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Congenital malformations of the lung

Chris Wright*

Department of Cellular Pathology, Royal Victoria Infirmary, Newcastle Upon Tyne, NE1 4LP, UK

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Summary Malformations of the lung are an important cause of morbidity and mortality, particularly in the neonatal period, and are a common finding at perinatal post-mortem examinations. This review relates the malformations to the underlying developmental processes and highlights recent literature.

Introduction

Satisfactory transition to extrauterine existence is dependent on adequate ventilatory function, and major malformations involving the lungs therefore frequently present in the early neonatal period with respiratory distress. Many are detected for the first time only at post-mortem examination, although diagnosis is increasingly made by antenatal imaging. Some malformations may remain asymptomatic or present later in life with complications such as infection. For this reason, and because of the rarity of many of the individual disorders, it is not possible to obtain an accurate overall assessment of the frequency of lung malformations.

Embryology, growth and development

As with other organ systems, a knowledge of the processes of normal lung morphogenesis provides a basis for the understanding of malformations.

The respiratory diverticulum appears as a ventral outpouching of the embryonic foregut at about 28 days. This elongates to form the trachea, which divides first to form two primary bronchi, and then

*Tel.: +44 191 282 0982; fax: +44 191 282 0980.
E-mail address: chris.wright@nuth.northy.nhs.uk.

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again at about 33 days to give three buds on the right and two on the left.[1] Each of these secondary (lobar) bronchi then undergoes a series of further divisions by the process known as branching morphogenesis to lay down the framework for the bronchi and bronchioles.

By the end of the so-called *pseudoglandular phase* (approximately 17 weeks after conception), the pattern for all the pre-acinar airways has been laid down, together with clusters of tubules thought to represent the early acinar structures.[2] During the subsequent *canalicular stage* (approximately 17–26 weeks post-conception), these distal structures undergo further branching, lengthening and widening, and the first capillary–epithelial contacts appear. Airway formation and growth is accompanied by ongoing centrifugal differentiation. The *saccular stage* (from about 24 to 38 weeks after conception) starts with groups of terminal saccules, and these undergo further subdivision (initially by secondary crests) to form the peripheral gas-exchange part of the lungs. The point at which definitive alveoli are said to be present has been a matter of controversy, dependent on the criteria used for identification, although it is likely that they are already numerous by term.[3]

There is increasing knowledge of the molecular mechanisms controlling normal lung morphogenesis. This is beginning to provide some insights into the mechanisms of development of individual malformations but currently has limited application in diagnosis.[4–6] The role of physical factors such as lung fluid volume is discussed below under 'pulmonary hypoplasia'.

Abnormalities during the early stages of airway formation lead to a spectrum of malformations including aberrant bronchi, bronchopulmonary foregut malformations, pulmonary sequestration and pulmonary agenesis.

Bronchial malformations

The normal asymmetry of the main bronchi may be lost in laterality disorders. Anomalous branching of the upper airways leads to variety of abnormalities including an origin of the upper lobe bronchi from above the carina (tracheal bronchus), and bronchial supply for part of one lung arising from bronchi of the other lung (bridging bronchus).

Bronchopulmonary foregut malformations and lung sequestration

The formation of separate additional buds from lower down the developing gastrointestinal tract leads to so-called bronchopulmonary foregut malformation in which an aberrant mass of lung tissue is connected to the oesophagus or stomach (see below). Bronchogenic cysts probably also arise from aberrant additional lung buds, and lesions with connections to the gut have been described. These cysts are usually found within the lung around the lung hilum or in the mediastinum; the fibromuscular wall may contain cartilage and glands, and is lined by respiratory type epithelium.

Lung tissue that is not connected to the upper airways by a normally sited bronchus is said to be sequestered; such tissue frequently has a systemic arterial blood supply. Subclassification into intralobar or extralobar types (below) depends on whether the sequestered lung lies within or outside the visceral pleura of the normal lung. The term 'total sequestration' has been used to designate lungs with a bronchial connection to the oesophagus and systemic arterial blood supply.

Some lungs with normal bronchial connections have varying degrees of systemic arterial supply. This is seen in the so-called scimitar syndrome, in which at least a partial systemic supply to a hypoplastic lung is accompanied by anomalous venous drainage of the same lung to the inferior vena cava (forming a scimitar-shaped X-ray shadow). Fusion of the lungs behind the heart (horseshoe lung) is frequently associated with scimitar syndrome.

Extralobar sequestrations

Extralobar sequestrations are generally held to represent accessory lung buds. Most have no identifiable bronchial supply, but some are connected to the foregut (and are then termed bronchopulmonary foregut malformations). The lung tissue forms a mass that commonly lies within the pleural cavity (usually on the left) but may be found within the mediastinum, or within or just below the diaphragm. Typically, the arterial supply is from the aorta or its major branches (Fig. 1), but on occasion it can be from the pulmonary arteries. Histologically, the mass often comprises lung tissue showing dilated and distal airspaces, but a proportion have features of type 2 adenomatoid malformation (see below).[7] There is frequently lymphangiectasia. Bronchial structures may be present. Given the likely pathogenesis of these sequestrations, it is not surprising that they may occur in association with anomalies such as tracheo-oesophageal fistula and gastrointestinal duplications.