CASE REPORT

Trilogy of foregut atresia without genetic abnormality: exception to the Martinez-Frias syndrome

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SUMMARY

We present a case of oesophageal atresia with distal tracheo-oesophageal fistula and duodenal atresia, which later on was detected to have cystic variant of biliary atresia. He underwent primacy repair of oesophageal atresia with ligation of distal tracheo-oesophageal fistula and duodenoduodenostomy. He later developed features of obstructive jaundice, and on investigation was diagnosed to have cystic variant of biliary atresia which was initially confused with iatrogenic biliary obstruction. Exploration and operative cholangiogram with biopsy confirmed cystic variant of biliary atresia and underwent successful Kasai procedure. Our case effectively demonstrates a rare trilogy of foregut atresia without an apparent genetic association. It highlights stepwise systematic management of foregut atresias in this patient and demonstration of cystic variant of biliary atresia. Even though these are rarely seen, still the clinician should be aware of such a possibility and should adopt a multimodality approach to diagnose and an aggressive approach to manage the condition.

BACKGROUND

Oesophageal atresia (OA) with or without tracheo-oesophageal fistula (TOF) are relatively common malformations occurring in approximately 1 in 4000 births. The aetiology is unknown. The incidence of associated anomalies is about 50%, with cardiac anomalies being the most common, followed by the gastrointestinal anomaly. The incidence of duodenal atresia is approximately 1 in 7000 births, with a high frequency of associated anomalies, particularly Down's syndrome. Here we report a case of antenatally detected OA and duodenal atresia, which later on was diagnosed also to have biliary atresia. Trilogy of foregut atresia with genetic abnormality has been reported as the Martinez-Frias syndrome.^{1 2} Our case had no genetic abnormality, and hence it represents an exception to this syndrome.

CASE PRESENTATION

We present the case of a boy child born at 38 weeks of gestation by forceps delivery in good condition, with birth weight of 3100 g, for parents who had no consanguineous marriage. Therefore, autosomal recessive inheritance for consanguineous marriages was ruled out. He had antenatal diagnosis of polyhydramnios, double fluid bubble sign with possible duodenal atresia and right multicystic kidney. There was no resuscitation required

at birth. He had a hypoplastic left thumb and an upper abdominal distension. A large bore size of 10 nasogastric tubes got arrested at 10 cm length. He was suspected to have OA with TOF and possibly duodenal atresia.

INVESTIGATIONS

Postnatal babygram showed the tip of nasogastric tube coiled in the upper oesophagus, a gaseous distension of the stomach and proximal duodenum with double air bubbles, segmentation anomalies in the upper thoracic region and 13 rib on the left side (figure 1A).

An ultrasound examination showed multiple cysts in the right kidney consistent with the diagnosis of multicystic dysplastic kidney (figure 1B).

The cranial ultrasound showed an anatomically normal brain, with an incidental finding of an ependymal cyst in the frontal horn of the right ventricle, likely to be of no significance. The echocardiogram was reported to be normal.

He was also examined by the geneticist, and was reported to have a normal 46XY karyotype, normal genetic tests. There was no evidence of trisomy 13, 18, 21, and fluorescence in situ hybridisation for 22Q deletion was negative.

DIFFERENTIAL DIAGNOSIS

VACTERL (V vertebral, A anorectal, C cardiac, T tracheal, R renal, E esophageal, L limb) association with or without the Martinez-Frias syndrome was considered.

TREATMENT

He underwent posterolateral right thoracotomy, ligation of distal TOF and primary repair of the OA over a transanastomotic tube (TAT), followed by exploratory laparotomy, diamond-shaped duodenoduodenostomy on day 1 of life. An incidental Meckel's diverticulum was found, which was not resected in view of incidental finding with wide base and no evidence of palpable ectopic tissue.

On the seventh postoperative day, he underwent a contrast study to check the integrity of oesophageal anastomosis through the TAT, which demonstrated no leak but the contrast remained in the stomach, even on delayed image although the child was very much settled apart from bilious nasogastric aspirates (figure 2A). A chest X-ray on the following day showed bilateral pleural infusion, and no bowel gas was seen beyond stomach. The on-call surgeon over the weekend was worried

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To cite: Patel RV, Kumar H, More B, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-200477

Figure 1 (A) Babygram with arrested repleg tube in the upper pouch (arrow), 13 ribs, thoracic hemivertebra in the chest and double bubble appearance in the abdomen. (B) An ultrasound scan showing multicystic dysplastic right kidney with non-communicating cysts and dysplastic parenchyma. NGT, nasogastric tube.

about anastomotic leak or obstruction based on the radiological features although the baby was very well settled.

He, therefore, underwent re-exploratory laparotomy on the 10th day of life, for possible walled-off perforation or anastomotic stenosis. On exploration, there was no evidence of any perforation or stenosis but had adhesions around the duodenal anastomotic site and no distal small bowel atresia. A redo duodenoduodenostomy was performed with insertion of transanastomotic jejunal feeding tube for the purpose of early enteral feeding. The feed was

started through the jejunal tube on the third postoperative day, which was well tolerated. Postoperative contrast study of the upper gastrointestinal tract showed contrast and gas beyond the anastomosis (figure 2B). He was started on nasojejunal transanastomotic feeding tube and weaned-off from total parenteral nutrition gradually by the seventh postoperative day.

On the third day of second laparotomy, a rising trend of bilirubin with predominant conjugated fraction (70–80%) was noted. The ultrasound examination of the abdomen suggested

Figure 2 Postoperative barium meal: (A) Seventh postoperative day following first surgery and (B) Eighth postoperative day following second operation.

an abnormality of the biliary system. A diagnosis of type 4 choledochal cyst was suggested. After receiving 5 days of phenobarbitone, he had Tc-99m mebrofenin scan, which showed no excretion of radioisotope into the gallbladder or bowel by 24 h, feature consisting with biliary obstruction (figure 3A,B). Possibility of iatrogenic injury or ligation of common bile duct due to re-exploration and reanastomosis was considered.

He was opening bowel with pale stools, and dark coloured urine. His γ -glutamyltransferase level was 324 mmol/L and serum bilirubin level was high. The serum albumin, alanine transaminase and clotting factors were normal. He was started on vitamins A, D, E and K, and ursodeoxycholic acid, which was stopped on the advice of the liver unit. He was transferred to the liver unit in the regional paediatric hepatobiliary unit of a children's hospital, and the diagnosis of biliary atresia with cystic variety was confirmed at exploratory laparotomy, operative cholangiogram and intraoperative liver biopsy. He, therefore, underwent successful Kasai portoenterostomy on the 30th day of his life under the same anaesthesia.

OUTCOME AND FOLLOW-UP

His postoperative recovery was uneventful. At 9 months follow-up, he was doing well, tolerating 6–7 oz of milk every 4 h and opening bowel normally with yellow coloured stool.

DISCUSSION

Our case was very unusual in having three foregut atresias in the same child—the oesophageal, duodenal and biliary, and the postulated hypothesis of embryogenesis of all three is varied and has no single theory connecting and explaining their occurrence together. There was no consanguinity of marriage, and therefore genetic basis of autosomal recessive inheritance was ruled out. Moreover, although it followed the features of the Martinez-Frias syndrome, there was no genetic abnormality on detailed investigations.

The association of OA with distal TOF with other congenital anomalies, particularly as part of the VACTERL, is well recognised.^{1–8} The VACTERL association comprises vertebral defects, anal atresia, cardiac defects, TOF, renal malformations and limb dysplasias. Children with VACTERL association do not have typical facial dimorphic features, learning disability or abnormalities of growth.^{1–3} Sibling and offspring risks are low, usually quoted around 1%.

There have been few less common reports of duodenal atresia, associated with OA+TOF. The prevalence of this association is approximately 6%. The overall survival after surgical repair, in a recent review by Ein *et al*,⁴ was 75%. They also recommended the staged repair as a safe method of management. With the improved imaging technology, the diagnosis of the entity can be made early in the gestation, allowing appropriate antenatal counselling and early management plan at birth.

Figure 3 (A) Ultrasound scan showing cystic variety of biliary atresia simulating dilated bile duct and gallbladder. (B) Nuclear medicine scan showing no excretion even at 24 h.

The typical ultrasound appearance of a fetus with combined OA +TOF with duodenal obstruction is by dilated stomach. Ancillary findings such as polyhydramnios, gastric wall thickening, a funnel-shaped narrowing of the gastric antrum and a relatively shapeless lesser curvature are sometimes seen in fetus with gastric outlet obstruction. The diagnosis of congenital hepatobiliary anomalies on the antenatal ultrasound remains difficult.⁸ The MRI of the fetus, if available, can facilitate the diagnosis.

At birth, the diagnosis of OA+TOF with duodenal atresia can be made on the basis of plain X-ray of the chest and abdomen, with or without contrast. However, the diagnosis of the congenital duodenal obstruction can be missed until oesophageal continuity is established, or when gastrostomy feeding fails.

Most neonatal surgical centres have stopped performing routine postoperative contrast studies even if a TAT is used for early feeding. Our case is the usual reminder of the fact that especially if there is an associated duodenal atresia, the anastomotic dysfunction is bound to be, and the contrast may not necessarily cross the anastomosis especially in the absence of a TAT, and radiological pictures may simulate walled-off perforation or obstruction to an unwary surgeon. Therefore, post-operative interpretation of the contrast should be carried out keeping in mind that the grossly dilated proximal duodenum could sometimes take a few weeks to start effective peristalsis and one should not rush to theatre too early. However, the re-exploration caused a lot of anxiety and apprehension to all concerned when the obstructive biliary picture emerged following reanastomosis, raising the possibility of an iatrogenic bile duct injury, which is very common in this traffic jam area especially during re-explorations and redo surgery.

There are several reports of a lethal syndrome of multiple gastrointestinal atresias in the oesophagus, small intestine and biliary system.^{5–7} Mali *et al* encountered the association of foregut atresia and bile duct anomalies in five referrals to a paediatric liver unit in 2 years and concluded that the association may not be that rare as previously reported. Parental consanguinity and sibling recurrence in these families point to autosomal recessive inheritance. The pathogenesis of this syndrome is most probably of blastogenic in origin, mainly affecting midline developmental biliary pancreatic junction. The evolution of apparent choledochal cysts to biliary atresia in outpatients is a known and reported presentation of biliary atresia.

These cases emphasise the importance of identifying anomalies beyond the VACTERL association spectrum in OA+TOF, and also challenges for the management strategies in infants with multiple anomalies. The management resides in the early recognition and a well-organised approach to their repair. Antenatal ultrasound suggesting either a foregut atresia or biliary anomaly will alert one to the other association. Full imaging investigation may be indicated prior to corrective surgery of the primary anomaly. In summary, we present an unusual case report of a child with three atresias—oesophagus, duodenum and biliary tract. There are few reports available in the literature of the same kind. This case differs from the rest owing to the fact that our case has no genetic basis.

Learning points

- ▶ Three foregut atresia having different embryogenesis are very rare in the same patient with other multiple congenital anomalies.
- ▶ Triology of gastrointestinal atresia has genetic basis with evidence of Martinez-Frias syndrome but our case was an exception to the rule.
- ▶ Absent gallbladder and cystic variety of biliary atresia can be missed even after two exploratory laparotomy and possibility of iatrogenic injury to common bile duct and acquired choledochal cyst can create confusion and delay.
- ▶ Routine contrast after primary repair of oesophageal atresia and tracheo-oesophageal fistula, and associated functional motility disorder of grossly dilated proximal duodenum can lead to erroneous interpretation of anastomotic dysfunction due to increased aspirates.
- ▶ Cystic variant of biliary atresia is very rare and only recently described. It may simulate choledochal cyst on ultrasound scan. Nuclear medicine Tc-99m mebrofenin scan, exploratory findings and operative cholangiogram with liver biopsy clinches the early diagnosis.

Acknowledgements The authors are grateful to Mr Shawqui Nour for re-exploration in the postoperative period and Mr Khalid, Consultant Hepatobiliary Surgeon at Birmingham Children's Hospital, for management of cystic variant of biliary atresia.

Contributors All authors have actively participated in the clinical and operative management of this patient and have contributed significantly in preparation, editing and appraising the manuscript.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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