Perinatal Management of Common Neonatal Thoracic Lesions

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ABSTRACT

Esophageal atresia, congenital diaphragmatic hernia, bronchopulmonary malformations and cystic lung diseases are the common neonatal thoracic surgical lesions encountered in practice. The availability of antenatal ultrasonography has lead to these lesions being detected before birth. Antenatal diagnosis can be made with a fair degree of accuracy in tertiary fetal medicine centres. Antenatal intervention is limited in a very few centres in the western world and not being done in India at present. The outcome of these babies with antenatal diagnosis of thoracic lesions has changed in the last decade. Earlier intervention is now possible in cystic lung disease before infectious complication has set in. All these lesions are managed exclusively in well developed neonatal surgery units with excellent outcome in the western world. The present study reviews the antenatal detection, clinical presentation, interventional/surgical procedures [antenatally and postnatally] and outcome of these common neonatal thoracic surgical lesions. **[Indian J Pediatr 2008; 75 (9) : 931-937]** *E-mail : naren_are@yahoo.com*

Key words : *Neonatal surgical lesions, Fetal thoracic surgical lesions, Perinatal management, Bronchopulmonary malformations*

Every pregnancy should ideally undergo a screening fetal ultrasonography at 18 to 20 weeks gestation principally to detect congenital fetal anomalies. The advent of routine antenatal ultrasonography has altered the mode of presentation and natural history of a number of congenital anomalies. An example for this has been the detection of various thoracic surgical conditions like congenital diaphragmatic hernia, bronchopulmonary malformations, cystic lung diseases and oesophageal atresia. Early detection and transfer, evolution of neonatal intensive care, refinements in neonatal surgical technique, has lead to a change in the outcome of these conditions in the tertiary centres. All these conditions are managed exclusively in limited tertiary neonatal surgery units in the western world leading to the significant change in outcome. The option of fetal interventions following antenatal detection of fetal thoracic lesions was limited to a few centres in the world and is not being practiced in India.

Esophageal Atresia

Esophageal atresia refers to a congenitally interrupted esophagus. It may be a pure atresia of both ends with blind ending on both ends or there may be a variety of termination of both ends. The upper or lower end may communicate at different levels with trachea. Esophageal atresia with its estimated life birth incidence of 1 in 3500 to 1 in 4500 remains the epitome of neonatal surgery.[1] The lack of esophageal patency prevents swallowing. In addition to preventing normal feeding, this problem may cause infants to aspirate and literally drown in their own saliva, which quickly overflows the upper pouch of the obstructed esophagus. If a (tracheoesophageal fistula (TEF) is present, fluid (either saliva from above or gastric secretions from below) may flow directly into the tracheobronchial tree. Currently, most authorities believe that the development of esophageal atresia has a non-genetic basis. Many anatomic variations of esophageal atresia with or without tracheoesophageal fistula have been described.[2,3]

• Clinical Presentation

The first sign of esophageal atresia in the fetus may be polyhydramnios in the mother, which occurs with approximately 33% of mothers with fetuses with esophageal atresia and distal tracteoesophagal fistula TEF and with virtually 100% of mothers with fetuses with esophageal atresia without fistula. The inability to identify the fetal stomach bubble on a prenatal ultrasonogram in a mother with polyhydramnios makes the diagnosis of esophageal atresia more likely.[4,5]

The diagnosis of esophageal atresia requires a high

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index of suspicion, the newborn with esophageal atresia presents with copious, fine, white, frothy bubbles of mucus in the mouth. The infant may have rattling respirations and episodes of coughing, choking and cyanosis. If a fistula between the esophagus and the trachea is present, abdominal distention develops as air builds up in the stomach. The abdomen will be scaphoid, if no fistula exists. If esophageal atresia is suspected, a radiopaque 8 French (in preterm infants) or 10 French (in term infants) nasogastric or feeding tube should be passed through the mouth to the stomach. In patients with atresia, the tube typically stops at 10 to 12 cm and will curl up in upper pouch visible in the upper thoracic midline on chest radiograph.

Vertebral defects, anorectal malformations, cardiovascular defects, tracheoesophageal defects, renal anomalies, and limb deformities (VACTERL) are associated anomalies that should be readily apparent upon physical examination and further investigations *i.e.* ultrasonography and echocardiography.

After confirming the diagnosis based on plain xray of the chest showing curling of the lower end of a feeding tube, assessment for other congenital anomalies and stabilization of the baby is done. The preoperative care needs frequent oropharyngeal suction, respiratory support and risk stratification and assessment for other congenital anomalies. Primary repair of the esophagus is feasible in majority of the cases, however a long gap between the atretic ends precludes a primary repair.

Complications

Most neonates who undergo repair of esophageal atresia and tracheoesophageal fistula have some degree of esophageal dysmotility.[6] The length of the gap between atretic end and tissue quality of fistula dictates the severity of subsequent complications. Strictures at the site of the anastomosis are common and may subsequently require dilatation. Recurrence of tracheoesophageal fistula may occur due to paucity of tissue or tissue damage of the poorly vascularized distal esophagus and surgical dissection performed too close to the trachea.

Approximately, one half of patients with surgically corrected esophageal atresia develop gastroesophageal reflux disease (GERD). Approximately, one half respond to routine medical therapy with prokinetic agents, histamine H_2 receptor blockers, or both, and one half require surgical intervention for correction.

Prognosis

In 1962, Waterston developed a prognostic classification system for esophageal atresia that is still used today.[7] Spitz *et al*, 1994 recognized that the presence or absence of cardiac disease is a proven major prognostic factor. When comparing the prognostic classification systems, the Spitz classification appears to have the most applicability in current practice.[8]

Over the past 50 years, early identification, neonatal transport, evolution of neonatal intensive care and refinements in surgical technique have improved the outcome. The western countries have reported near 100% survivals in low risk newborns.[7] Limited Indian experience has been published, data is still evolving and the available literature available suggests survival of 70% babies in the low risk category and about 50% in high risk babies with esophageal atresia and tracheoesophageal fistula.

CONGENITAL DIAPHRAGMATIC HERNIA (CDH)

Congenital diaphragmatic hernia(CDH) is an uncommon condition affecting 1 in 2000 to 5000 . CDH results from a defect in the developing diaphragm leading to herniation of abdominal viscera into the chest and is almost always associated with an abnormal gastroesophageal junction and abnormal mesentry with malrotation of bowel. The incidence of associated anomalies in CDH varies between 39%-50%. Cardiac anomalies constitute around 63% of the associated anomalies. The diaphragmatic defect has three anatomical types, commonest being posterolateral defect. However, the most important issue is the associated pulmonary hypoplasia and persistent pulmonary hypertension which dictates eventual outcome.[9]

• Pathophysiology

The primary cause of mortality in patients with CDH is pulmonary hypoplasia with reduced alveolar surface area and surfactant deficiency leading to refractory pulmonary hypertension.

Kitagawa has shown that the number of arterial branches in CDH, are reduced along with an increased arteriolar wall thickness. Moreover, patients with CDH are known to have reduced left ventricular mass and left ventricular dysfunction. Among these factors, pulmonary hypoplasia is thought to be the most important in determining the outcome.[10] In addition to the effects of pulmonary hypoplasia and pulmonary hypertension, chest and abdominal wall compliance may play a substantial role in the pathophysiology of severe CDH, reducing the contents in the abdomen and closure of abdomen.

Clinical Presentation

The most severely affected babies presented with respiratory distress at birth. Cyanosis, tachypnea, grunting and retractions are noted with scaphoid abdomen. Mediastinal shift may be present. Breath sounds are absent on the affected side and bowel sounds may be heard in the chest. CDH may be seen beyond the

first hours of life in upto 20% of the cases. The symptoms in this group of patients are non-specific and include recurrent chest infections, failure to thrive and vomitings. These cases can also present as acute presentations secondary to acute bowel volvulus or strangulation. The diagnosis is made on chest radiograph which shows air filled bowel loops in the chest cavity and can be confirmed with contrast study in case of any doubt.

Prognostic Predictors

Although there are several prognostic indicators mentioned in literature, very few have been validated in large prospective series. The various indices evaluated included indirect predictors of lung hypoplasia prenatally using lung-head ratio, magnetic resonance lung volumetry, and postnatal modified McGoon index, these require further evaluation in larger series.[11]

Existing mortality-predictive models include those of the CDH Study Group (CDHSG) based on birth weight and 5-minute Apgar score, the Canadian Neonatal Network (CNN) based on gestational age and admission score in score for Neonatal Acute Physiology version II (SNAP), and the Wilford Hall/Santa Rosa clinical prediction formula (WHSRPF) derived from blood gas measurements which suggested that inability to achieve adequate oxygenation and/or ventilation was associated with a high mortality, The SNAP-II score, a validated outcome predictor in non-CDH neonatal populations, applies a weighted score to 6 physiologic variables within the first 12 hours of admission to the NICU. These predictor studies require further evaluation in larger series.[12]

Postnatal and Surgical Management

The antenatal and postnatal management of patients with CDH is still evolving, and none of the therapies used to treat CDH have been successful in all patients. Given the wide variations in the management of patients with CDH, it is not surprising that there are no predictors, that are reliable. The surgical aspects are relatively straight forward but the medical management still eludes us. The multitude of treatment options reflects the limited understanding of the pathophysiology and relatively fixed mortality rate seen. The management of a neonate with CDH without respiratory distress requires only the passage of nasogastric tube to avoid bowel distention, on the other hand, neonates presenting with distress at birth requires intubation and ventilation. Various levels of cardiopulmonary support *i.e.* conventional ventilation, high frequency oscillatory ventilation(HFOV), inhaled nitric oxide, surfactant therapy, liquid ventilation, intra tracheal pulmonary ventilation(ITPV), intra venous pulmonary vasodilators, and ECMO to stabilize the patient may be required before operative repair.

At present use of ECMO is reserved for severe cases of CDH with severe PPHN, who fail to respond to alternative modalities. Although ECMO is an invasive procedure, its use as such would not increase the mortality. Patients requiring ECMO support for more than 2 weeks are likely to have significant pulmonary hypoplasia and have a poor prognosis. The development of renal complications (requirement of CVVH) while on ECMO was associated with mortality. Although the exact cause(s) of renal failure in these patients are unclear, the present study believe this could be multifactorial, including the severe hypoxia in these neonates before instituting ECMO.

During the surgical repair, controlled ventilation using high frequency, low tidal volume, pressure limited is the ideal way. Trans abdominal route *via* subcostal incision is used traditionally for repair of diaphragmatic repair. The repair of the diaphragmatic defect is done by a single layer of horizontal mattress, non-absorbable sutures .

For larger defects the options are - synthetic mesh repair, intercostal muscle flaps, internal oblique and transversus abdominus flaps, rectus abdominus flaps, and reversed lattismus dorsi flaps. If the patient is stable, additional procedures like Ladds procedure is done if there is associated malrotation of midgut. If abdominal wall closure is under tension- ventral hernia creation by skin closure only, patch repair, or creation of silo are the options.

Right sided defects needs a careful reduction of liver with hemodynamic monitoring because of kinking of vena cava or hepatic veins can occur causing a decrease in venous return.

Antenatal Management

Fetal therapy for CDH was evolved by Harrison et al in San Francisco and remains confined to isolated research centres in the western world. The selection criteria for fetuses for prenatal therapy is based on identifying poor prognostic signs on antenatal ultrasound; *i.e.* lung-to-head circumference ratio, fetal cardiac ventricular disproportion, contralateral and liver herniation, intrathoracic stomach. The options available for in utero fetal interventions in CDH are-complete in utero repair, which may be done when there is no liver herniation. PLUG (plug the lung until it grows) is a procedure of temporary tracheal occlusion, developed by Harrison *et al,* is done on cases of CDH with liver herniation. These children are delivered by EXIT procedure(extrauterine-intrapartum tracheoplasty), in which umbilical circulation is maintained till airway is secured. Fetal PLUG is a video assisted fetal endoscopy, which avoids the need for hysterotomy.[10, 13]

Prognosis

Despite many advances in the treatment of CDH including ECMO, gentle ventilation, nitric oxide, and fetal

therapy the overall survival for CDH still remains approximately 65%. Infants with severe CDH require ECMO, with survival rate ranging from 50% to 65%. There have been many recent reports regarding the timing of surgery, when dealing with severe CDH. Treatment protocols have changed from immediate repair to delaying the operation until the patient has stabilized.[14]

The mortality rate in CDH cases, presenting in the first 6 hrs of life remains between 40-50%. Infants who have symptoms after 24 hr of life have nearly 100% chance of survival. The mortality is higher if CDH is diagnosed antenatally, and most of the series report figures between 56-86%.

The use of reduced size of lung grafts on ipsilateral side from living donors temporarily till the contralateral lung matures and PPHN resolves is being under evolving stage. Long term consequences in survivors of CDH, depend on the treatment modality used, associated anomalies, besides the effects of the diaphragmatic hernia itself.

• Bronchopulmonary malformations

Antenatal ultrasound scan is now a sensitive tool with the ability to detect a range of parenchymal lung abnormalities for which the outcome usually is excellent. Congenital abnormalities of the lung are characterized by cyst formation or increased echogenicity. Such abnormalities have included congenital cystic adenomatoid malformations (CCAM), pulmonary sequestration (EPS/IPS) and bronchogenic cysts and less commonly congenital lobar emphysema.[15] It remains important that appropriate postnatal investigations are undertaken to allow for appropriate selection of cases for excisional surgery. The natural history of parenchymal lung lesions such as CCAM and pulmonary sequestration (PS) has been altered by the advent of antenatal ultrasonography.

Congenital Cystic Adenomatoid malformation (CCAM)

The first report of CCAM was done by Chin and Tang in 1947. CCAM is the congenital lung malformation that accounts for 95% of the congenital cystic lung diseases. It usually occurs as a sporadic, non-hereditary lung disease but may be associated in 18% of cases with other anomalies predominantly with renal agenesis and cardiac defects. Today the most commonly used description and classification are based on clinical, gross and microscopic criteria described by stocker *et al* in 1977. Stocker added two additional types based on the site of origin of malformation and labeled them o-4 to indicate their progression down the airway. (tracheal, bronchial, bronchiolar, bronchiolar/alveolar duct, alveolar/distal acinar) CCAM is often diagnosed by antenatal ultrasound scan. Prenatal clinical course varies from hydrops in 40% of cases to complete regression in 15% of cases. Postnatal presentation varies from severe respiratory distress with neonatal death to lesions which are completely asymptomatic. When no prenatal diagnosis is made, children may remain asymptomatic or may present later in life with complications of recurrent pneumonia or spontaneous pneumothorax.

Antenatal Intervention

Active antenatal interventions were done in only 6 to 15% of overall cases in various centres. The option of open fetal surgery was restricted to a few selected centres. The largest experienced with fetal surgery remains that of Sanfranciso group. Adzick *et al* described the outcome for 13 fetuses subject to lung resection which formed about 10% of the their population diagnosed with CCAM. Surgery was performed at 21 to 29 weeks of gestations. Five (38%) died either during Surgery or immediately postnatally.

Currently a range of options are available for antenatal intervention in fetuses affected with CCAM. Ultrasonically defined macrocystic disease may be aspirated, shunted using thoracoamniotic shunt or excised using fetal surgical techniques. Whereas ultrasonically defined microsystic disease may be excised or fulgurated using percutaneous applied laser therapy.[16]

Postnatal Management

The postnatal management of antenatally diagnosed CCAM is now clear at present. All symptomatic lesions will undergo early thorocotomy to excise the expanding lesions and to allow appropriate growth of normal compressed lung. Surgical resection is the standard care for symptomatic CCAM. The treatment of asymptomatic CCAM is controversial. Many series recommend early surgical resection to avoid eventual development of complications like recurrent infections, Pneumothorax, or even rare development of lung malignancy.[16, 17] In case one waits for infection to set in, lung resection in a CCAM bearing lung can be life threatening due to all the adhesions in pulmonary hilum .The extent of surgical resection should be based on preoperative imaging and inspection.

CONGENITAL LOBAR EMPHYSEMA (CLE)

CLE is a rare anomaly of the lung development. It is defined as the post natal over distention of the air spaces of one or more segments or lobes of the lung, that usually presents in the neonatal period with respiratory distress. This over distended portion of the lung, compresses the adjacent lung lobes and compromises the ventilation.

In about 50% of cases, the exact cause of CLE is not known, in the remaining 50% several mechanisms have been postulated. Air-way trapping in the emphysematous lobe is caused by (a) dysplastic

bronchial cartilages causing a ball-valve –type obstruction. (b) endo-bronchial obstruction from inspissated mucus. (c) extrinsic bronchial obstruction from aberrant cardio-pulmonary vasculature (d) diffuse bronchial abnormalities that can be related to infection. (e) polyalveolosis, described by Hislop and Reid, has been found in association with CLE in some cases, it is not clear if this is the cause of CLE or affect of chronic bronchial obstruction.[18] Involvement of the left upper lobe occurs most frequently (42%), followed by right middle lobe (35%), right upper (21%). The lower lobes are involved in 1% of the cases. Males are affected three times as often as females.

Clinical Presentation

One half of the patients become symptomatic in the neonatal period, others may present months later. The presentation is with respiratory distress, which can be of varying severity. Physical examination reveals a hyper resonance in the affected area with diminished air entry on auscultation.

Chest radiography is the best diagnostic tool. Initial films may show an opaque mass on chest radiograph due to delayed clearance of lung fluid from affected lobe. The later films show an hyper lucent over expanded area of the lung with compression or actelectasis of the adjacent lobes of the lung, depression of the diaphragm and mediastinal shift to the opposite side. The emphysematous segment may also herniate anterior to the heart and great vessels. CT of the chest is a useful adjunct. Ventilation perfusion scanning can show un-ventilated and hypo perfused lung segments. Diagnostic bronchscopy is rarely indicated, rather may be harmful.

These lesions were detected by midgestation using a combination of ultrasonography and ultrafast fetal MRI a valuable tool in prenatal diagnosis of congenital anomalies. Prenatal diagnosis of CLE from microcystic CCAM was difficult. About 20% of patients with CLE will have associated congenital cardiac lesions.

Most of the patients are symptomatic and require treatment. The indication for surgical treatment is life threatening, progressive, pulmonary insufficiency from compression of adjacent normal lung. Prompt resection of the involved lobe is the ideal treatment in symptomatic

PULMONARY SEQUESTRATIONS

Pulmonary sequestration were first described in 1861 by Rokitansky as accessory pulmonary lobes but later renamed as pulmonary sequestrations by Pryce in 1946. Sequestration refers to a mass of non-functioning lung tissue without normal bronchial or vascular connections. The sequestration may be of bronchial elements alone, or pulmonary arterial supply alone or most commonly of both elements. Traditionally the sequestrations are divided into either intra-lobar or extralobar variants depending on pathological criteria such as pleural investment. It is possible that both CCAM and EPS are two entities at either end of a single bronchpulmonary developmental defect spectrum. Upto 50 anatomical extra lobar sequestrations with histological features of CCAM have been reported, often in association with congenital diaphragmatic hernias and occasionally as intra-abdominal masses with an intact diaphragm.

• Clinical Features

Intra-lobar sequestration may present during infancy with cardiac failure due to the significant arterio venus shunt or associated cardiac anomaly. After the period of infancy they may present with recurrent lower respiratory tract infection, inadequate response to treatment or persistent changes on chest radiography.[19] Rare presentations are with hemoptysis and hemetemesis. extra-lobar sequestration are generally asymptomatic and discovered incidentally.

Natural History

The natural history of intra lobar sequestration is of recurrent infections. Initially the sequestrated lung tissue is non-aerated. After infection, with development of communication, aeration occurs in the sequestrated area. It can compress the surrounding lung tissue causing collapse. Occasionally the air loculated within the sequestration may ruptured causing pneumothorax.[20]

Diagnosis

An abnormal shadow may be found on chest radiography in intra lobar sequestration in the posterior medial basal segment near the mediastinum. Diffuse infilterations of the lobe, cavitations/fluid level may sometimes be found. Duplex Doppler ultrasound can demonstrate anomalous blood supply. Contrast enhanced CT scan and MR angiography can provide adequate anatomical details and visualization of arterial inflow.

Treatment

Asymptomatic extra lobar sequestrations rarely require any treatment, however if found during another operative procedure they may be resected. Intra lobar sequestrations when asymptomatic may be observed but are more likely to developed secondary infective complications, resection of the sequestration by segmental resection preserving normal lung tissue is the ideal surgical treatment.

BRONCHOGENIC CYSTS

Bronchogenic cysts arise from abnormal buds from the primitive esophagus and tracheobronchial tree, which do not extend to the site were alveolar differentiation occurs.

If this separation occurs early, the system migrates into mediastinum. If it occurs late, it forms an intra pulmonary broncogenic cyst. Bronchogenic cyst account for 20-30% of congenital broncopulmonary foregut cystic malformation.[21]

Potential locations for Broncogenic cyst includes cervical, para tracheal, sub-carinal, hilar, mediastinal and intra pulmonary. Ectopic sites for broncogenic cyst includes para vertebral, para esophageal, peri cardial locations. Bronchogenic cysts are typically unilocular mucus field lesions arising from posterior membraneous wall of the air way. The cyst wall has structural elements of the air way including cartilage, smooth muscle, mucous glands and respiratory epithelium. Malignancies have been reported in these lesions.

The spectrum of congenital cystic disease of the lung ranges from hydrops and neonatal respiratory distress to asymptomatic lesions. Clinical presentations range from asymptomatic to recurrent non-specific respiratory symptoms or infections to life threatening respiratory distress. In new borns the cyst adjacent to the trachea and proximal air ways can lead to severe respiratory distress, lobar emphysema which can be life threatening. Plain chest-radiograph is the standard initial study. Ultrasound may show the fluid content. CT and MRI are the best confirmatory studies. Antenatal intervention is therefore rarely indicated.

Risk of gradual expansion with compression of the adjacent lung, infections, hemorrhage, sudden death from rapid enlargement and risk of malignancy justify the excision[22]. The bronchogenic cysts are usually treated by thorocotomy and excision of the cyst. In case of intra parenchymal bronchogenic cysts wedge resection, segmental resection or lobectomy may be required. The long term outcome for infants and children with broncogenic cysts is excellent because they generally do not require sacrifice of significant normal lung parenchyma.

Risk of Malignancy

The association of CCAM, but probably not pulmonary sequestrations with malignancies such as pulmonary rhabdomyosarcoma (RMS) and broncho alveolar carcinoma (BAC) is real but currently unquantifiable.[23] The literature suggests that RMS occurs early in childhood (about 3 yrs) in these cases and should be treated by excision and combination cytotoxic chemotherapy. The broncho alveolar carcinoma occurs in an younger population (20 yrs) in those cases associated with CCAM.[24] Such tumors often have prominent mucinous component.

CONCLUSIONS

The congenital thoracic conditions in newborns and early childhood are not common and are usually complex to manage.The diagnosis can be based on a screening antenatal ultrasound or as an investigation for refractory respiratory distress or infectious complication of the lung with contrast enhanced CT scan.

It is not uncommon in our country to see these children with delayed complications of unrecognized lesions in the lung and long drawn medical treatment. The drastic improvement in the results of these conditions in the western units have been obtained by early recognition, transfer to dedicated units and early surgical intervention with background intensive care support.

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