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PICTORIAL ESSAY

Medical Pulmonary Diseases That Cause Neonatal Respiratory Distress: A Radiological Pictorial Essay

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INTRODUCTION

Respiratory distress is a common condition affecting up to 7% of all neonates.[1] It is a common manifestation of different underlying conditions that include pulmonary, cardiovascular, metabolic, and systemic diseases. It is recognised as the presence of signs of increased respiratory difficulty, including tachypnoea, nasal flaring, retraction, and abnormal breathing sound. Neonates are at risk of respiratory failure and subsequent cardiopulmonary arrest if the increased respiratory effort cannot be sustained. Early recognition of the presence and the cause of respiratory distress is important to enable prompt and appropriate treatment and to reduce morbidity and mortality.

Medical pulmonary diseases account for most cases of neonatal respiratory distress; the more common ones include hyaline membrane disease (HMD), transient tachypnoea of the newborn (TTN), meconium aspiration syndrome (MAS), and pneumonia. They primarily relate to saccular (25-36th week of gestation) and alveolar (≥37th week of gestation) stages of lung development.[2] This pictorial essay reviews these common pulmonary conditions that cause neonatal respiratory distress and demonstrates the typical radiological findings.

When approaching imaging for neonatal respiratory distress, most commonly chest radiographs (CXRs), it is important to understand the distinctive clinical and radiological features of common conditions that cause neonatal respiratory distress, and to communicate with the clinician about the detailed clinical information and findings.

First, some conditions, especially surgical ones such as congenital pulmonary airway malformation and congenital lobar overinflation, may have been detected by antenatal ultrasonography or magnetic resonance imaging.[3] Review of any antenatal imaging is essential to guide further evaluation and management.

Second, antenatal, perinatal, and postnatal history is important to identify risk factors for different conditions. For example, a history of maternal chorioamnionitis is a significant risk factor for congenital pneumonia, perinatal fetal distress increases the risk of MAS and

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mechanical ventilation is a common cause of air leak including pneumothorax.

Third, knowing the maturity of the affected neonate is vital because various degrees of lung maturity predispose neonates to different pathologies. Preterm neonates are at higher risk of HMD and neonatal pneumonia, whereas term and post-term neonates are at higher risk of TTN and MAS.

Finally, an appreciation of the pathophysiology of different conditions will help understand their radiological appearance and distinctive features. Presence of a mass lesion, mediastinal shift, an abnormal lung that is radio-opaque or radiolucent, lung volume, and characteristics of lung opacities are all important features for distinguishing medical conditions.

Combined with clinical information and laboratory results, a CXR is usually sufficient to diagnose a medical pulmonary condition. Lung volume and lung opacity are important features to distinguish these conditions (Figure 1).

HYALINE MEMBRANE DISEASE

In preterm neonates, HMD is the leading cause of respiratory distress. The immature lungs and deficiency of surfactant underlie the disease mechanism. Affected neonates present with respiratory distress immediately or within a few hours of birth and usually require ventilatory support and exogenous surfactant. As the lungs mature with increased endogenous surfactant production after birth, respiratory distress often improves or resolves after 3 to 4 days.[1,4,5]

Pathophysiology and Risk Factors

In immature lungs, there is reduced alveolisation and excessive connective tissue matrix. In addition, surfactant synthesis by type II pneumocytes is not mature until the 35th week of gestation. As a result, there is increased alveolar surface tension leading to alveolar microatelectasis and poor lung compliance. Epithelial injury and oliguria in the first few days of postnatal life contribute to pulmonary oedema. Inflammation and necrosis of lung epithelium occurs, and the accumulation of fibrin and cellular debris form the hyaline membrane.[4,6] The resultant effects lead to impaired gaseous exchange with development of hypoxia and acidosis.

Prematurity is the most important risk factor, with risk increasing with decreasing gestational age. Antenatal corticosteroids promote fetal lung surfactant synthesis and reduce the incidence of HMD. Other risk factors include maternal factors, especially diabetes mellitus, fetal factors such as low birth weight and male sex, and labour factors such as Caesarean section.[1]

Radiological Findings

Classic CXR findings include reduced lung volume, bilateral symmetrical diffuse fine granular infiltrates with ground glass appearance or white-out of the lungs in more severe cases, and air bronchogram. Pleural effusion is typically absent (Figure 2).[4]

With assisted ventilation, application of exogenous surfactant and gradual production of endogenous surfactant, the CXR appearance improves in 3 to 4 days, showing increased lung volume and patchy reduction

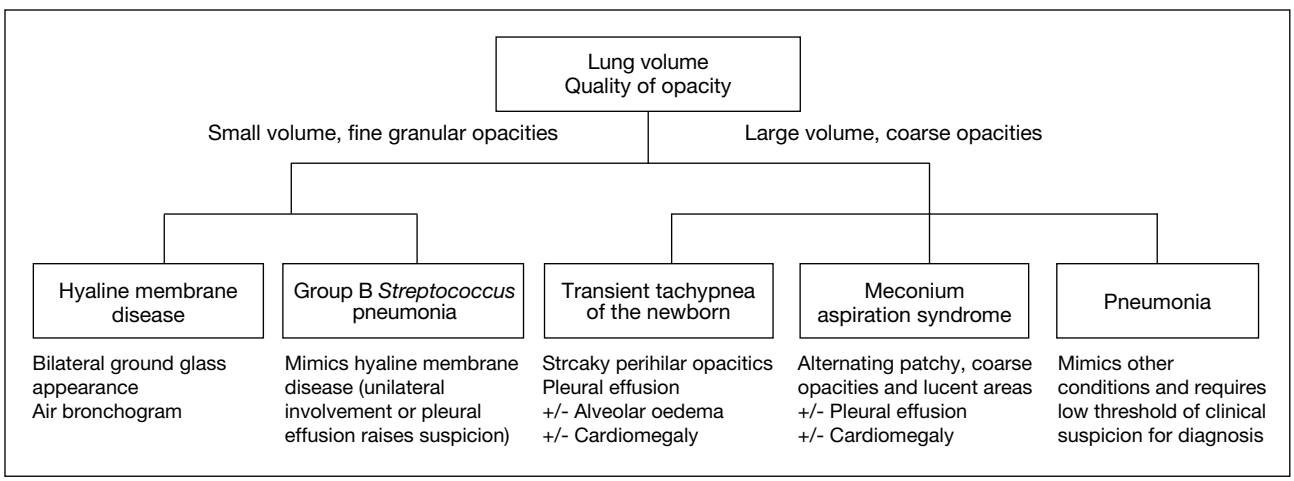

Figure 1. Summary of typical radiographic findings of different medical pulmonary diseases causing neonatal respiratory distress.

of air space opacities, related to uneven distribution of exogenous surfactant (Figure 2c).[6]

In the absence of expected improvement, concomitant patent ductus arteriosus or other congenital heart diseases should be considered. The typical radiographic appearance of pulmonary plethora in patent ductus arteriosus resulting from left to right shunt may not be obvious in the presence of HMD. Clinical assessment and echocardiogram play important roles for diagnosis (Figure 3).[4,7] Deterioration after initial improvement raises the possibility of superimposed nosocomial infection. Other complications including air leak and pulmonary haemorrhage are not uncommon (Figure 4).

TRANSIENT TACHYPNOEA OF THE NEWBORN

In term neonates, TTN is the most common cause of respiratory distress. It is caused by failed mechanism of fetal lung fluid clearance with consequent excessive retained fluid that impairs gaseous exchange. Neonates with TTN usually develop symptoms within the first few hours of delivery. Fortunately, the presence of a normal surfactant system in term neonates helps protect the lungs from injury by maintaining alveolar capillary membrane integrity and allowing gradual absorption of lung fluid. TTN is usually a self-limiting condition lasting for up to about 3 days, requiring minimal to modest respiratory support.

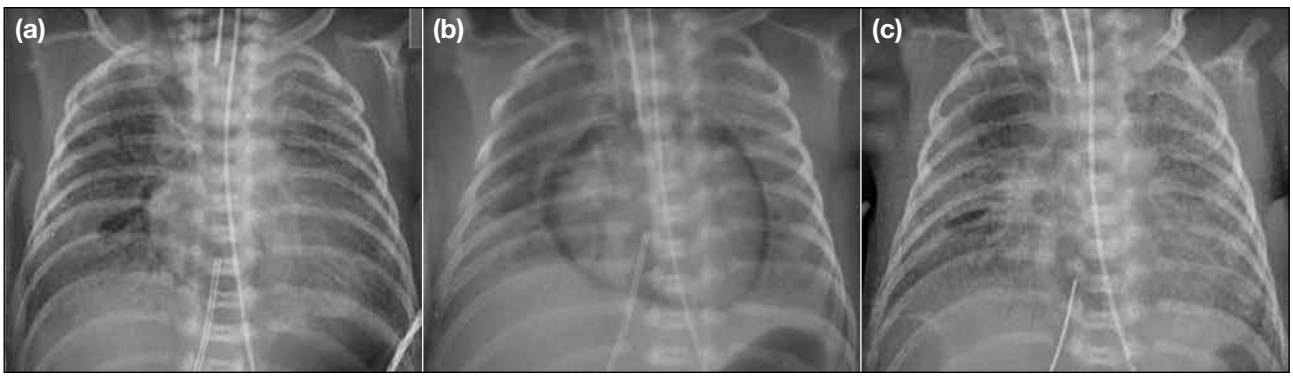

Figure 2. Typical example of hyaline membrane disease radiographic appearance. A 28+4 weeks preterm baby girl, delivered by emergent Caesarean section for severe maternal pre-eclampsia, presented with respiratory distress at birth. (a) Chest X-ray on day 0 showing bilateral small lung volume, diffuse symmetric infiltrates with white-out of the lungs, air bronchogram, and absence of pleural effusion, typical of hyaline membrane disease. Note the presence of pneumomediastinum and pneumopericardium as complications of positive pressure ventilation, more obvious in chest X-ray on day 1 (b). (c) Chest X-ray on day 2 after treatment with exogenous surfactant showing typical patchy areas of improvement due to uneven distribution of administered surfactant. Note the significant improvement of air leak.

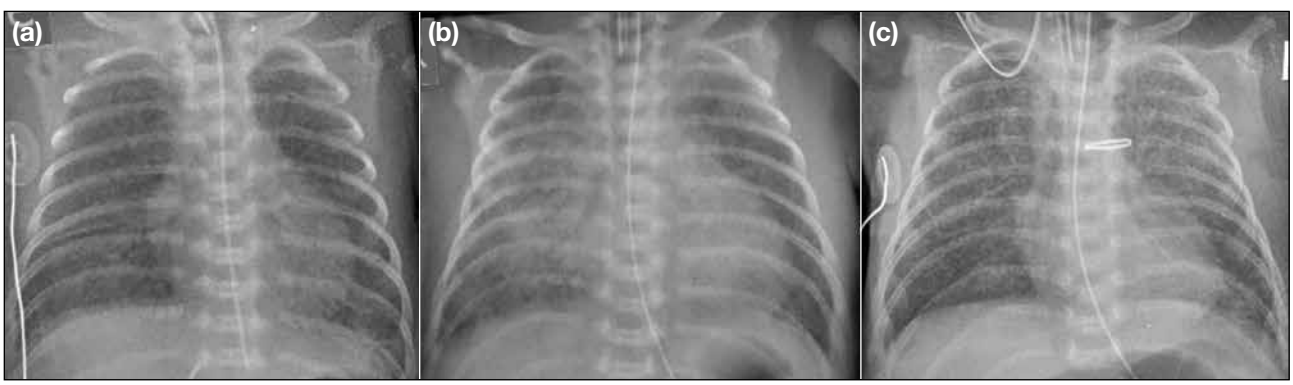

Figure 3. Deterioration after initial improvement of hyaline membrane disease. Same patient as Figure 2. (a) Chest X-ray on day 7 showing significant improvement of hyaline membrane disease after ventilatory support and exogenous surfactant. (b) Chest X-ray on day 11 showing sudden deterioration with increased infiltrates in both lungs, more on the right. She developed late-onset sepsis and echocardiogram revealed haemodynamically significant patent ductus arteriosus, both could contribute to the new pulmonary infiltrates. (c) Chest X-ray on day 24 showing significant improvement of pulmonary infiltrates after treatment with antibiotic and surgical ligation of patent ductus arteriosus.

Pathophysiology and Risk Factors

In utero, fetal lungs are filled with fluid for normal lung development. In term foetuses, there is a physiological reduction in fluid secretion by lung epithelia at least a few days before labour onset. There is also increased fluid absorption by active transport of Na+ and Cl-, followed by water. This mechanism is also enhanced by an increased fetal catecholamine level in response to labour stress. A resultant net absorption of fetal lung fluid is therefore achieved during labour.[8] Squeezing of the fetal lungs during passage through the birth canal during labour is also important for expelling fetal lung fluid through the airways. Bypassing or impairment of these mechanisms can result in excessive retained fetal lung fluid.

Elective Caesarean section before the 39th week of gestation is the most important risk factor for TTN because of the lack of normal mechanisms for fetal lung fluid absorption and expulsion. Other common risk factors include maternal factors such as maternal diabetes mellitus, fetal factors such as low birth weight or macrosomia, and labour factors such as precipitous delivery or maternal sedation.[5]

Radiological Findings

Frontal CXR typically shows hyperinflated lungs secondary to air trapping, streaky perihilar opacities due to prominent vascular and lymphatic structures, and evidence of interstitial oedema, such as pleural effusion which may extend along pulmonary fissures (with right horizontal fissure as the best seen one in frontal CXR) or Kerley's B lines. Alveolar oedema is a less common finding; transient cardiomegaly has also been reported. Follow-up CXR in 1 to 2 days typically shows rapid improvement or resolution (Figures 5 and 6).

MECONIUM ASPIRATION SYNDROME

Meconium-stained liquor is encountered in about 12% of all deliveries, of which 5% are complicated by MAS. In neonates with MAS, 4% will die, accounting for about 2% of all perinatal deaths.[9] MAS is defined as respiratory distress in an infant born through meconium-stained

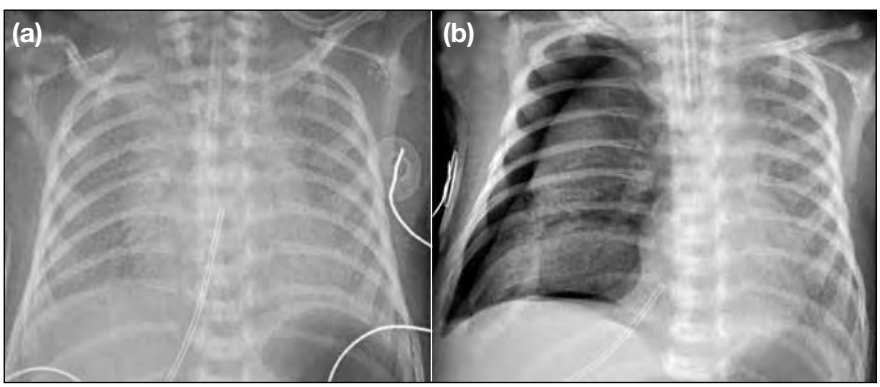

Figure 4. Pneumothorax complicating hyaline membrane disease. A 29+1 weeks preterm baby boy delivered by emergent Caesarean section for maternal antepartum haemorrhage. (a) Chest X-ray after birth showing bilateral small lung volume, diffuse symmetric infiltrates, air bronchogram, and absence of pleural effusion, typical of hyaline membrane disease. (b) Chest X-ray on day 3 after intubation showing right pneumothorax.

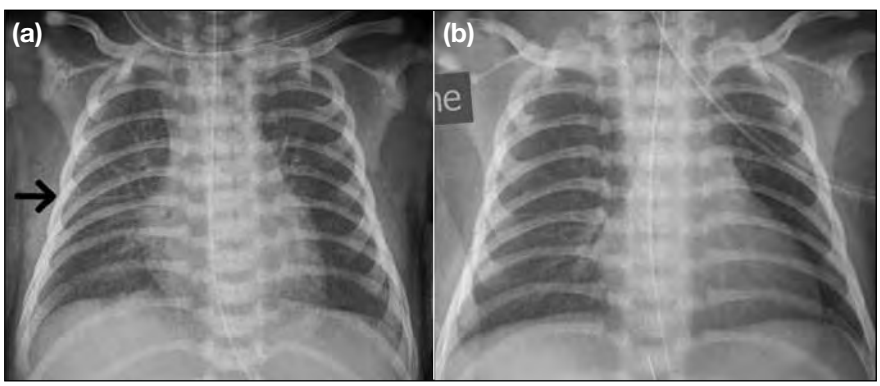

Figure 5. Typical radiographic appearance of transient tachypnoea of the newborn. A 39+4 weeks term baby girl delivered vaginally developed respiratory distress soon after birth. (a) Chest X-ray on day 0 showing hyperinflated lungs, increased perihilar streaky opacities and thickened right horizontal fissure (arrow). (b) Chest X-ray on day 1 after minimal ventilatory support showing clearance of perihilar opacities and improvement of pleural effusion.

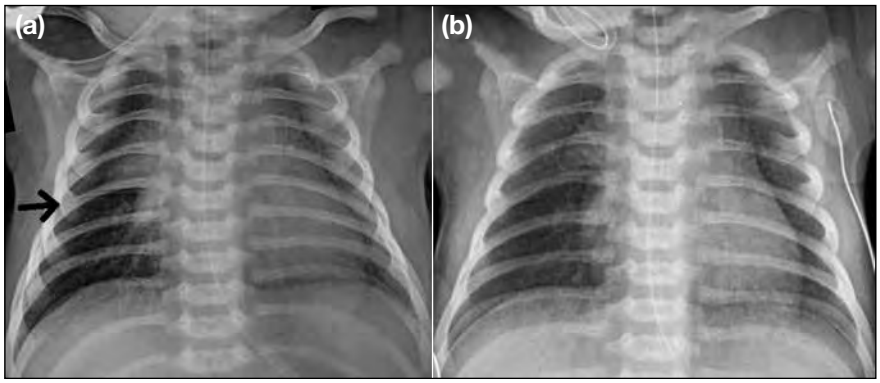

Figure 6. Transient cardiomegaly in transient tachypnoea of the newborn. A 40+4 weeks post-term baby girl delivered by emergent Caesarean section due to failed induction of labour, presented with respiratory distress at birth. (a) Chest X-ray on day 0 showing hyperinflated lungs, increased perihilar streaky opacities and thickened right horizontal fissure (arrow), as well as prominent cardiac shadow. (b) Chest X-ray on day 1 showing interval improvement.

liquor with characteristic CXR changes and whose symptoms cannot be otherwise explained.[10] As MAS can result in significant morbidities, e.g. air leak and superimposed infection and mortality, prevention, early recognition and prompt treatment are essential.

Pathophysiology and Risk Factors

Meconium is viscous fetal colonic content comprised of a mixture of desquamated epithelial cells, bile, pancreatic enzymes, swallowed amniotic fluid, lanugo (fetal hair), and vernix caseosa (waxy fetal skin coating). Meconium does not pass to the lower descending colon until the 34th week of gestation, hence MAS is seldom seen before the 37th week of gestation and affects mainly term and post-term neonates.[5]

Advanced fetal maturity and fetal distress are the most important risk factors for MAS. With advanced fetal maturity, there is a higher risk of passing meconium in utero. In the presence of fetal distress, e.g. hypoxia, fetal neuronal stimulation causes fetal anal sphincter relaxation and meconium passage.

Aspirated meconium causes partial or complete obstruction of medium to small airways due to its high viscosity, leading to air trapping and atelectasis; chemical pneumonitis with epithelial injury due to acidity, bile and pancreatic enzymes; and inactivation of surfactant by the presence of bile, contributing to atelectasis. These compromise gaseous exchange and predispose to a wide range of complications from air leak and superimposed infection to persistent pulmonary hypertension.[11]

Radiological Findings

The appearance of MAS on CXR depends on its severity. Mild disease can manifest as perihilar streakiness and reticular opacities that may be difficult to distinguish from TTN. The classic CXR appearance of MAS includes hyperinflation due to air trapping and patchy coarse irregular or band-like opacities with intervening lucent areas, corresponding to alternating areas of atelectasis and hyperinflation. Pleural effusion and cardiomegaly (possibly related to persistent pulmonary hypertension) are also possible findings. Absence of air bronchogram is typical (Figures 7 and 8). Complications, especially air leak, including pneumothorax and pulmonary interstitial emphysema, should be carefully sought (Figure 9).

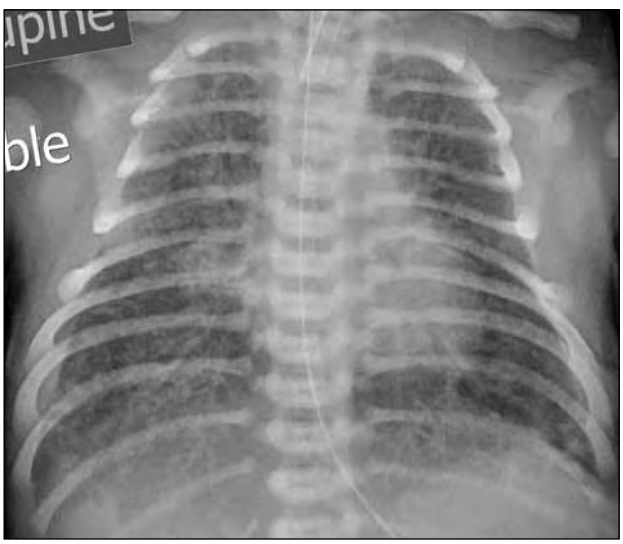

Figure 7. Typical radiographic appearance of meconium aspiration syndrome. A 38+5 weeks baby boy following spontaneous vaginal delivery with thick meconium-stained liquor, with persistent low Apgar score of 6 at 10 minutes and respiratory distress. Direct laryngoscopy showing thick meconium-stained liquor pooled at the vocal cords and oesophagus. Intubation and aspiration yielded thick meconium-stained liquor. Chest X-ray on day 0 showing hyperinflation, patchy, coarse irregular opacities with intervening lucent areas and small right pleural effusion.

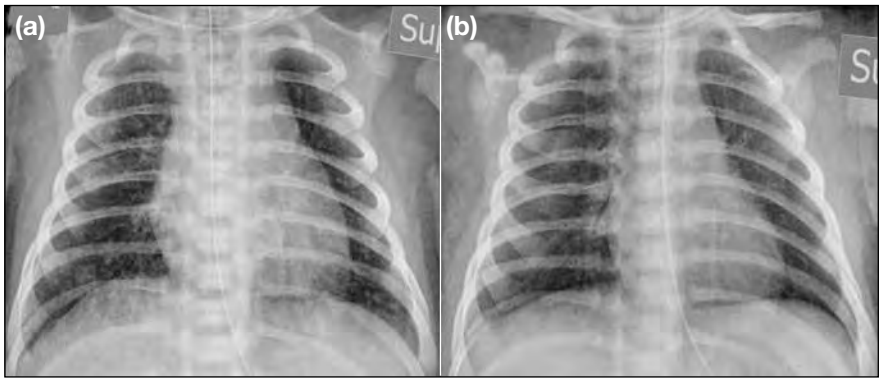

Figure 8. Cardiomegaly in meconium aspiration syndrome. A 38-week baby girl delivered by emergent Caesarean section due to suboptimal cardiotocography, presented with moderate meconium-stained liquor and respiratory distress. (a) Chest X-ray on day 0 showing typical appearance of meconium aspiration syndrome with hyperinflation and patchy, coarse irregular opacities, accompanied by cardiomegaly. (b) Chest X-ray on day 7 showing interval resolution of parenchymal changes and cardiomegaly.

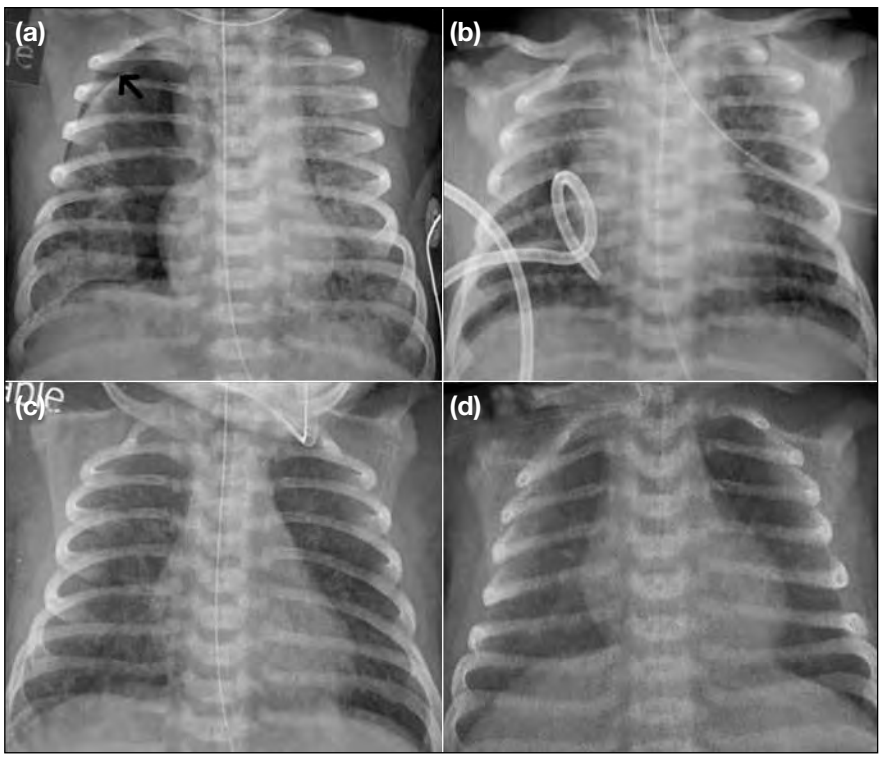

Figure 9. Pneumothorax complicating meconium aspiration syndrome. A 40+6 weeks baby girl delivered by vacuum extraction delivery for non-reassuring fetal status, presented with respiratory distress. (a) Chest X-ray on day 0 showing hyperinflation and patchy, coarse irregular opacities, typical of meconium aspiration syndrome. It was complicated by a right pneumothorax (arrow). (b) Chest X-ray on day 1 showing interval insertion of right chest drain with resolution of right pneumothorax. (c, d) Chest X-ray on day 4 and 6 showing progressive interval radiographic improvement of meconium aspiration syndrome.

Radiographic changes may show gradual resolution over time, ranging from 7 to 10 days to weeks, as the aspirated meconium is cleared by macrophages (Figure 10).[10,11]

PNEUMONIA

The estimated incidence of pneumonia during the neonatal period is about 1% in term and 10% in preterm neonates. It accounts for about 10% of global child mortality, especially in developing countries and regions.[12] Pneumonia during the neonatal period can be classified as early-onset (in first week after birth) or late-onset (after first week after birth).[12] Early- and late-onset pneumonia have different mechanisms of transmission and spectrums of causative agents. Bacterial infection is the most common culprit for both early- and late-onset pneumonia, followed by viral or fungal infection.

The diagnosis of pneumonia in neonates is often challenging, not only because there is significant overlap of clinical and radiological findings with other neonatal respiratory conditions, but also because laboratory results may be non-specific and causative pathogens may not be identified.[1] Pneumonia can also co-exist with other causes of respiratory distress. A low threshold of

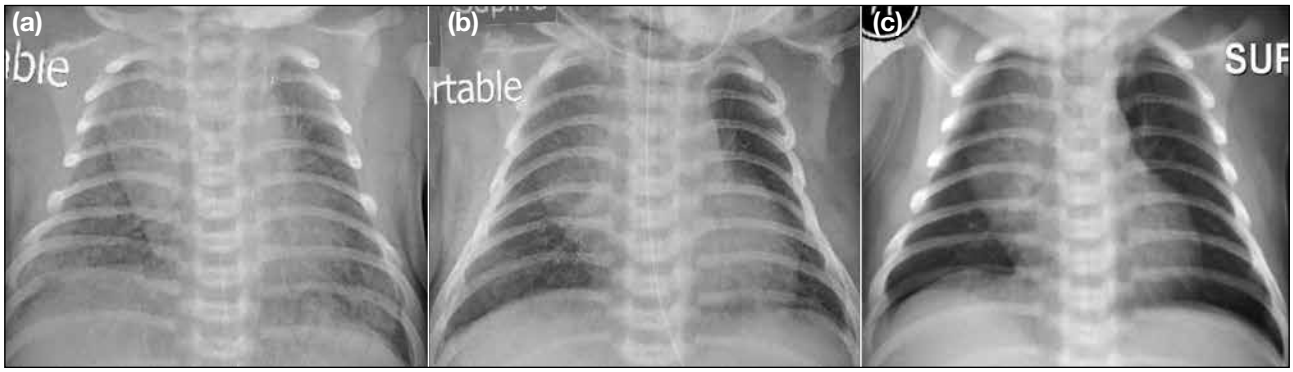

Figure 10. Temporal changes in meconium aspiration syndrome. A 41-week baby girl following vacuum extraction delivery for non-reassuring fetal status showing thin meconium-stained liquor and desaturation. (a) Chest X-ray on day 0 showing hyperinflation, patchy, coarse irregular opacities and small right pleural effusion, suggestive of meconium aspiration syndrome. (b, c) Chest X-ray on day 1 and 7 showing gradual improvement of radiographic findings.

clinical suspicion and the combination of all clinical, radiological, and laboratory findings are essential to reach a diagnosis and provide timely antimicrobial treatment, so reducing morbidity and mortality.

Pathophysiology and Risk Factors

Early-onset Pneumonia

Early-onset pneumonia includes congenital pneumonia transmitted by transplacental spread or infected amniotic fluid, and that contracted perinatally by aspiration of infected liquor or vaginal organisms during labour. Common risk factors include maternal factors such as chorioamnionitis or vaginal colonisation with group B *Streptococcus*, fetal factors such as prematurity, and labour factors such as prolonged labour or premature rupture of membrane. Most common pathogens include bacteria, especially group B *Streptococcus* and *Escherichia coli*, viruses (e.g. herpes simplex virus and adenovirus), and fungi (e.g. *Candida* species).[1,12,13]

Late-onset Pneumonia

Late-onset pneumonia is usually acquired during the postnatal period and may be nosocomial or community-acquired. Exceptions include *Chlamydia trachomatis* that is usually acquired during labour by aspiration of the pathogen from the birth canal and presents 1 to 2 weeks after birth. Common risk factors include environmental factors such as prolonged hospitalisation, suboptimal hand-washing technique of caregivers, or home environments including infection of family members; and neonatal factors such as assisted ventilation or conditions predisposing to aspiration, including neuromuscular disorders and tracheaoesophageal fistula. Most common causative agents are bacteria such as *Staphylococcus aureus* and *Streptococcus pneumoniae*; viruses such as respiratory syncytial, influenza and parainfluenza viruses; and fungi such as *Candida* species.[1,12,13]

Radiological Findings

CXR findings of pneumonia in neonates show a wide range of patterns, overlapping with other neonatal respiratory conditions, such as diffuse parenchymal infiltrates with air bronchogram similar to HMD (Figure 11), especially for group B *Streptococcus* infection[14];

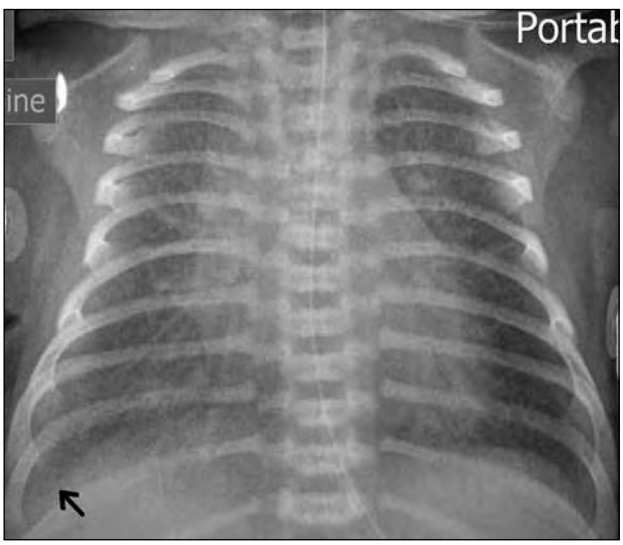

Figure 11. Pneumonia in a 38+4 weeks baby girl delivered by normal spontaneous vaginal delivery with clear liquor, presented with respiratory distress after birth. Chest X-ray on day 0 showing bilateral diffuse lung infiltrates, more on the right, with air bronchogram in the right lower lung zone and a small right pleural effusion (arrow). White cell count increased to 29.7 × 10^9/L and C-reactive protein to 296.2 nmol/L. She was treated as pneumonia with antibiotics.

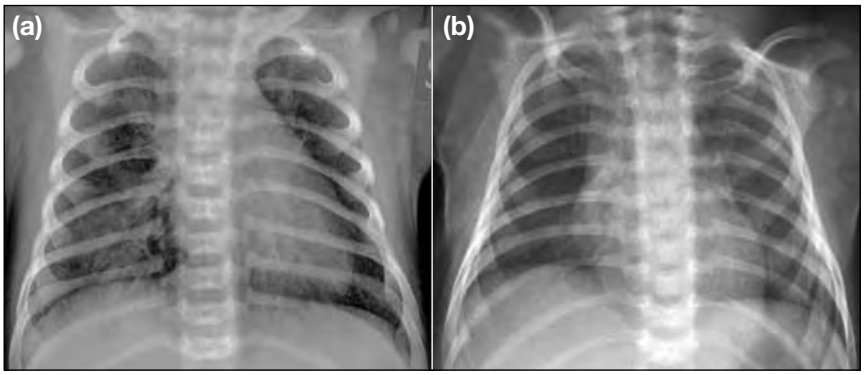

Figure 12. Pneumonia. A 40+4 weeks baby girl delivered by emergent Caesarean section for failed induction of labour, liquor was clear. Maternal vaginal swab was culture positive for group B *Streptococcus*. The patient had respiratory distress and fever since day 2, with elevated white cell count and C-reactive protein. (a) Chest X-ray showing large consolidation with air bronchogram in the right lower zone and patchy coarse opacities in both lungs, more in the bilateral upper zones (mimicking meconium aspiration syndrome). She was treated with empirical antibiotics. Blood culture was positive for group B *Streptococcus* and sensitivity to penicillin. (b) Chest X-ray 3 weeks later showing resolution of consolidation.

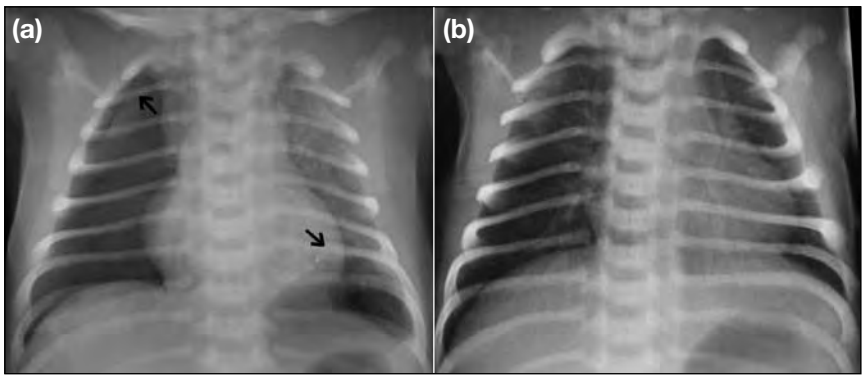

Figure 13. Pneumonia complicated by pneumothorax. A 40-week baby girl delivered by emergent Caesarean section for failed induction of labour presented with respiratory distress. Maternal vaginal swab was culture positive for group B *Streptococcus*. The patient was treated as pneumonia. (a) Chest X-ray on day 0 showing diffuse infiltrates in the left lung and bilateral pneumothorax (arrows), both of which were resolved by day 7 (b).

perihilar streakiness with or without effusion, mimicking TTN; and coarse irregular patchy opacities resembling MAS (Figure 12). Other possible radiographic findings range from normal, lobar consolidation to central perihilar airspace opacities mimicking pulmonary oedema. Complications such as pulmonary interstitial emphysema, pneumothorax, and pneumomediastinum may also be encountered (Figure 13).[15]

Certain features should raise a radiological suspicion of underlying pneumonia, such as unilateral involvement, normal lung volume, and presence of pleural effusion in a pattern similar to HMD (Figure 14); lack of an expected rapid radiographic improvement in a pattern mimicking TTN; and presence of air bronchogram in a pattern resembling MAS (Figure 15).[14]

It is again stressed that the diagnosis of pneumonia in neonates requires a low threshold of suspicion and consideration of all clinical, radiological, and laboratory findings.

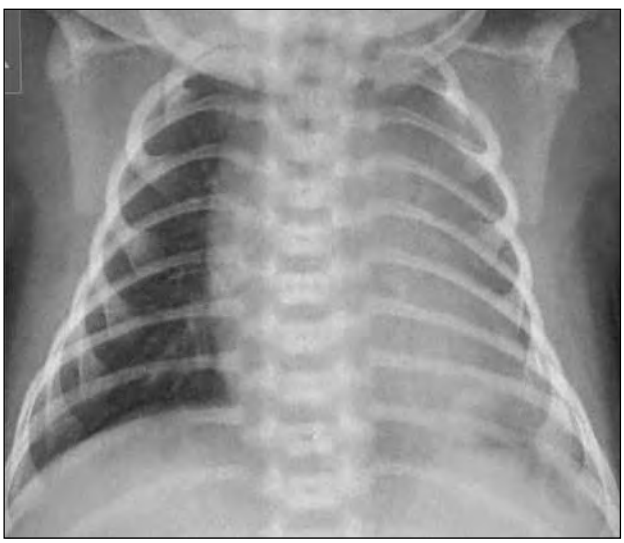

Figure 14. Distinguishing pneumonia from hyaline membrane disease. A 38+1 weeks baby girl delivered by Caesarean section presented with respiratory distress. Chest X-ray on day 0 showing diffuse infiltrates in the left lung. The maturity of the neonate and unilateral involvement of the lung infiltrates argued against hyaline membrane disease. The patient was treated as pneumonia.

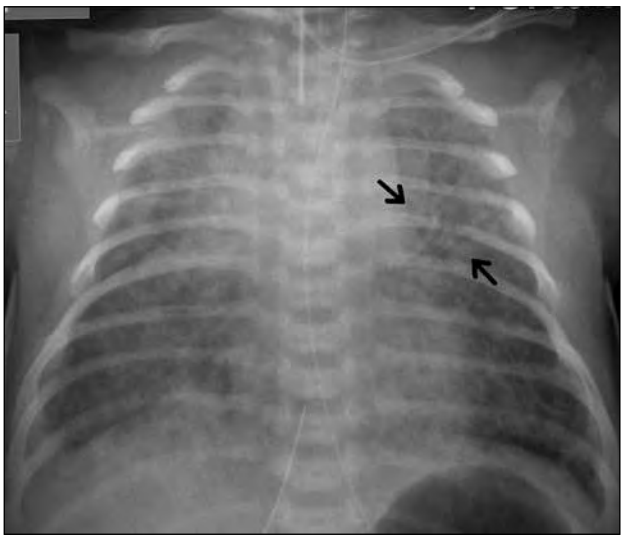

Figure 15. Distinguishing pneumonia from meconium aspiration syndrome. A 40+3 weeks baby boy presented with respiratory distress following a normal spontaneous vaginal delivery. Chest X-ray on day 0 showing patchy infiltrates in both lungs, with alternating opaque and lucent areas. A small right pleural effusion was present. Presence of air bronchogram (arrows) argued against a diagnosis of meconium aspiration syndrome. White cell count was slightly raised and C-reactive protein was elevated. The patient was treated as pneumonia.

CONCLUSION

Understanding the pathophysiology, risk factors, and radiological appearance of pulmonary diseases that cause neonatal respiratory distress is essential for timely diagnosis and treatment.

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