile hypertrophic pyloric stenosis, Twins, Dizygotic

INTRODUCTION

IHPS occurs in 2 to 3.5 per 1000 live births approximately, although the rate and trend vary from region to region(;). It is found more common in Caucasians and less commonly seen in Indian, Asian, and African populations. The incidence is 2.4 per 1000 in Caucasians, 0.7 in Africans, and 0.6 in Asians(). There is a male preponderance (4:1 to 6:1 in male and female babies respectively)(;). And is more common in preterm babies as compared to term babies(). The occurrence of IHPS in Dizygotic twins is rare as compared to monozygotic twins. Monozygotic twins are identified to have a 200-fold increase in risk as compared to dizygotic twins where an increase in risk is only 20-fold without known affected relatives(). Here we report a rare case of IHPS in dizygotic twins having different sexes with a similar presentation in terms of symptoms and severity. We have reviewed various literature to discuss the possible etiology of IHPS in this case.

Case report

Dizygotic twins, 'Twin A' & 'Twin B' were referred to Indraprastha Apollo hospital on day 36 of life with complaints of recurrent episodes of non-bilious vomiting for 8-10 days. Twins were born to a 37-year-old G2A1 mother (IVF conception) at 35 to 36 weeks of gestation by caesarian section. Both babies cried immediately after birth but developed respiratory distress in form of grunting respiration so were shifted to NICU and oxygen support was given by nasal prongs. Distress settled and babies were weaned off oxygen to room air. Babies were discharged on day 7 of life on full feeding (both formula feed and breastfeed).

Twins were observed to have episodes of non-bilious vomiting from day 24-25 of life which increased in frequency leading to decreased urine output. So babies were hospitalized because of recurrent vomiting with moderate dehydration and hypokalemia. Ultrasounds done on day 33 of life were indicative of hypertrophic pyloric stenosis. No history of IHPS was found in both maternal and paternal families. Babies were further referred to Indraprastha Apollo hospital for further management.

On admission, both babies were hemodynamically stable. Twin A- male baby weighing 2.44 kg at birth was admitted with a weight-2.335 kg. And Twin B- a female baby weighing 1.78 kg at birth was admitted with weight-1.83 kg. The blood parameters of both babies were in the normal range except the coagulation profile which was deranged so plasma was transfused. And in both babies, CRP was raised and blood culture showed growth of Pantoea species so antibiotics were started.

An Upper GI contrast study and ultrasound were done for both babies. A contrast study of twin A showed evidence of over distension of gastric fundus, body, and antrum with no evidence of contrast passing into pylorus and no evidence of extravasation of contrast seen. Findings were correlated with ultrasound findings. Ultrasound of twin A showed pyloric wall thickness of 5-6 mm with narrowed lumen suggestive of hypertrophic pyloric stenosis. A contrast study on twin B showed evidence of elongation and narrowing of the pyloric region (approx. Segment of 10mm) with a thin stream of contrast passing through with proximal gastric distension and no evidence of the distal passage of contrast. An ultrasound showed pyloric wall thickness of 5-6 mm with narrowed lumen, both suggestive of hypertrophic pyloric stenosis.

Treatment- After confirmation of the diagnosis surgery was planned for both babies. After preoperative stabilization and hydration, both babies underwent laparotomy and pyloromyotomy on day 3 of admission. Babies tolerated the procedure well. Feeds were reintroduced and gradually increased as babies tolerated feeds well. Because of culture-positive sepsis CSF analysis was done for both to rule out meningitis. Out of both Twin, B had normal CSF reports and Twin A had CSF analysis suggestive of partially treated meningitis. After 2 weeks of antibiotics, CSF analysis was repeated in twin A. CSF analysis was within normal range. Babies were discharged after two weeks of antibiotics on full feeds and gained weight.

DISCUSSION

IHPS is one of the most common causes of vomiting and abdominal surgeries in infancy. The incidence reported was about 1-3.5 cases in 1000 live births. Usually these babies present with non-bilious, non-bloody projectile vomiting leading to dehydration at 4 to 6 weeks of life(). The baby appears to be hungry and dehydrated and has vomiting when fed. Frequent episodes of vomiting lead to furthermore dehydration, and decreased urine output and later lead to electrolyte imbalances (classically hypochloremic, hypokalemic metabolic alkalosis). Like in our case both twins had a moderate degree of dehydration with hypokalemia at the time of presentation.

Although the clinical presentation, diagnosis, and treatment of IHPS are well known, etiopathogenesis remain unclear. Both genetic as well as and environmental factors have been proposed to affect the occurrence of the IHPS. Features that point towards genetic origin include male predominance, the high incidence in Caucasians, and significant familial predisposition(;). Also, a high incidence of IHPS in twins is reported in the literature(). Studies have found that male babies are four times more frequently affected than females and the occurrence of IHPS is seen in 5.5% of the sons and 2.5% of the daughters of an affected father as compared to 20% of the sons and 7% of the daughters of an affected mother. Siblings have 30 times the greater high risk and a similar risk of affecting both the babies in a pair of twins, particularly in mono-zygotic twins have been reported().

IHPS in Dizygotic twins, as in the present study are rare (;). These all suggest its hereditary nature(;).

However, IHPS does not follow a classic Mendelian mode of inheritance due to which the researchers have proposed another 2 modes of inheritance. MFT (Multi-factorial threshold) model was proposed by Carter and Evans in 1961 (). According to the MFT model IHPS has polygenic inheritance involving several genes and discounts the genetic etiology being autosomal recessive or sex-linked recessive(). As IHPS is more prevalent in males the MFT model proposes that the inheritance is sex-modified. So according to it, females are protected because of their sex from developing this disease. A high concordance rate in monozygotic twins was found when compared to dizygotic, however, in the mono-zygotic twins, 50% of the pair are unaffected. This is inconsistent with Mendelian genetics but can be explained by the MFT model().

The second model proposed was the SML (Single Major Locus) model, in which only one two-allele locus is involved, which is likely to be a very rare but dominant allele. Despite the differences in the two models, both models attribute a role to environmental modification of the genes involved in the causation of IHPS. Carrying the gene(s) only increases the risk of development of IHPS while the environmental factors are required for the disease to manifest(;). Capon et al.(), have recently mapped some cases to chromosome 16, but this monogenic linkage of IHPS to chromosome 16p12- p13 was found inconsistent, again justifying the polygenic inheritance explained by the MFT model.

Several environmental factors have been proposed to have the potential for the causation of IHPS. High androgen levels in intrauterine & early postnatal life have been found associated with the high prevalence in males(). The use of erythromycin in early life has been also suggested as a risk factor(). Neonatal hypergastrinemia and gastric hyper-acidity may also play a role in causation(). On contrary, it has been proposed that low gastric acidity in the perinatal period may cause the gut to be more susceptible to infections and such infections can disrupt the wall integrity leading to muscle hypertrophy and IHPS(). Alternatively, Paulozzi explained that mucosal thickening in IHPS can be due to infectious agents, specifically Helicobacter pylori().

Many have postulated the dysfunction of neuronal nitric oxide synthase as a potential cause of hypertrophy of smooth muscle cells of the pylorus. Nitric oxide is an inhibitory neurotransmitter that leads to the relaxation of smooth muscle and its deficiency can lead to prolonged constriction and hypertrophy of smooth muscle cells(;).

Another environmental modifier maternal smoking has been found to increase the risk by 1.5 to 2-fold(). Many studies have reported that bottle-fed infants and infants who were both bottled and breastfed (like in our case) were at high risk than an exclusively breastfed infant–(;).

CONCLUSION

In this case, twins presented here can be explained to have poly-etiologic origins including genetic as well as environmental factors in the development of IHPS. Being the case of twins genetic factors may contribute to the occurrence of IHPS but paying attention to certain factors like zygosity of twins, having different sexes, having shared same prenatal and postnatal conditions (like the feeding habits & sepsis), and having a similar presentation of the disease, the fact of environmental modification of gene(s) and impact of environmental factors itself cannot be ignored. Therefore, it can be concluded that the etiology of IHPS is still not completely understood and the occurrence can be attributed to having an impact of both genetic and environmental factors.

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